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SHORT REVIEW

Pharmacological Properties of *Leucas aspera*: A Review

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Abstract

The *Lamiaceae,* previously called *Labiatae*, is a part of the mint group of blossoming plants. *Leucas aspera* commonly known as '*Thumbai*' possesses diverse ethno-medical values with proven medicinal properties. Traditionally, it is widely used as an anti-insecticide and antipyretic. Studies show that it imparts medicinal properties like antioxidant, antimicrobial, antifungal, antinociceptive, cytotoxic, antiulcer, anti-inflammatory and larvicidal activity. Its abundant availability across India makes it a more reliable source of medicinally active substances. Existing work on the pharmacognostic study of the plant *L. aspera* reveals phytochemical characteristics and it indicates the existence of bioactive substances such as terpenoids, flavonoids, tannins, carbohydrates, alkaloids, saponins and phenols. There are reported studies which show that this plant has activity against skin infection-related disease-causing pathogens like *Aspergillus niger*, *Pseudomonas aeruginosa* and *Candida albicans*. This review centres around the accumulation of the pharmacological qualities of *L. aspera* that have been studied beforehand by various researchers and compiling its outcome.

Major Findings: *Leucas aspera* possesses numerous and vulnerable pharmacological properties so plant has a potential to act a source of reliable herbal medicine, particularly against pathogens that cause skin infections.

Keywords: Anti-fungal Activity, Antimicrobial Activity, *Leucas aspera*, Pharmacological Properties, Phytoconstituents

1. Introduction

For thousands of years, plants have been used for medical purposes as well as human health. For therapeutic utilisation, it is assessed that more than 70000 plant species have been utilised across the globe. A very important medicinal plant family is the *Lamiaceae* family, otherwise called the mint family[1]. It represents more than 3000 types of plants spread in the temperate districts everywhere. The most known plants from this family are different fragrant spices such as wise, mint, exquisite, lemon emollient, thyme, hyssop, basil, oregano and rosemary[2].

One such notable species found with incredible importance in therapeutic use is *L. aspera* because of its huge medicinal results. This species corresponds to the *Leucas* genus and from the well-known medicinal family *Lamiaceae*, having aromatic characteristics[3]. Phytochemical screening studies uncover the presence of functional groups like tannin, saponin, alkaloid, phenol, flavonoid and carbohydrate[4]. Years of research carried out on this herb established tremendous useful pharmacological activities like but not limited to analgesic, anti-diarrheal, antipyretic, antioxidant, antimicrobial and anti-fungal. Also, traditionally it is being utilised for skin rashes, painful swelling and cough[5]. Further various researchers have proved its properties like cytotoxic activity, antinociceptive, anti-inflammatory and insecticidal[6]. Plants extracts derived from *L. aspera* show huge powerful for dealing with skin infection related disease like scabies, psoriasis and ulcer[7]. Juices derived from plant found to be effective to treat psoriasis[8,9].

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2. Botanical Description

Morphological behaviour suggests that *L. aspera* is a 10-55 cm raised and stretched herb. Its stem is quadrangular in shape with comparable branches (Figure 1), light greenish to yellow coloured stem whereas its surface is hairy and rough. Roots are either zigzag or cylindrical shaped roots, smooth and long with multiple wiry branches. Linearly lanceolate furrow leaves are shortly petiolate or sometimes sub-sessile. Sessile leaves have sharp to pointy tips and are arranged opposite each other (Figure 2). White-coloured flowers are dense terminal or axillary whorls of tiny, sessile flowers. The corolla is 1cm in length with 5mm long tube with a circinate in the middle[10-13].

3. Phytochemical Screening

As per the reported studies, standard techniques in light of compound assessments are utilised to affirm the presence of various phytochemicals. Investigation of phytochemical compounds reveals the presence of phenols, terpenoids, alkaloids, flavonoids, carbohydrates, saponins and tannins[2]. Details of the identified phytochemicals found in *L. aspera* roots and aerial parts are mentioned in Table 1.

4. Pharmacological Activities

Reported writing stresses that *L. aspera* is an efficacious medicinal herb utilised for relieving various illnesses. The pharmacological and biological effect shown by plants is the virtue of different phytochemical active constituents; that are present in the aerial part of the plant. To identify and isolate those phytochemicals, researchers used a variety of extraction techniques. The first list of these ingredients includes long-chain compounds, glycosides, and fatty compounds, among others. Further list extends to terpenoids, flavonoids, terpenes, alkaloids and sterols. To evaluate



Figure 1. The plant *Leucas aspera*.



Figure 2. *Leucas aspera* flower and leaf.

Table 1. List of phytochemicals found in roots and aerial part of *Leucas aspera*

Tissue	Phytochemicals	References
Whole plant	β-sitosterol and oleanolic acid	14
Aerial parts	licarin A and sterols, diterpenes, nicotine, linifolioside, glucoside	13, 15-19
Leaf	xthujene and ufarnesene(in the form of volatiles)	20
Flower	isoamyl propionate and amyl propionate	20
Seed	linoleic acid, stearic acid, ceryl alcohol, palmitic acid and oleic acid	21, 22
Shoot	aliphatic ketols, βsitosterol, long-chain compounds nonatriacontane, and triacontanol, novel phenolic compounds	23-26
Root	leucolactone	25

the biological activities derived from the extraction studies, extensive research has been carried out. The reported activities are anti-inflammatory, antipyretic, antimicrobial, anticancer, phytotoxic, antioxidant, analgesic and antimalarial.

The literature survey tells us more about the different types of pharmacological activities shown by *L. aspera* as mentioned below,

4.1 Antimicrobial Activity

There are a few microorganisms like *P. aeruginosa*, *Salmonella choleraesuis, Staphylococcus aureus*, *Shigella flexneri* and *Salmonella typhimurium* against which the leaf, flower, stem and root of *L. Aspera* have showed good antibacterial activity[19]. At the point when the aerial part of the plant is extracted using polar solvents like ethanol found to be effective against *Klebsiella pneumonia* and *Staphylococcus epidermidis* was more prominent. The disc diffusion method is used in this study to demonstrate antibacterial activity at the lowest extract concentrations 20 µg/mL and 35 µg/mL respectively. Additionally, extraction carried out using methanol exhibited antibacterial properties against *E. coli*. Methanol and ethyl acetate of *L. aspera* extract act against *Streptococcus pyogenes* by forestalling biofilm formation[16]. *L. aspera* flowers contain phyto compounds like tannin and phenol which make them more viable antimicrobial agents causing inhibition of pathogens. Scalbert has studied this behaviour of *L. Aspera* to demonstrate antimicrobial activity by tannin[27]. Hebbar *et al*., studied that *L. aspera* has an antibacterial impact against most of the bacteria causing oral disease. *L. aspera* extract was tested *in vitro* using the time-kill method to determine its effectiveness against *Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis,* and *Prevotella intermedia*[28].

In terms of medicine, it has been demonstrated that *L. aspera* shows multiple therapeutic values including anti-microbial activity[27]. Ileana Cocan studied that petroleum ether and chloroform extracts of *L. aspera* exhibit strong antimicrobial activity when studied on the fungi *Microsporum gypseum* and *Trichophyton*. According to this study, 5mg/mL is the lowest potent concentration value[15]. It was found that the *Aspera* plant has both fungicidal and fungistatic action. The methanolic extracts of *L. aspera* have a higher range of antimicrobial activity against *M. gypsum, Epidermophyton floccosum, Trichophyton mentagrophytes, Candida tropicalis, Aspergillus flavus, Microsporum nanum* and *Penicillium* spp. Both the extracts obtained from chloroform and ethanol revealed antimicrobial activity against *M. gypseum* and *Trichophyton*[13]. Atomic Force Microscopy (AFM) was used to observe the plant extract's antibacterial activity against the dermatophytes mentioned. AFM found that the pathogens' size and shape significantly changed in response to the extracts' treatment**.** The expressed flower juice, the methanolic extract of flowers, its fractions and the alkaloidal residue showed good antimicrobial activity against *Cryptococcus neoformans, C. albicans, Trichophyton mentagrophytes* and *A. niger* in the zone of inhibition method. Ethanolic and Chloroform extracts showed antimicrobial activity against *M. gypseum* and *Trichophyton*. The alkaloidal residue has the best antimicrobial activity against *C. albinos, Cryptococcus neoformans, A. niger* and *Trichophyton mentagrophytes* whereas according to reports, the methanolic extracts of *L. aspera* flowers exhibit fungistatic and fungicidal properties. At concentrations between 250 ppm and 1500 ppm, the fungicidal effect against *A. niger, Fusarium moniliforme* and *Sclerotium rolfsii* was investigated.

4.2 Antioxidant Activity

Many researchers have established the antioxidant properties of *L. aspera* with proper substantiation. A potent antioxidant activity is reported in ethanol extract[15]. Specifically root of the plant when extracted in ethanol exhibited antioxidant activity and in his subsequent investigation suggested that the whole plant has the highest antioxidant activity. A study performed by Sadhhu proved that *L. aspera* shows prostaglandin inhibition and antioxidant activity[13]. Aqueous extracts of whole plants contain antioxidant enzymes like superoxide dismutase, catalase and glutathione peroxidase which effectively works on lipid peroxidation by decreasing its levels in D-GalN-induced hepatotoxic rats[29]. Mother tinctures derived from the plant have shown significant antioxidant activity as studied by Mishra R[29]. Methanol extract has shown more potent activity compared to other fractions[30]. In a comparative study on different plants, it was found that *L. aspera* shows antioxidants lower than those shown by *Adhatoda vesica* and *Phyllanthus niruri*[31].

Adhatoda vesica could scavenge 56.6% of radicals whereas *P. niruri* and other plant extracts *L. aspera* showed 45.7% scavenging potential. Earlier studies have proved that plants contain metabolite compounds diosmetin (bioflavonoid), cosmosiin hexaacetate, 4H-1-benzopyran-4-one,3-hydroxy-2-phenyl, rutin and 2-isoprenylemodinis responsible for antioxidant activity[32-34]. Vasudha K. has assessed antioxidant study in plant extract by DPPH (2,2-diphenyl-1-picrylhydrazyl) and scavenging of H_2O_2 free radicals[35]. Using scavenging assay on *L. aspera* flower Gulnaz has proved the activity[36]. The phosphomolybdenum assay method was used by scientists to determine Ascorbic acid which has given equivalent antioxidant activity[37]. Researchers have found the presence of a phenolic group in plants which corresponds to flavonoids. These groups are responsible for producing an antioxidant effect. Ganga Rao B and team have studied regional variation in antioxidant activity in terms of phenolic content present in the plant[38]. S Meghashri has studied antioxidant properties in *L. aspera* leaves with repeated fractionation of the methanol extract[39].

4.3 Antinociceptive Activity

Researchers have performed studies on the extract of *L. aspera* in different solvents with multiple dilutions and found comparatively higher antinociceptive activity in whole plants' methanolic extract at doses between 50 to 400mg. Also, the roots of *L. aspera* show significant characteristics of antinociceptive activity[40]. Rahahmtulla has studied the effect of the combination of *L. aspera* and *Zingiber officinale* rhizomes and proved that extract of both the plants in combination gives good antinociceptive and antihyperglycemic activity[41]. A comparative study of acetic acid-induced gastric pain models in Swiss albino mice by Farhad Hossan found that the whole plant extract of *L. aspera* showed superior antinociceptive action in comparison to the leaves of *Xanthium indicum*[28]. In the case of *X. indicum* number of writhings was inhibited by 31.8, 36.6, 41.2 and 42.9%. In comparison, the number of constrictions was reduced as shown by *L. aspera* methanolic extract as 50.1, 51.9, 55.8 and 57.7%.

4.4 Cytotoxic Activity

Researchers found that *L aspera* roots show cytotoxic activity[12]. Also, methanol extract of whole plants exhibits similar activity[5]. Whereas in another study researchers found a cytotoxic activity which was dose dependent[42]. Significant cytotoxic activity was reported in the roots of *L. aspera* where a study was carried out using the brine shrimp nauplii bioassay method at 80% ethanolic extract. Further, 52.8µg/ml is the concentration that has been identified as LC_{50}. Research has proved that how root extract of *L. aspera* shows cytotoxic activity[6]. It shows enhanced anti-cancer activity in the form of stable nanoparticles obtained by nanoprecipitation with methanol[27-29,43].

Rajeev *et al.*, studied cytotoxic properties shown by *L. aspera* and discovered that flowers of *L. aspera* possess moderate anti-cancer activity[44]. Scientists have studied and established anti-cancer properties from plants against tumour development[45]. Leaves of *L. aspera* showed a strong cytotoxic effect when a study was performed on dichloromethane fractions from plant extract[46]. The presence of secondary metabolites like glycosides, flavonoids, steroids and phlobatannins in plants is responsible for a cytotoxic effect[47].

4.5 Antiulcer Activity

When stomach acid erodes the intestinal lining, ulcers develop. Among the frequent causes is bacterial infection, because *L. aspera* contains secondary metabolites, it has a pharmacologic action that is hostile to ulcers. Hydro-alcoholic leaf extract of *Leucas aspera* acts through the restraint of cell wall biosynthesis which kills the bacteria[48]. Nagarajan studied that the calming property of *L. aspera* would be advantageous in the treatment of aphthous ulcers[49]. A study has been performed utilising ethanol-induced ulcer models and the pylorus ligation technique to evaluate *in vitro* antiulcer activity of methanolic extract[50]. In a comparative study with the standard drug lansoprazole, *L. aspera* stands equivalent to its activity against ulcers through gastric protective effect[51].

4.6 Anti-inflammatory Activity

The anti-inflammatory activities of herbal plants are generally exerted through their secondary metabolites. In the case of *L. aspera*, oleanolic acid found in the leaf

is responsible for giving anti-inflammatory activity[52]. Scientific research has been carried out by Bhuvaneswari *et al.*, to study the anti-inflammatory properties of Cu nanoparticle which has been synthesised from *L. aspera* and proven that it has dose-dependent activity[53].

In another study, using standardised assay methods, multi-model assays were carried out on plants to prove their anti-inflammatory activity. Since *L. aspera* shows the presence of polyphenolic compounds hence mixtures of *L. aspera* can be utilised as effective compounds for planning strong anti-inflammatory drug[54]. Scientists have successfully isolated apigenin 7-O-glucoside from *L. aspera,* exhibiting a significant anti-inflammatory activity. This has been established by comparing the activity with standard diclofenac sodium[55]. The anti-inflammatory activity is accessed in terms of the paw volume reduction which was 3.83± 0.126 obtained from *L. aspera* extract as compared to 3.63 ± 0.126 due to the diclofenac standard. Gold nanoparticles integrated utilising the restorative plant *L. aspera* extract show a better anti-inflammatory effect when compared with the pure *L. aspera* extract[56].

4.7 Larvicidal Activity

An insecticide called a larvicide is used to keep mosquitoes away from houses, both indoors and outdoors. They function by eliminating mosquito larvae before they have a chance to develop into adults. In rural areas, the leaves of *L. aspera* are utilised as an insect poison and mosquito repellent. Eswaralakshmi and Shakila, carried out research using methyl alcohol extracts from *L. aspera* leaf for mosquitocidal activity and the study showed significant larvicidal action[57]. In another study, the larvicidal capability of rejuvenating oil separated from leaves of *L aspera* was assessed against three medicinally significant types of mosquito vectors, *Ae. aegypti*, *C. quinquefasciatus* and *An. stephensi*[58]. Studies have been conducted using *L. aspera* aqueous leaf extracts to create silver nanoparticles in a green way on *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus* and laid-out plants is successful in controlling mosquito larvae[58]. Research lead by Elumalai *et al.*, successfully established plant extract capability versus *Anopheles stephensi* and *Culex quinquefasciatus* to prove plant potent larvicidal efficacy[59].

4.8 Hepaprotective Activity

It is crucial to defend the liver against the damaging effects of hepatotoxins, which can be consumed, or to reverse changes in the antiradical defense systems. Many plants with bioactive flavonoids and polyphenols have the potential to protect the liver damage. Sattar *et al.*, and team studied hepaprotective activity shown by *L. aspera* leaves through an *in-vivo* study on albino rats[60]. The experiments were conducted by assessing the influence of pre-treatment of ethanolic extract of *L. aspera* **leaves in** simvastatin-induced hepatotoxicity and concluded that plant leaves have hepaprotective potential. In another study, scientists have proved the hepaprotective potential of the plan by conducting experiments against Carbon tetra chloride-induced acute liver and proven scientifically that plant can be considered for curing hepatic disorders[61]. Research conducted by Banu S *et al.*, on the Hepatoprotective activity of *L. aspera* d-GalN caused liver damage and demonstrated that *L. aspera* extract could repair the damage to the hepatic tissue brought on by GalN[62].

4.9 Anti-hyperglycemic Activity

The primary cause of the plant's antihyperglycemic action is their capacity to restore pancreatic tissue function by either increasing insulin production or preventing intestinal glucose absorption. In light of a previously performed study, the antihyperglycemic capability of *L. aspera* was assessed by involving *in vivo* techniques in streptozotocin-actuated diabetic rats. The study outcome confirmed that methanol extract from plants possessed anti-hyperglycemic activity[63]. In another study, Abdul Mannan *et al.*, and team explored a study on methanol extract of leaves and stems of *L. aspera* in oral glucose resilience tests led with glucose-tested Swiss pale-skinned person mice and established antihyperglycemic impact[64]. The two extract combinations i.e. *L. aspera* and *Z. officinale* showed fantastic antihyperglycemic and antinociceptive properties. Plant extracts at 50, 100, 200, and 400 mg doses significantly reduced blood glucose levels in glucose-administered mice by 32.3%, 45.0%, 51.2%, and 54.0%, respectively, demonstrating a dose-dependent effect[39].

4.10 Miscellaneous Properties

It was accounted for that all parts of the plant had pharmacological properties and were helpful in different

fields of medication. The whole plant was utilised as an antipyretic in fever conditions and to treat colds, scabies, psoriasis and persistent skin contaminations. Using chloroform as extracting solvent a flavonoid was extracted from *L. aspera* in a study and it was identified as apigenin-7-O-(6"-O-E-caffeoyl)-β-D–glucopyranoside. An investigation study on this compound successfully shows wound healing activity[53]. In another study, Prabakaran *et al*., isolated baicalein-7-O- β-D-glucuronide (baicalin) from *L. aspera* flower and proved that plants possess wound healing activity[65]. The study evaluated the wound-healing activity of baicalin from *L. aspera*, comparing its effectiveness to standard soframycin ointment.

Immunizing agent toxin impact of methanolic leaf concentrate of *L. aspera* Linn. was concentrated by confinement and refinement of a functioning Compound-Triterpenoid. This study affirmed that Triternoid obtained from *L. aspera* irritates the cobra toxin harmfulness[66]. Referring to different examinations done beforehand, researchers demonstrated that and announced extracts from *L. aspera* activity against wounds by causing wound healing, pan oral disorders, asthma and diabetes.

4.11 *Leucas aspera* as a Herbal Drug

Several homoeopathic formulations under the herbal category have been produced by drug manufacturers due to the high therapeutic potential of *L. aspera*, which has been confirmed by numerous studies. A homoeopathic remedy '*L. aspera* 30CH' is mainly used to treat respiratory conditions like asthma, coughing, jaundice and dysentery as well as sporadic fever. appropriate for recurrent fevers and respiratory issues. '*L. aspera* MT' is used to treat skin issues, venomous animal bites, asthma, coughing, diarrhoea, jaundice and intermittent fever. In Indian medicine, it is applied externally to treat chronic skin eruptions, psoriasis, and scabies. Mother Tincture of *L. aspera* has cytotoxic, antimicrobial, antinociceptive, antifungal, and antioxidant properties. beneficial for bacterial infections and fevers. 'Dr Willmar Schwabe India *L. aspera* dilution' is a homeopathic medicine, which is primarily used for the treatment of intermittent fever and respiratory diseases including asthma, cough, jaundice, dysentery and jaundice.

5. Conclusion

As per a literature survey, *L. aspera* is a very important medicinal plant. Investigated studies uncover the presence of different phytochemicals when aerial parts and roots of the plant are extracted using different solvents. Phytocompounds are distinguished tannins, carbohydrates, flavonoids, alkaloids, phenols, saponins and which are in charge of vital biological functions such as cytotoxic, antimicrobial, antioxidant, antifungal, anti-ulcer, anti-inflammatory, larvicidal, hepatoprotective, and anti-hyperglycemic effects. Also, the plant shows effective action against dermatophytes belonging to the genera *Trichophyton, Epidermophyton* and *Microsporum*. These findings motivate scientists to isolate and characterise the phytoconstituents of the *L. aspera* plant, investigate their potential against particular disease-causing microbes, and utilise them to create novel pharmaceuticals.

6. Author Contribution

In order to recognize the author's participation, we highlight each individual contribution: Veena Khilnani - Guidance for literature search and designing of the article; Sameer Hajare - Literature search, writing the article and crafting the graphical abstract; Yogesh Naik – Literature search; Yogesh Ghalsasi - Guidance for literature review. review. All authors have read and agreed to the published version of the manuscript.

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