JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Phytochemical Delineation and Depiction of Phytopharmacological Properties of *Leucas aspera*

Jeevankumaar V, Nithishkumar P, Thyagarajan R*, Ramesh Kumar V*

Department of Biotechnology, School of Bio

and Chemical Sathyabama Institute of

Science and Technology

Abstract: This review is about *Leucas aspera*, a medicinal weed, focusing on its botany, phytochemical spectrum, and broad therapeutic potential. The research starts with an assessment of the entire Leucas genus, identifying and studying the many bioactive components. *Leucas aspera* shines as a species of interest due to its huge phytochemical profile. Its anti-cancer properties & anti-inflammatory properties are highlighted, as is its ability to induce programmed cell death and limit the spread of various cancer cell lines and its effect on prostaglandins respectively. In addition to its anti-cancer properties & anti-inflammatory properties, the journal also analyses the broader phytopharmacological properties of *Leucas aspera*, which include antibacterial, antioxidant and analgesic activity. The review provides a detailed evaluation of various plant extraction techniques, emphasizing solvent systems and innovative methods like supercritical solvent extraction and ultrasonic extraction, which have demonstrated enhanced purity and phytochemical yields. By integrating botanical, phytochemical, and pharmacological data, this review has pinpointed *Leucas aspera* as a potential candidate for future therapeutic applications, especially in oncology. The findings presented here aim to direct upcoming research and encourage exploration of the medicinal properties of this distinctive plant, thereby establishing a robust basis for its increased application in contemporary medicine.

***Index Terms - Leucas aspera*, Medicinal Aromatic Weed, Phytochemicals, Phytopharmacological Properties, Anti-cancer**

I. INTRODUCTION

The following is a summary of the main points: Medicinal plants have always been an essential part of medical treatment. These plant resources have long been prized for their curative properties, establishing the framework for traditional medicinal systems including Ayurveda, Siddha, Unani, and Traditional Chinese Medicine (TCM). Plants have been utilised as cures for thousands of years, as demonstrated by writings from ancient societies such as the Sumerians, Chinese, Indians, Egyptians, and Greeks (Hosseinzadeh et al., 2015; Petrovska, 2012). The trend to look for therapeutic plants has only just begun. Researchers and scientists have conducted studies to determine the medicinal potential and the active ingredients contained in these natural sources. The medicinal value of plants cannot be precisely defined. Some 70000 plant species have been used for medicinal purposes, mainly in Asian medical traditions (Nasim et al., 2022). Ongoing research on medicinal plants is vital to the progress of modern medicine. Researchers can find new pharmaceutical compounds and develop innovative treatments by combining traditional knowledge with state-of-the-art scientific techniques. This collaborative approach not only honours the knowledge of historical medical systems, but it also holds the prospect of transforming how we approach healthcare in future.

Many expert researchers, like Sabri et al. (2015), and Srinivasan et al. (2011), record and discuss taxonomic categorization and anatomical observations. The Lamiaceae family, particularly the genus Leucas, comprises over 80 species figuring prominently in Indian traditional medicine in the treatment of numerous ailments. Among such various species, *Leucas aspera*, a little branched herbaceous erect weed that sizes to a height of up to 2 feet per annum, is widely distributed throughout India. It is a stinging odoriferous weed that is spread abundantly in highland cultivable lands, shallow meadows, roadsides and fallow sites throughout Indian Landmass. Tribals and herbal medicine practitioners use the whole plant or its components orally or applied as paste topically to inflamed areas (Gani 2003).

The aim of this journal is to provide a comprehensive and sophisticated synthesis of the pharmacological properties and bioactive phytocomponents of *Leucas aspera*, a thorough analysis of the advanced techniques for increasing the production of these compounds to facilitate their large-scale application in cancer treatment. *Leucas aspera* has been chosen as the main theme because of its proliferative and communal growth patterns, which make it an easily available and sustainable resource. Its well-documented therapeutic abilities, as well as its astonishing tolerance to a variety of environmental conditions, make it an excellent candidate for future pharmacological research. By delving deeper into its complex chemical composition and optimising extraction methods, this revision is intended to unlock the full therapeutic potential of *Leucas aspera* and contribute to the development of revolutionary cancer therapies.

Figure 2 Wild growth of Leucas aspera

TABLE 1 Taxonomic Relations of *Leucas aspera*

TAXONOMIC	RELATIONS
KINGDOM	PLANTAE
SUB-KINGDOM	TRACHEOBIONTA
SUPER DIVISION	SPERMATOPHYTA
DIVISION	ANGIOSPERMAE
CLASS	DICOTYLEDONAE
SUB-CLASS	GAMOPETALAE
ORDER	LAMIALES
FAMILY	LAMIACEAE
GENUS	LEUCAS
SPECIES	ASPERA
BOTANICAL NAME	*Leucas aspera*
VERNACULAR NAME	THUMBAI (TAMIL)

II. BOTANY

2.1 Morphological Characteristics

Leucas aspera is a herbaceous plant that grows to a height of 15 to 60 cm and has a square stem. The leaves are small, linear-lanceolate and hairy, up to 80 mm long and 12.5 mm wide. Produces white, stylised flowers in terminal or axillary whorls. The leaves are 6 mm long, linear and spiny, while the cylindrical cup is 0.7-1.5 cm long and tapers above the seed. The inflorescence is 10 mm long, with a hairy tube and differentiated upper and lower lips. The fruit is a smooth, chestnut-brown nut which is 2.5 mm long (Hooker, 1984).

2.1 Anatomical Characteristics

The cross-section (TS) of the *Leucas aspera* strain shows a symmetrical structure with four choline burrows and a thin inner bark. The epidermis is covered by a thick porous cuticle and also contains isolated trichomes. Along the ridges, choline-like cells form and a distinctive endoderm surrounds the vascular bundles. The xylem is surrounded by the phloem radially and calcium oxalate crystals are present in the parenchymal cortex. The leaf surface of the leaf reveals a convex abaxial surface, a flattened adaxial surface, and a convoluted meristem with a parenchymal pericyclid. The cuticle with stomapores and trichomes covers the epidermis.

Figure 3 Apical Shoot Leaves of Leucas aspera

III. PHYTOCHEMICAL SCREENING OF *Leucas aspera*

3.1 Phenolic Compounds

Plant phenolic compounds are various compounds with important medicinal properties, often in the form of complex structures bound to oxygen-containing heterocycles. This group includes coumarins, flavonoids and benzoic acid derivatives (Harborne et al., 1999). Phenolic compounds are abundant in Leucas species. For example, organic acids such as 4-hydroxybenzoic acid and methoxybenzoic acid have been isolated from *Leucas urticifolia* (Fatima et al., 2008). In the absence of any other relevant information, the use of the test chemical should be evaluated.

Lignans formed from dimerized phenylpropanoid units are found in various plant parts (Ayres and Loike, 1990). Sadhu et al. (2003) discovered several lignans, including Nektan-Drin B and Masaerignan. Flavonoids that play a key role in plant physiology include Baicaleína from *Leucas aspera* (Manivannana and Sukumar, 2007) and Cirsimaritin from *Leucas mollissima* (Ku et al., 2000). Acecetin, chrysoerol and apigenin have also been detected in *Leucas aspera* (Sadhu et al., 2003), while *Leucas cephalotes* contains compounds such as trichotin and gonzalitosin I (Miyaichi et al., 2006).

Coumarins with physiological effects on humans and animals include coumarsabine and 8-methoxycoumarin from Leucas inflata (Kennedy and Thornes, 1997). Chromoderivatives such as leucazone have also been found in *Leucaena inflata* (Al Yousuf et al., 1999).

3.2 Steroids

Sterols derived from the ring structure of perhydrocyclopentane-phenanthrene are widely distributed in higher plants (Harborne et al. 1999). Leucas species include several plants possess sterols, such as β-sitosterol, stigmasterol, campesterol, and ursolic acid (Al Yousuf et al., 1990; Sadhu et al., 2003). Leucosterol, a new steroid derived from the methanolic derivative of *Leucas urticifolia*, differs from stigmasterol in that it has a side chain structure, specifically a -OH group and an alkene bond at C-20.

3.3 Terpenes

Terpenes are the extensive and configurationaly disparate families of phytoconstituents found in plants that contribute to their flavour, aroma, and bioactivity. (Humphery and Beale, 2006). Terpenes are plentifully available in the Leucas genus of plants. Vagionas et al. (2007) found monoterpenes in the essential oil produced from *Leucas glabrata* using GC/MS analysis. The essential oil derivatives from the leaves and flowers of *Leucas aspera* showed hoisted levels of α-farnesene, α-thujene, and menthol according to Gerige et al. (2008) and Mangathayaru et al. (2006), while the essential oil extracted from the leaves of *Leucas deflexa* exhibited significant amounts of β-cubebene, α-pinene, trans-caryophyllene, limonene, and α-terpinolene. *Leucas deflexa* has high concentrations of sesquiterpene hydrocarbons, including germacrene-D, β-caryophyllene, and α-humulene according to Mve-Mba et al. (1994).

Furthermore, two triterpenes, Leucastrinas A and B, coupled with oleanolic acid, were recovered from the methanolic derivative of the entire plant, *Leucas cephalotes Spreng*, whereas oleanolic acid-3-acetate was discovered in the methanol solvent derivative of *Leucas mollissima*. Wall. Variant. Chinensis Benth. (Ku et al. 2000). A triterpene lactone, 3β,16α-hydroxylean-28→13β-olide, was isolated from the benzene solvent root extraction of *Leucas aspera*. (Pradhan et al., 1990).

3.4 Glycosides

Two new flavonoid glycosides, Leufol A and Leufol B, were isolated from the ethyl acetate fraction of *Leucas urticifolia* and showed significant inhibition of butyrylcholinesterase in vitro (Noor et al., 2007). In addition, the phenylethanoid glycoside 3-O-methylpolyumosate has been identified with Angoroside-C and Incanoside-D in *Leucas indica*, which have remarkable free radical scavenging activity due to their hydroxyl groups (Mostafa et al., 2007). Baicalin from *Leucas aspera* flowers demonstrated protective effects against red blood cell hemolysis (Manivannana and Sukumar, 2007). Iso-pimarane-type diterpenoid glycosides, such as leucasperosides A, B, and C, from *Leucas asperainhibited* intestinal contractions in guinea pigs (Mahato and Pal, 1986; Sadhu et al., 2003). Other flavonoids have also been identified, including apigenin-7-O-{p-cumaroil} β-D-diglucoside from *Leucas aspera* and the cosmosin and luteolin derivatives from *Leucas cephalotes* (Sadhu et al., 2003; Miyaichi et al., 2006). In the case of a test for the determination of the test chemical, the test chemical should be used as a solvent.

3.5 Fatty Acids

Aitzetmuller et al. (1997) and Sinha et al. (1978) identified a significant presence of labalenic acid (28% w/w) in the seeds of *Leucas cephalotes* and *Leucas urticaefolia*. The levels of oleic and linoleic acids in *Leucas aspera* changed depending on the cultivation conditions, as indicated by the findings of Chen et al. (1979) and Mahato and Pal (1986).

3.6 Miscellaneous Compounds

Leucas aspera is appreciated for its high nutritional value, particularly its protein content, which is 21.3% (Prakash, 1988; Chen et al., 1979). Both *Leucas aspera* and *Leucas cephalotes* have been found to contain compounds such as 1-dotriacontanol, 1-hydroxy tetratriacontane-4-one, and 32-methyl tetratriacontane (Mishra et al., 1992). Aliphatic cetoles, including 28-hydroxy-pentatriacontan-7-one and 7-hydroxy-dotriacontan-2-one, were identified in *Leucas aspera* shoots (Mishra et al., 1992). *Leucas nutans* contain n-hentriacontane, l-dotriacontanol, phytol, and trans-phytyl palmitate (Hasan et al., 1991). Essential oils from *Leucas aspera* inflorescences are rich in amyl and isoamyl propionate (Mangathayaru et al., 2006). Additionally, *Leucas linifolia* grown in northern India exhibits high concentrations of Zn, Fe, and Sr (Mohanta et al., 2003; Rai et al., 2001).

IV. EXTRACTION METHODOLOGIES

The acetone extract of juvenile leaves had the highest phenol content (6.00±0.12 mgCE/g), followed by aqueous extracts of inflorescence and methanol extracts of juvenile leaves and flower heads (Chetia and Saikia, 2020). The methanol extract of mature leaves (3.32±0.95 mgCE/g) and acetone extract of young leaves (3.05±0.04 mgCE/g) showed the highest flavonoid content.The ethanol extracts from the stalks had the lowest levels of phenol and flavonoids (1.03 0.00 mg EC/g and 0.70 0.00 mg EC/g). In the absence of any other relevant data, it is appropriate to use the method described in this Annex to determine the concentration of ethanol in the ethanol extract.

Methane extracts from both young and mature leaves demonstrated notable antioxidant activity inhibition in the DPPH tests (Latha et al., 2013). According to Rahman and Islam (2013), an ethanol extract exhibited an inhibition rate of 86.62 ± 0.49%, while Morshed et al. (2011) noted purification properties in extracts from flowers, leaves, and stems.The fluctuations in antioxidant activity have been attributed to various methods.

Methanol and ethanol extracts showed remarkable antibacterial activity against *Shigella, Salmonella typhii and E. coli* (Shiny Ramya et al., 2012). Ethyl acetate and methanol derivatives also showed antibacterial activity (Ilango et al., 2008). However, n-hexane and ethanol extracts did not show efficacy against 14 microbial species (Morshed et al., 2011). Methanol leaf extracts inhibited *Candida albicans and Penicillium* spp. In the absence of such data, the Commission considers that the MET/IT claimed by the applicant is invalid.

V. PHARMACOLOGICAL PROPERTIES

5.1 Antifungal Activity

Leucas aspera is known for its dual fungicidal and fungistatic properties. This is the case in the United Kingdom (Thakur et al., 1987). In addition, the use of the test chemical should be limited to the use of the test chemical in the test vessels and the test chemical should be used in the test vessels.It was also found that both chloroform and ethanol derivatives are antifungal against *Trichophyton mentagrophytes and Microsporum gypseum* (Vijay Kumar et al., 2016). Because of their alkaloidal components, methanolic extracts derived from*Leucas aspera* flowers exhibit strong antifungal activity against *Candida albicans, Cryptococcus neoformans, Aspergillus niger, and Trichophyton mentagrophytes* (Mangathayaru et al., 2005).

5.2 Anti-Diabetic Activity

Mannan et al. (2010) found that methanol derivatives from the leaves and stem of *Leucas aspera* lowered blood glucose dose-dependently when administered to albino Swiss mice. In addition, Tukaram et al. (2011) showed that the ethanol extract of the leaf can lower blood sugar levels.

5.3 Anti-inflammatory effects

Leucas aspera has been shown to exhibit significant anti-inflammatory properties. According to Reddy et al. (1993), *Leucas aspera* has anti-inflammatory properties and promotes the breakdown of mast cells. Sundane et al. (2000) found that several extracts, including the ethanol, methanol and aqueous forms, had different levels of anti-inflammatory potency. Studies show that both aqueous and alcohol extracts of *Leucas aspera* exhibits anti-inflammatory effects through various assays like membrane stabilization, inhibition of protein saturation, and reduction of lipoxygenase activity (Kalpana and Rajeswari, 2016; Tahareen and Shwetha, 2016). In addition, the extracts of this plant show antioxidant abilities by eliminating free radicals and enhancing the activity of antioxidant enzymes (Kripa et al., 2011; Tahareen and Shwetha, 2016). In animal models used in arthritis research, extracts from *Leucas aspera* significantly reduced inflammatory markers such as TNF-α, CRP and IL-2 while improving antioxidant enzyme levels (Kripa et al., 2010; Kripa et al., 2011). Phytochemical evaluations identified catechins, flavonoids, phytosterols and other bioactive components that may contribute to their therapeutic effects (Kripa et al., 2011; Tahareen & Shwetha, 2016). The present findings lend credence to the claims of a tradition employing *Leucas aspera* as a treatment for inflammatory diseases and support the potential of *Leucas aspera* for developing anti-inflammatory medicinal products. *Leucas aspera* leaf extract also showed anti-inflammatory effects in rat models of carrageenan-induced paw edema and cotton pellet granuloma (N. Patil et al., 2014). The anti-inflammatory properties of *Leucas aspera* seem to be the result of phenolic phytochemicals such as alkaloids, flavonoids, and tannins contributing to its therapeutic effects (Tahareen S. et al., 2016). The extracts were shown to block prostaglandin-induced contractions of guinea pig ileum and displayed DPPH scavenging activity. From the extract, eight lignans and four flavonoids were isolated, and of these compounds, some showed prostaglandin-inhibiting action and antioxidant properties In addition, very little data is available to support the efficacy of the treatment. (S.K. Sadhu et al., 2003). The extracts of the plant, especially the leaves, were shown to inhibit xanthine oxidase with an IC50 value of 0.026 µg/ml, indicating anti-inflammatory potency (R. et al., 2023). From the docking studies, it is found that many of the evaluated bioactive compounds are found to possess strong binding affinities against various inflammatory proteins; thus, they can be used in the development of anti-inflammatory agents (Islam et al., 2023). It is perhaps the rich presence of various phytochemicals, with particular emphasis on oleanolic acid, that further substantiates in its attributes aiding against inflammation (Soujanya et al., 2024)(R. et al., 2023).

5.4 Anti-Ulcer Activity

Phytochemical studies showed that hydroalcoholic solvent extract of *Leucas aspera* leaves contained flavonoids, tannins, and saponins. The extract was therapeutically effective in gastric ulcers by inhibiting cell growth of the bacterial cell wall, causing cell death, especially in indomethacin-induced gastric ulcers. The study also established the efficacy of the extract by inhibiting ulcer surface area and ulcer scores as reported by Kumar et al. (2021). Besides, the antioxidantal and histo-pathological findings support the use of *Leucas aspera* in traditional medicine for treating various gastrointestinal disorders. Methanol solvent extract of *Leucas aspera* was found to possess good antisecretory and ulcer-protective properties in all the ulcer models tested. (Augustine et al. 2014).

5.5 Anti-asthmatic Activity

Whole-plant methanol solvent extractive of *Leucas aspera* very likely may show great anti-histaminic, bronchodilatory, anti-inflammatory, mast cell-stabilizing, anti-allergenic, and antiplasmodial effects in various staged anti-asthmatic models. The extract was therefore pronounced to possess a powerful anti-asthmatic activity (Limbasiya et al., 2012).

5.6 Cytotoxicity Studies

5.6.1 Brine Shrimp Lethality Assay

Artemia salina lethality test is widely also applied in pharmacology and toxicology to evaluate the cytotoxicity of natural products. This test is an efficient, initial tool for determining the cytotoxicity of bioactive chemicals, such as those from Leucas *aspera* extracts, providing a rapid toxicity assessment (Rahman and Islam, 2013). Research indicates the high toxicity of Leucas *aspera* extracts relative to the conventional drugs vincristine sulfate. This reveals their clinical application in the killing of cancerous cells and pests (Rahman and Islam, 2013).

Researchers have used this assay to show the cytotoxicity of plant extracts, such as Leucas *aspera*, to provide insights into their pharmacological activity (Rahman and Islam, 2013). Other plant extracts, such as *Dillenia indica and Croton gibsonianus*, have also been evaluated using the brine shrimp test, indicating its applicability in cytotoxicity screening (Apu et al., 2010; Prashith et al., 2013). The test has also been used to evaluate the cytotoxic activity of medicinal plants such as *Ceriops decandra and Centaurea gigantea* against cancer cells (Sukasini and M., 2018).

Aside from plant extracts, the assay has also been employed to investigate the cytotoxicity of nanoparticles, including silver oxide and graphene (Nasim et al., 2020), and *Leucas aspera* roots and whole plant extracts (Chew et al., 2012). It has also been useful in forecasting the cytotoxicity of organic extracts, including mahogany seed extracts (Assaduzzaman et al., 2020). The brine shrimp lethality test provides a good estimate to determine the cytotoxicity of natural products, which aids in further evaluation of their pharmacological properties and clinical potential.

5.6.2 Anti-migratory Study

Assorted literature depicts the anti-migratory action of *Leucas aspera* extracts. An experiment to characterise the phytochemicals of *Leucas aspera* leaf extracts and study their anti-proliferative and anti-migratory effects was carried out in vitro using MDA-MB-231 cells (Begum and Sankarram, 2024). The scratch assay served as the means of calculating extracts' inhibition of cell migration and suggested that *Leucas aspera* is capable of limiting cell mobility.

TABLE 2 Leucas species, their Extraction Solvent and Pharmacological Activity

s/no	Part	Solvent	Activity	Author
1.	Leaves	Aqueous	Madras eye condition.	Sandhya *et al*., 2006
2.	Flowers, Stem, Root	Aqueous	Antivenom,insect-stings, anti-asthma	Singh *et al*., 2002
3.	Leaves	Ethanol, Hexane	Oil extracted from plants has antimicrobial activity against *Pseudomonas aeruginosa, Haemophilus influenzae etc...*	Gerige *et al*., 2007
4.	Root	Methanol	Cytotoxicity Acitivity	Rahman *et al*., 2007
5.	Root	Methanol	Cytotoxicity Acitvity	Augustine *et al*., 2014
6.	Root	Methanol	Root exhibit the cytotoxic activity.	Sadhu *et al*., 2014
7.	Whole plant	Methanol	Anti-inflammatory activity.	Sundane *et al*., 2000
8.	Leaves and Flower	Aqueous	Antifungal activity against Epidermophyton floccosum etc..	Mangathayaru *et al*., 2016

9.	Whole plant	Alcohol	Cytotoxicity activity	MA Rahman *et al.*, 2013
10.	Leaves	Methanol	Hepatoprotective activity	Latha *et al.*, 2012
11.	Whole plant	Ethanol	Antidiabetic activity	Gupta *et al.*, 2011
12.	Whole plant	Methanol	Antifungal Activity	Babu et al., 2016
13.	Stem and Leaves	Methanol	Antidiabetic Activity	Mannan et al. (2010)
14.	Leaves	Ethanol	Antidiabetic Activity	Tukaram et al. (2011)
15.	Whole plant	Methanol	Anti-Asthmatic Activity	Limbasiya et al., 2012

VI CONCLUSION

This review focuses on the phytochemical constituents and their extensive pharmacological uses, although *Leucas aspera* possesses immense therapeutic potential in this direction. The raw material affords an intellectual wealth of bioactive compounds: flavonoids, alkaloids, terpenoids, saponins, and phenolic acids. It is opined that all these should bring in antibacterial, antioxidant, anti-inflammatory, analgesic, antipyretic, and anticancer properties, justifying its traditional use as a sub-optimal therapeutic resource. The plant would be subjected to solvent extraction with ethanol, methanol, and dichloromethane for optimum extraction of these bioactive constituents. These phytochemicals exhibit varying antibacterial, antioxidant, anti-inflammatory, analgesic, antipyretic, and anticancer effects helping bolster its use for alternative medicine and prospect for contemporary therapeutic uses. Efficient extraction procedures should mark the isolation of these bioactive compounds; particularly, solvent extraction involving conjugates like alcohols (ethanol and methanol) and dichloromethane is essential. New extraction techniques include supercritical fluid extraction (SFE) and ultrasound-assisted extraction (UAE) that offer high extraction yield with lower solvent consumption and greater preservation of sensitive components. These technologies allow selective extraction of high-value phytochemicals for useful exploitations. New technologies such as supercritical fluid extraction (SFE) and ultrasound-assisted extraction (UAE) increase yield, lower solvent consumption, and conserve delicate compounds. These technologies facilitate the selective extraction of high-value phytochemicals for their therapeutic uses. The antibacterial and antifungal activities of the plant are due to alkaloids and flavonoids, whereas antioxidant activity, with high phenolic content, is protective against oxidative stress associated with chronic diseases. Leucas aspera also has potential in treating inflammation, pain, and cancer, as its extracts have the ability to induce cell death and inhibit the growth of cancer cell lines.

REFERENCES

[1] Abdullah F, Fazira Mohd Salleh NA, Luqman Selahuddeen M. Phytochemical and toxicity analysis of *Leucas zeylanica* crude extracts. Environ Toxicol Manag. 2021;1(2):1–8.

[2] Aitzetmüller K, Tsevegsüren N, Vosmann K. A new allenic fatty acid in phlomis (*Lamiaceae*) seed oil. Lipid Fett. 1997;99(3):74–8.

[3] Asase A, Oteng-Yeboah AA, Odamtten GT, Simmonds MSJ. Ethnobotanical study of some Ghanaian anti-malarial plants. J Ethnopharmacol. 2005;99(2):273–9.

[4] Assaduzzaman A, Amin MZ, Rahman MH, Uddin MR, Shohanuzzaman M, Mandal P, et al. Evaluation of antibacterial, anti-oxidant and cytotoxic activity of organic extracts of mahogany seeds. Eur J Med Plants. 2020;31:1–7.

[5] Augustine BB, Pitta S, Lahkar M, Dash S, Samudrala PK, Thomas JM. Ulcer protective effect of *Leucas aspera* in various experimental ulcer models. Asian Pac J Trop Dis. 2014;4:S395–S402.

[6] Ayres DC, Loike JD. Lignans: chemical, biological and clinical properties. Cambridge (UK): Press Syndicate of the University of Cambridge; 1990.

[7] Babu A, Mohamed MSN, Jaikumar K, Anand D, Saravanan P. In-vitro antifungal activity of leaf extracts of *Leucas aspera* and *Leucas zeylanica*. Int J Pharm Sci Res. 2016;7(2):752.

[8] Begum SM, Sankarram M. Phytochemical characterization by GC-MS and in vitro evaluation of antiproliferative and antimigratory studies of *Leucas aspera* leaf extracts on MDA-MB-231 cell line. BioTechnologia. 2024;105(1):55–68.

[9] Borah U, Dash B, Dash S, Kalita L. Preliminary phytochemical screening and in vitro antimicrobial activity of ethanolic extract of whole aerial part of the herb *Leucas plukenetii* Spreng (family-Lamiaceae). Int J Curr Pharm Res. 2017;9(3):87.

[10] Chandrashekar KS, Arun BJ, Satyanarayana D. Flavonoid glycoside from *Leucas lavandulaefolia* aerial parts. Asian J Chem. 2005;17:2853–4.

[11] Chauhan NS. Medicinal and aromatic plants of Himachal Pradesh. New Delhi (India): Indus Publishing Company; 1999. p. 260.

[12] Chen SC, Elofson RM, MacTaggart JM. Carbon-13 nuclear magnetic resonance studies of lipids and starch digestion in intact seeds. J Agric Food Chem. 1979;27(2):435–8.
[13] Chew AL, Jessica JJA, Sasidharan S. Antioxidant and antibacterial activity of different parts of *Leucas aspera*. Asian Pac J Trop Biomed. 2012;2(3):176–80.
[14] Dixit V, Irshad S, Agnihotri P, Paliwal AK, Husain T. Evaluation of antioxidant and antimicrobial potential of *Leucas urticaefolia* (Lamiaceae). J Appl Pharm Sci. 2015;5(4):39–45.
[15] Ethnobotanical investigation of some medicinal plants used by tribes of Mandla District, Madhya Pradesh, India. Int J Sci Res. 2015;4(12):1694–6.
[16] Fatima I, Ahmad I, Anis I, Malik A, Afza N, Iqbal L, Latif M. New butyrylcholinesterase inhibitory steroid and peroxy acid from *Leucas urticifolia*. Arch Pharm Res. 2008;31(8):999–1003.
[17] Gani A. Medicinal plant of Bangladesh: chemical constituents and uses. Dhaka (Bangladesh): Asiatic Soc of Bangladesh; 2003. p. 277.
[18] Gerige SJ, Yadav MK, Rao DM, Ramanjeneyulu R. GC-MS analysis and inhibitory efficacy of *Leucas aspera* L. leaf volatile oil against selected microbes. Niger J Nat Prod Med. 2008;11(1).
[19] Gupta N, Agarwal M, Bhatia V, Sharma RK, Narang E. A comparative antidiabetic and hypoglycemic activity of the crude alcoholic extracts of the plant *Leucas aspera* and seeds of *Pithecellobium bigeminum* in rats. Int J Res Ayurveda Pharm. 2011;2(1):275–80.
[20] Gupta V, Guleri R, Gupta M, Kaur N, Kaur K, Kumar P, et al. Anti-neuroinflammatory potential of *Tylophora indica* (Burm. f) Merrill and development of an efficient in vitro propagation system for its clinical use. PLoS One. 2020;15(3):e0230142.
[21] Harborne JB, Baxter H, Moss GP. Phytochemical dictionary: a handbook of bioactive compounds from plants. London (UK): Taylor & Francis Ltd.; 1999. p. 773.
[22] Hasan M, Burdi DK, Ahmad VU. Diterpene fatty acid ester from *Leucas nutans*. J Nat Prod. 1991;54(5):1444–6.
[23] Hooker JD. The flora of British India. London (UK): Muston Company; 1984. p. 690.
[24] Hosseinzadeh S, Jafarikukhdan A, Hosseini A, Armand R. The application of medicinal plants in traditional and modern medicine: a review of *Thymus vulgaris*. Int J Clin Med. 2015;6(9):635–42.
[25] Humphrey AJ, Beale MH. Terpenes. Plant secondary metabolites. 2006;47–101.
[26] Ilango K, Ramya S, Gopinath G. Antibacterial activity of *Leucas aspera* Spreng. Int J Chem Sci. 2008;6(2):526–30.
[27] Islam, M. S., Bhagawati, H., Tanjim, A., Mehboob, M., Sarma, M. K., Borah, C., Islam, A., & Basumatary, P. (2023). In-silico anti–microbial, anti-inflammatory and hypoglycemic evaluation of active phytoconstituents of the plant: Leucas aspera (Willd.).
[28] Jayaprakasam, R., Abinaya, R., Gandhimathi, M., & Ravi, T. K. (2023). Estimation of Oleanolic Acid by HPTLC and HPLC Methods in Successive Leaf Extracts of Leucas aspera and Tridax procumbens and their In vitro Anti- Inflammatory Activity. European Journal of Medicinal Plants.
[29] Kalpana, V. N., & Rajeswari, V. D. (2016). Phytochemical and Pharmacological investigation of an indigenous medicinal plant Leucas aspera. *International Journal of PharmTech Research*, *9*(8), 2455-9563.
[30] Kanneboina, S., Kumari, A., & Jyothsna, E. (2024). Leucas aspera: A wild traditional green leafy vegetable with immense pharmacological properties. International Journal of Advanced Biochemistry Research, 8(2S), 504–508.
[31] Kennedy RO, Thornes RD. Coumarins: biology, applications, and mode of action. New York (NY): Wiley Publication; 1997. p. 1.
[32] Kripa, K. G., Chamundeeswari, D., Thanka, J., & Uma Maheswara Reddy, C. (2011). Modulation of inflammatory markers by the ethanolic extract of Leucas aspera in adjuvant arthritis. *Journal of Ethnopharmacology*, *134*(3), 1024– 1027.
[33] Ku CT, Chen SC, Wang JP, Wu JB, Kuo SC. Studies on anti-inflammatory constituents of *Leucas mollissima* Wall. var. *chinensis* Benth. Chin Pharm J. 2000;52:261–73.
[34] Kumar S, Patel N, Budholiya P. Evaluation of anti-ulcer activity of hydroalcoholic leaves extract of *Leucas aspera*. Int J Pharm Biol Sci Arch. 2021;9(2).
[35] Limbasiya VR, Modi PR, Tigar TR, Desai TN, Bhalodia TN. Evaluation of anti-asthmatic activity of dried whole plant extract of *Leucas aspera* using various experimental animal models. Indian J Pharm. 2012;3(3):291–8.
[36] Mahato SB, Pal BC. Structure of linifolioside, an isopimarane rhamnoglucoside from *Leucas linifolia*. Phytochemistry. 1986;25(4):909–12.
[37] Mangathayaru K, Amitabha G, Rajeev R, Kaushik VK. Volatile constituents of *Leucas aspera* (Willd.) Link. J Essent Oil Res. 2006;18(1):104–5.
[38] Manivannana R, Sukumar D. The RBC membrane stabilization in an in vitro method by the drug isolated from *Leucas aspera*. Int J Appl Sci Eng. 2007;5:133–8.
[39] Mannan A, Das H, Rahman M, Jesmin J, Siddika A, Rahman M. Antihyperglycemic activity evaluation of *Leucas aspera* (Wild.) Link. leaf and stem and *Lannea coromandelica* (Houtt.) Merr. bark extract in mice. Adv Nat Appl Sci. 2010;385–8.
[40] Misra TN, Singh RS, Pandey HS, Singh S. Long-chain compounds from *Leucas aspera*. Phytochemistry. 1992;31(5):1809–10.
[41] Misra TN, Singh RS, Prasad C, Singh S. Two aliphatic ketols from *Leucas aspera*. Phytochemistry. 1992;32(1):199– 201.
[42] Miyaichi Y, Segawa A, Tomimori T. Studies on Nepalese crude drugs. XXIX. Chemical constituents of dronapuspi, the whole herb of *Leucas cephalotes* SPRENG. Chem Pharm Bull. 2006;54(10):1370–9.

[43] Mohanta B, Chakraborty A, Sudarshan M, Dutta RK, Baruah M. Journal of Radioanalytical and Nuclear Chemistry. 2003;258(1):175–9.

[44] Morshed MA, Uddin A, Saifur R, Barua A, Haque A. Evaluation of antimicrobial and cytotoxic properties of *Leucas aspera* and *Spilanthes paniculata*. Int J Biosci. 2011;1(2):7–16.

[45] Mostafa M, Nahar N, Mosihuzzaman M, Makhmoor T, Choudhary MI, Rahman AU. Free radical scavenging phenylethanoid glycosides from *Leucas indica* Linn. Nat Prod Res. 2007;21(4):354–61.

[46] Mvé-Mba CE, Menut C, Lamaty G, Zollo PHA, Tchoumbougnang F, Bessière JM. Aromatic plants of tropical central Africa. Part XIX. Volatile components from leaves of two Lamiaceae from Cameroon: *Leucas deflexa* Hook and *Solenostemon monostachyus* (P. Beauv.) Briq. Flavour Fragr J. 1994;9(6):315–7.

[47] Nasim N, Sandeep IS, Mohanty S. Plant-derived natural products for drug discovery: current approaches and prospects. Nucleus. 2022;65(3):399–411.

[48] Noor A, Fatima I, Ahmad I, Malik A, Afza N, Iqbal L, et al. Leufolins A and B, potent butyrylcholinesterase-inhibiting flavonoid glucosides from *Leucas urticifolia*. Molecules. 2007;12(7):1447–54.

[49] Patil, N. (2013). A Study of Anti-Inflammatory Activity of Alcoholic Extract of Leaves of Leucas Aspera in Albino Rats (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).

[50] Petrovska BB. Historical review of medicinal plants' usage. Pharmacogn Rev. 2012;6(11):1–5.

[51] Pradhan BP, Chakraborty DK, Subba GC. A triterpenoid lactone from *Leucas aspera*. Phytochemistry. 1990;29(5):1693–5.

[52] Prakash D, Jain RK, Misra PS. Amino acid profiles of some under-utilised seeds. Plant Foods Hum Nutr. 1988;38(3):235–41.

[53] Punjani BL. Herbal folk medicines used for urinary complaints in tribal pockets of northeast Gujarat. Indian J Tradit Know. 2010;9:126–30.

[54] Reddy KM, Viswanathan S, Thirugnanasabmantham D, Santa R, Lalitha K. Analgesic activity of *Leucas aspera*. Fitoterapia. 1993;151–4.

[55] Rahman MA, Islam MS. Antioxidant, antibacterial and cytotoxic effects of the phytochemicals of whole *Leucas aspera* extract. Asian Pac J Trop Biomed. 2013;3(4):273–9.

[56] Rahman MA, Sultana R, Bin Emran T, Islam MS, Rahman MA, Chakma JS, et al. Effects of organic extracts of six Bangladeshi plants on in vitro thrombolysis and cytotoxicity. BMC Complement Altern Med. 2013;13(1).

[57] Rai V, Kakkar P, Khatoon S, Rawat AKS, Mehrotra S. Heavy metal accumulation in some herbal drugs. Pharm Biol. 2001;39(5):384–7.

[58] Sabri G, Vimala Y, Mandlik P. *Leucas aspera*: Medicinal plant review. Int Res J Multidiscip Stud. 2015;1(3):1–8.

[59] Sadhu SK, Okuyama E, Fujimoto H, Ishibashi M. Separation of *Leucas aspera*, a medicinal plant of Bangladesh, guided by prostaglandin inhibitory and antioxidant activities. Chem Pharm Bull. 2003;51(5):595–8.

[60] Sandhya B, Thomas S, Isabel W, Shenbagarathai R. Ethnomedicinal plants used by the Valaiyan community of Piranmalai hills (reserved forest), Tamilnadu, India. A pilot study. Afr J Tradit Complement Altern Med. 2005;3(1).

[61] Shiney Ramya B, Ganesh P, Suresh Kumar R. Phytochemical screening of *Coleus aromaticus* and *Leucas aspera* and their antibacterial activity against enteric pathogens. Int J Pharm Biol Arch. 2012;3(1):162–6.

[62] Shoeb M, Jaspars M, MacManus SM, Celik S, Nahar L, Kong-Thoo-Lin P, et al. Anti-colon cancer potential of phenolic compounds from the aerial parts of *Centaurea gigantea* (Asteraceae). J Nat Med. 2006;61(2):164–9.

[63] Shwetha, R. J., Tahareen, S., & Myrene, R. D. Journal of Chemical, Biological and Physical Sciences.

[64] Singh AK, Raghubanshi AS, Singh JS. Medical ethnobotany of the tribals of Sonaghati of Sonbhadra district, Uttar Pradesh, India. J Ethnopharmacol. 2002;81(1):31–41.

[65] Sinha S, Ansai AA, Osman SM. *Leucas cephalotes* a new seed oil rich in laballenic acid. Chem Ind. 1978;1:67.

[66] Srinivasan D, Nathan S, Suresh T, Lakshmana Perumalsamy P. Antimicrobial activity of certain Indian medicinal plants used in folkloric medicine. J Ethnopharmacol. 2001;74(3):217–20.

[67] Sukasini S, M B. Cytotoxic activity of a medicinal mangrove plant *Ceriops decandra* (Griff.) Ding Hou leaves on human breast adenocarcinoma cell line MCF-7. Asian J Pharm Clin Res. 2018;11(12):296.

[68] Sundane AR, Ulla KMH, Satyanarayan ND. Anti-inflammatory and analgesic activity of various extracts of *Leucas aspera* Spreng. (Labiatae). Indian J Pharm Sci. 2000;144–6.

[69] Tukaram T, Parvati CV, Rao NV, Prakash P, Rao KS. Evaluation of the extracts of *Leucas aspera* on biochemical profiles in experimental model of diabetes mellitus (Type - I) in rats. Int Res J Pharm. 2011;246–8.

[70] Vagionas K, Ngassapa O, Runyoro D, Graikou K, Gortzi O, Chinou I. Chemical analysis of edible aromatic plants growing in Tanzania. Food Chem. 2007;105(4):1711–7.

[71] Varol M. Anti-breast cancer and anti-angiogenic potential of a lichen-derived small molecule: Barbatolic acid. Cytotechnology. 2018;70(6):1565–73.

[72] Vijay Kumar G, Devanna N. An update of *Leucas aspera* - A medicinal plant. Int J Sci Res Methodol. 2016;1–19.

[73] Wesley JJ, Smith AA, Balakrishnan N. Anti-diabetic effects of *Leucas urticaefolia*–Ham. in STZ-induced diabetic rats. J Coast Life Med. 2022.

[74] Yousuf MHA, Bashir AK, Blunden G, Yang M-H, Patel AV. Coumarleucasin and leucasone from *Leucas inflata* roots. Phytochemistry. 1999;51(1):95–8.