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A CONCISE REVIEW: CURRENT DEVELOPMENT AND FUTURE PROSPECTS OF PHARMACOLOGICAL ACTIVITIES OF *LEUCAS ASPERA*

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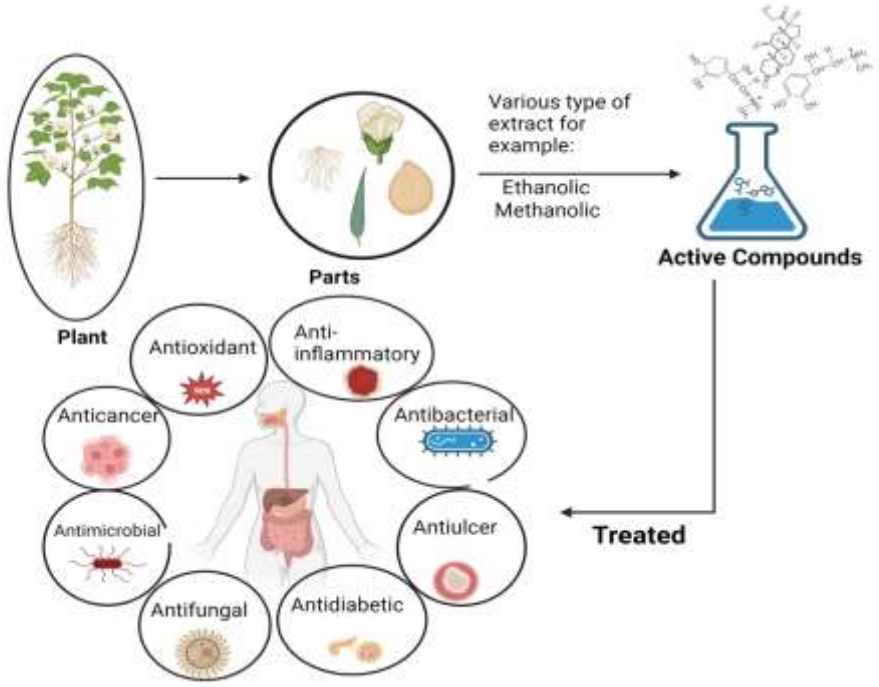
ABSTRACT

Leucas aspera, commonly known as "Thumbai" or "Dronapushpi," is a medicinal plant that has been traditionally used in various cultures for its therapeutic properties. This review explores the current state of research on the bioactive compounds derived from *Leucas aspera* and their potential applications in medicine. The plant is rich in secondary metabolites such as alkaloids, flavonoids, terpenoids, and essential oils, which contribute to its diverse pharmacological activities. Several studies have demonstrated the antioxidant, anti-inflammatory, antimicrobial, and anticancer properties of *Leucas aspera* extracts. These bioactive compounds have shown promising results in preclinical studies, indicating their potential for the development of novel therapeutic agents. Additionally, the plant has been recognized for its traditional use in treating various ailments, including respiratory disorders, skin diseases, and digestive issues. The review also highlights the ongoing efforts to isolate and characterize specific bioactive compounds from *Leucas aspera*, providing insights into their molecular mechanisms and pharmacokinetics. Furthermore, advancements in extraction techniques, formulation strategies, and biotechnological approaches are discussed, aiming to enhance the bioavailability and efficacy of these compounds. Looking toward the future, the review outlines potential directions for further research, emphasizing the need for clinical trials to validate the safety and efficacy of *Leucas aspera* derived compounds in humans.

KEYWORDS: *Leucas aspera*, Biocompounds, Pharmacological, Antimicrobial activity, Medicine.

GRAPHICAL ABSTRACT



INTRODUCTION

Leucas aspera (Willd.) Linn, an herb from the Lamiaceae family, contains a variety of biologically active compounds. These compounds include diterpenes, b-sitosterol, nicotine, oleanolic acid, ursolic acid, sterols, glucoside, and phenolic compounds, specifically 4-(24-hydroxy-1-oxo-5-n-propyltetracosanyl)-phenol.

Commonly known as "Thumbai," this herb displays a broad range of pharmacological properties.[1] In South India and has been used for a long time in conventional medicine[2] For thousands of years, people have utilized plants as medicine to treat a variety of illnesses. These plants are a source of several strong and effective medications that are utilized extensively in traditional medicine throughout several nations[3] Traditionally, medicinal plant extracts have been utilized to treat a variety of infectious disorders brought on by fungi and bacteria.[4] There have been reports that the plant contains insecticidal and antipyretic properties.[5] Flowers serve various purposes, including being used as emmenagogues, pesticides, diaphoretics, expectorants, aperients, and stimulants. It is believed that leaves possess properties that help alleviate psoriasis, chronic rheumatism, and other persistent skin conditions. Moreover, the topical application of crushed leaves is used as a remedy for snake bites.[6] The plant's root ethanolic extract possesses cytotoxic, antioxidant, and antinociceptive properties.[7] Liver problems are responsible for roughly 20,000 fatalities annually. Drugs derived from plants have demonstrated the ability to preserve the liver's typical functioning state. Approximately 80% of the global population depends on traditional medicine.[8] The plant genus *Leucas*, which is part of the Lamiaceae family, contains roughly 80 species. Traditional healers use these species to treat a wide range of illnesses.[9] The roots of this plant have been found to contain 3□,16α-dihydroxyoleanan-28→13□-olide, a triterpenoid lactone, according to recent reports. Unfortunately, this plant has not been the subject of a thorough chemical analysis; for this reason, the current study was started.[10] recently, there has been a significant increase worldwide the academic research of conventional plants and its potential therapeutic benefits. The research on plants for their medicinal properties has been driven by their strong pharmacological effects, low toxicity, and economic feasibility.[11] The fact that many antibiotics are becoming multidrug resistant and that there is a general belief that herbal therapy is more dependable and safe than costly synthetic medications, the majority of which have side effects, are the main causes of this renewed interest in plant-derived medications.[8] Exploration of novel indigenous herbal remedies may result from this belief and perspective. Because of the strong radical scavenging abilities of plants, scientific research on their therapeutic qualities has been conducted worldwide since ancient times.[12]

Fig. 1: Plant of *Leucas Aspera*.[13]

CLASSICAL CATEGORIZATION

Madhuva dravyaguna - Vividaushadi varga
Shaligrama Nighantus - Guduchyadi Vargas
Nighantu Adrasha - Tulasyadi vargas
Madanapala Nighantus - Abhayadi varga
Raja Nighantus - Parpatadi varga
Kaiyadeva Nighantus - Osadhi Vargas
Bhavaprakasha Nighantu - Guduchyadi Varga, Shaka Varga[8]

GEOGRAPHICAL DISTRIBUTION

It is found in various regions including China, Southern United State, Africa, Asia, and the Pacific Islands. It is spread across all of India, from Ceylon to the Himalayas. It is also common in Africa and the temperate and tropical regions of Asia, as well as Bangladesh, Indo-China, and Malesia.[14]

Table 1: Species and Country.

SPECIES	COUNTRY
Leucas aspera	India
Leucas alluaudii	Republic of congo
Leucas aspera	India
Leucas biflora	India
Leucas calostachys	Ethiopia
Leucas capensis	South africa
Leucas capitata	India
Leucas cephalotes	India
Leucas ciliate	China
Leucas decurvata	South africa
Leucas deflexa	Republic of congo,Ethiopia
Leucas hirta	India
Leucas Indica	Bangladesh, india
Leucas jamesii	Kenya
Leucas lanata	India
Leucas lavandulaefolia	India
Leucas linifolia	India
Leucas martinicensis	Ghana, Brazil, Tanzania
Leucas mollissima	India
Leucas abyssicica	Ethiopia
Leucas Plukenetii	India
Leucas stricta	India
Leucas urticaefolia	India
Leucas zeylanica	Bangladesh, india(24)[15]

BOTANICAL CLASSIFICATION

Leucas aspera is a yearly herb that usually grows to tallness of 15 to 60 Centimetre. The stem and branches of this plant are strong and covered in stiff hairs, giving them a sharp, four-sided appearance. The nutlet of Leucas aspera are elongated, measuring approximately 25 nm in length, and have a smooth surface. Importantly, these nutlets have clearly defined inner and outer faces that are darker in colour and have a well are defined shape.

LEAVES: The leaves are covered with fine hairs, called pubescence, and are up to 8.0 centimetre extended and 1.25 centimetre wide. They have a straight or lanceolate shape, a rough texture, and are either sub-sessile or have a short petiole. The petiole itself ranges from 2.5cm to 6cm long.

FLOWER: Bracts measuring 6 mm in length are observed to be linear in shape, with sharp and bristle-tipped characteristics. These bracts are also ciliate, with long and slender hairs. The blooms, on the other hand, are white and appear to be sessile and tiny, forming dense terminal or axillary whorls.

CALYX: Varying in appearance, the tubular structure measures between 8 and 13 mm in length. Typically, the upper half of this structure is characterized by ribbing and a rough texture, while the lower half is smooth and thin. The tube itself is curved and becomes narrower towards the top where the nutlets are located. The teeth present on this structure are small and triangular in shape, with each tooth ending in a fine bristle and having ciliated edges. The upper tooth is the largest in size. The mouth of this structure is small and inclined at a steep angle, lacking a hairy texture, and with the upper half extending outward.

CLORAL: The calyx varies in length, ranging from 8 to 13 mm. It has a tubular shape with a curved tube that narrows over the nutlets. The bottom half of the calyx is usually smooth and membrane-bound, while the upper segment is rib-shaped and covered with fine hairs. The calyx has small triangular teeth, each with a bristle-like tip. These teeth are adorned with fine hairs, and the largest tooth is situated at the top. The calyx mouth is small and highly oblique, without a hairy texture, and the upper half of the mouth protrudes forward.

FRUIT: The nutlets are smooth, brown, oblong, and measure approximately 2.5 mm in length. They have an angular inner surface and a rounded outer surface.[16][17]

A. Flower **B. Leaves**

C. Root **D. Seeds**

Fig. 2: Parts of Plants.[14],[18]

Table 2: Pharmacological Activities of Different Parts of *Leucas Aspera.*

Part	Extract	Animal	Dose	Route of Administration	Activity	Reference
Leaf	Ethanol extract	Wistar Albino rat (150-200) gram	2000mg/kg	Oral route	Hepatoprotective activity	[19]
	Menthol leaf Extract, Triterpenoid From methanol extract	Swiss Albino mice (18-22) g	0.2ml	Intramuscular, intraperitoneal, subcutaneous, intravenous	Antivenom activity	[20] [21]
	Ethanol extact	Wistar albino rat(150-200g)	5mg/kg	Intraperitoneal administration	Anti-diabetic activity,	[22] [23]
		Male wister rat (150-180g)	200 - 400mg/kg	Oral administration	Anti-hyperlipidemic activity	[24] [3] [14]
Root	Ethanol Extract	Male as well as female swiss Mice webstar stain (20-25g)	250-500 mg	Oral administration	CNS depressant activity	[14] [3]
	Methanol Methanol and petroleum ether extract	Male as well as female swiss webstar stain (20-25) gram	250-500mg/kg	Oral administration	Antioxidant Analgesic	[27]
	Hydro-ethanol and Aqueous extract	Male wistar rats(150-200mg)	100-200mg	Oral administration	Chemoprotective effect	[25]
	Ethanol Extract	Male swiss Albino mice (25-30)gram	400mg/kg	Oral administration	Antiepileptic Activity,	[26]
		Male swiss albino mice (25-30gram)	250-500mg/kg	Oral administration	Cytotoxic effect,	[27]
		Male in swiss Albino mice (25-30gram)	250-500mg/kg	Oral administration	Antinociceptive Activity	[27]
Flowers	Ethanolic Extract	Healthy albino mice (8-10 weeks old)	200-400mg	Intraperitoneal	Anticancerous Activity	[14] [28]
Whole plant	Ethanolic Extract	Male wistar albino rats (160-200g)	200mg/kg	Subcutaneous	Antipyretic Activity,	[29] [14]
		Wistar rats (150-200)	100mg/kg	Oral administration	Anti-inflammatory activity	[32]
	Methanol Extract	Healthy adult albino rat of wistar strain (150-200mg)	100-400mg/kg	Oral administration	Anti-hyperglycemic activity,	[30] [3]
		Adult swiss albino mice	200mg	Intraperitoneally	Anti-mutagenic activity	[31]
Aerial parts	Ethanol extract	Balb/c mice	(100mg/cm^2)	Topical	Anti-Psoriatic Activity	[33] [34]
	Methanol Extract	Swiss Albino mice (25-30) gram and wistar albino rat (150-200g)	2000mg/kg	Oral administration	Ulcer Protective effect	[3] [35]

PHARMACOLOGICAL ACTIVITEIS OF *LEUCAS ASPERA*

Antifungal Activity

It appears that the study investigated the antifungal activities of organic and water-based extracts obtained from the leaf of Leucas aspera in opposition to four fungal strains. The crude extract of Leucas aspera showed promising antifungal activity against Trichoderma viride, Candida Albicans, Aspergillus Flavus, and Epidermophyton floccosum (E. floccosum). The results indicate that, among the tested extracts, the dichloromethane (DCM) extract of Leucas aspera leaves demonstrated the highest antifungal potency. This was supported by the maximal area of inhibition observed against Trichoderma Viride (29.2 ± 2.00 milimeter), Candida Albicans (24.4 ± 0.80 milimeters), Aspergillus flavus (22.8 ± 0.36 milimeter), and E. floccosum (19.5 ± 2.17 milimeter) at a concentration of Ten milligrams /disc.The antifungal activity of the crude extracts was considerably higher in DCM extract and this is in agreement with the findings of Epidermophyton floccosum and Trichophyton mentagrophytes.[4] It was done agar diffusion method by Antifungal activity.[36] The antifungal action was conducted using Czapek Dox Agar medium. Stock societies were reactivated by the immunized them in Czapek Dox Agar soup medium and allowing them to grow for 48 hours at 27°C. The mentioned media were prepared on agar plates. The forty eight hour-old cultures (10−4 CFU/100 µl) were uniformly distributed over each plate .The wells were filled with 100 µl of *Leucas aspera* floral ethyl acetate extract after being perforated with a sterile cork borer measuring 6 mm after 20 minutes. An effective control was fluconazole. The inhibitory zone diameter was measured in millimeters during the 96-hour incubation period at 27°C on each plate.[37]

Table 3: Example of fungus.

Moulds	Aspergillus fumigatus
	Botryodiplodia theobromae
	Colletotrichum corchori
	Curvularia lunata
	Fusarium equiseti
Yeasts	Candida albicans
	Saccharomyces cerevisiae

The antifungal properties of all three extracts were evaluated against two yeasts and five molds. But normal clotrimazole shown very robust action against both yeasts and molds, while none of the extracts demonstrated any activity against the yeasts tested. Furthermore, the extracts appeared to encourage the growth of certain molds. The antimicrobial activity of an aqueous extract of the whole *Leucas aspera* plant was assessed in a prior investigation. It has been discovered that S. aureus, E. coli, and P. aeruginosa showed a larger range of zone of inhibition. This finding is consistent with the zone of inhibition for the ME extract found in the current investigation, with the exception of E. coli. experiment or study involving E. coli and plant extracts, specifically considering the differences in results that may arise from using different solvents for extraction and using different parts of the plant.[38]

Mosquito Repellence

It is discovered that the *Leucas aspera* are Ocimum americanum treated fabrics had mosquito-repelling efficacies of 68% and 64%, respectively. It is evident from the outcome that fabric treated with Leucas aspera exhibits greater repellence than fabric treated with Ocimum americanum. This could be because *Leucas aspera* has a higher concentration of farnesene.[39] The experiments employed larvae in the early stages of their fourth instar. The larvicidal activity was assessed using the WHO-recommended standard techniques. DMSO was used to prepare the concentrations of 1.25, 2.25, 5, 10, and 20 ppm. There were twenty larvae present in a 250 millilitres a glass beaker filled with 199 millilitres of tap water, along with One millilitre of the fraction and the corresponding concentrations of the separate substance. After a 24-hour exposure period, the dead larvae were counted from five replicates kept for each concentration.[40]

Hepato-Protective activity

The trichloromethyl free radical is created during the biotransformation of the toxin (CCl4) by cytochrome P450 in experimental hepatopathy. In the presence of oxygen produced by metabolic leakage from mitochondria, this in turn elicits lipid peroxidation of membrane lipids. The end result of all these processes is the destruction of hepatic tissue and the loss of cell membrane integrity.[19] Hepatotoxicity was induced by carbon tetrachloride in a model using a methanol extract. The hepatoprotective effectiveness of ethanol extracts from *Leucas aspera* leaves (400 milligram/kilogram) was discoverd to be significant in reducing simvastatin (Twenty milligram /kilogram p.o) caused hepatotoxic, similar to the standard medication silymarin (Twenty milligram per kilogram).[9] Fresh juice extracted from the leafs of *Leucas aspera* was examined to Assess its effectiveness in combating liver damage caused by carbon tetrachloride. The results revealed that the chilly methanol excerpt of the complete plant showed notable hepatoprotective properties. Alkaline phosphatase, glucose, bilirubin, cholesterol, overall protein, Transaminase Glutamic Oxaloacetic, and glutamic pyruvic transaminase were used as evaluation markers. To establish a comparison, The sillymarin was chosen as a normative. The fresh juice showed significant efficacy in treating liver diseases. Experimental studies conducted on male albinos Wistar rats using a hydrocarbon based leaf of extracted from *Leucas aspera* demonstrated a remarkable liver protective effect.[14]

Antioxidant Activity

Numerous diseases, such as atherosclerosis, aging, cancer, diabetes, and neurological disorders, are connected to the presence of unbound radicals. This responsive specie react with biological material, leading

to oxidative stress. Antioxidants catch these free radicals and neutralize oxidative stress, which in turn treats a variety of chronic illnesses. A potent bioactive substance called leucasin demonstrated significant potential for scavenging free radicals and inhibiting lipid peroxidation at a 40-ppm concentration. The results indicated that the methanol extract had stronger antioxidant properties than the ethanolic extract at 19.588 mm of ascorbic acid/gram of material. It was also determined that vitamins C and E were found to possess antioxidant attributes at dosages of 0.084 milligrams /gram of fresh weight and 645.69 milligram/gram of fresh weight, correlatively.[9] This suggests that a plant possessing the ability to effectively scavenge free radicals, there by mitigating tissue damage caused by them, may hold therapeutic significance.[41] The plant sample's ability to scavenge free radicals was assessed through various methods, including analyses of reducing power, phosphomolybdenum, nitric oxide scavenging, and hydrogen peroxide activities.[42]

The hydrogen peroxide scavenging percentages for both *Leucas aspera* extracts and typical substances were computed:

% Scavenged [Hydrogen peroxide] = [(Absorbances of control – Absorbance in presence sample of *Leucas aspera*)/Absorbance of control] x 100

Where,

AC - Absorbance of the control

AS - Absorbances in presence sample of *Leucas aspera* standards.[43]

Results regarding the ability of several plant extracts and well-known antioxidants to scavenge free radicals are shown. The results of the one way Analysis of Variance test, along with after the fact tests, indicated a significant difference in the average percentages of scavenge among all the test excerpts was used Butylated Hydroxytoluene, Tocopherol, roots, flowers, leafs, and stems at a concentration of 2 milligram/millilitre .The findings indicated thats, among the various plant extracts, the root extracts demonstrate the highest activities in scavenging free radicals, registering a mean percentage of (32.36±1.19)%. Conversely, the extracts obtained from the flower, leaf, and stem demonstrated scavenging activities of (26.39±0.07)%, (17.04±0.82)%, and (13.42±0.56)%, correspondingly. These extracts' scavenging activity was less than that of vitamin E (41.67±0.58)% and BHT (65.67±0.58)%, two antioxidants. Given that the root had the strongest antioxidant activities, it was examined in further detail in relation to the DPPH radical liberation.[11] The current study presents the evaluation of the overall anti-oxidative action of *Leucas aspera* using distinct solvent extracts through the phosphomolybdate technique. The phosphomolybdated method, commonly employed for assessing the overall antioxidant capacity of plant extracts, revealed a notably high antioxidant activity in the ethanol extract, measuring at 19.588 millimetre of ascorbic acid per gram of the samples. Analysis of variance analysis indicated significantly variations in the antioxidative capacity of *Leucas aspera* among both acetone and methanol extracts, as well as acetone and ethanol extracts. However, there are does not statistics noteworthy distinction observed between ethanol and methanol extracts. The DPPH method was employed to assess the free radical scavenging activity of *Leucas aspera*. The findings revealed that the highly activities was observeted in the ethanol excerpt, with an IC50 value of 35.335 microgram/millilitre. This was followed by the acetone and methanol extracts, which showed IC50 virtue of 119.237 micrograms /millilitre and 157.765 microgram/millilitre, correspondingly. The student t-test analyses show a noteworthy difference in the DPPH radically scavenges activities between the various excerpts and the normative trolox.[44][11]

Antiulcer Activity

This research revealed that the hydrocarbon based excerpt of *Leucas aspera* leaves contained Flavonoid, Tannin, and Saponin, as indicated by the phytochemical analysis. It also exhibited a therapeutic effect for gastric ulcers caused by indomethacin by killing the bacteria by preventing its cell wall manufacturing. In this research, the outcomes from antioxidant and histopathological investigations lend support to the traditional usually of *Leucas aspera* in treating various digestive issues. The study concludes that the methanol excerpt of *Leucas aspera* exhibits significant antisecretories and ulcer-preventive effects in every ulceration prototype that has been evaluated.[8] This study looked at how hydroalcoholic extract of leaves from *Leucas aspera* affected ulcers. *Leucas aspera* hydroalcoholic leaf extract was found to have an impact on the healing of indomethacin-induced stomach ulcers. It functions inhibiting the biosynthesis the cells of wall, ultimately causing the demise the bacterias. The hydroalcoholic extract of *Leucas aspera* leaves demonstrated effectiveness in decreasing both the ulcer area and ulcer score, indicating its antiulcer properties. antiulcer effect has an *leucas aspera*. It enhanced the healing process of ulcers induced by indomethacin.[45] The current research intended to evaluate the potential of the methanol excerpt obtained from *Leucas aspera* in preventing ulcers in Swiss albino mice and Wistar rats, using amount of 100 and 200 milligram/kilogram. The results demonstrated that the administration of the methanol extract significantly protected against the formation of ulcers in both animal species. Moreover, histopathological images provided additional evidence of the ulcer-preventive action of the methanol extract. Furthermore, investigations into the toxicity of both intense and subclinical of the methanol excerpt of *Leucas aspera* confirmed its safety profile for use.[35]

Anti-Cancerous Activity

The anticancer potential of the plant extracts was observed across various concentrations ranging from 10µg/ml to 50µg/ml, with absorbance measurements conducted at 570nm. For the aqueous extract, the percentage of cell death was 43.4%, whereas for the

methanol extract, it was 56.7%.[46] The results of the In-vitro cytotoxicity and cellular feasibility assays show that the leaf of *Leucas aspera* have significant antioxidantive possible. This attribute was evaluated use assays that targeted DPPH scavenging, hydroxyl intense scavenging, and NO scavenge activities. Additionally, this research demonstrated the anticancer effects through the MTT assay on MCF-7 cell line, utilizing a moderate focus. The observed activity are credited to a highly concentration of flavonoids as compared to alkaloids. In both In-vivo as well as In-vitro studies, biological and histology evidence suggests that extracted ethyl acetate are obtained from the whole portion of *Leucas aspera* possess anticancer properties. These properties are attributed to the stimulation of macrophages, inhibition of angiogenesis, and scavenging of free radicals. Additionally, the research findings indicate that the anticancer effectiveness of ethyl acetate excerpts of *Leucas aspera* is similar to that of the normative drug five-Fluorouracil.[8]

Anti-Diabetic Activity

The whole plant's methanol extracted, administered a dosage 400milligram/kilogram body weight, led to 34.45% reduce in blood glucose amounts in diabetic rats caused by streptozotocin. This extract containing ethanol from the entire plant on display significant anti-diabetic efficacy in glucose oral tolerance tests, as well as in diabetic rats induced by alloxan and streptozotocin. The ethanolic extract derived from the leaves demonstrated a doses depending on reduction a blood glucose levels and alleviated pathobiochemical alterations induced by experimental type 1 diabetes mellitus in rats.[47] The research findings show the leaves extracted of *Leucas aspera* exhibits antidiabetic potential in an in-vivo model using streptozotocin-induced diabetic Wistar albino rats.[8] In summary, this study systematically investigated the diabetes patterns induced by Streptozotocin and oral glucose loading in experimental rats. The responses of these rats to anti-diabetic agents were analyzed to assess the appropriateness of chemically introduction as a prototype for researching diabetic mellitus in experiments of animal. The results affirm the potential *Leucas aspera* for effectively managing diabetes mellitus in the human population.[23]

Anti-Inflammatory Activity

The entire plant extract of *Leucas aspera* was noted for its anti-inflammatory properties and induced mast cell degranulation. Notably, the yellow-colored chromatographic fraction from In models of both intense and persistent inflammation, the extract demonstrated strong anti-inflammated properties. The observed activities are attributed to the inhibition of histamines and serotonins.[15] The anti-inflammatory properties of various components of *Leucas aspera* have been extensively documented. The application of leaf juice, specifically extracted from *Leucas aspera*, is commonly used to address conditions such as skin condition, persistent skin eruptions, and persistent rheumatism. Notably, studies haved demonstrated a noteworthy anti-inflammated effect of *Leucas aspera* leaf ethanol extract across distinct doses in each of them intense and persistent inflammatory conditions.[9]

Anti-Psoriatic Activity

The anti-psoriatic activity of *Leucas aspera* was investigated using ethanol and petroleum ether extracts of C. juncea. The results showed that lipid peroxidation and nitric oxide generation had a strong negative effect on the proliferation of skin keratinocytes. This suggests that the activity of anti-psoriatic is attributed to antioxidant mediated[8] *Leucas aspera* ethanol extract influences lipid peroxidation, nitric oxide generation, and skin keratinocyte proliferation, indicates activity of anti-psoriatic associated with antioxidant mechanisms. The historical record reveals a longstanding tradition of utilizing herbal remedies for managing various skin conditions since the earliest days of human civilization.[14] The assessment of extracts was conducted in vitro using the HaCaT cell line, and the viability of cells was determined through the MTT assay. The experiment established the linearity range by evaluating the experiment's linearity range and determined the seeding density of cells from the growth curve.[33]

Antibacterial Activity

The plant has historically served as a crucial reservoir of medicinal compounds, prompting extensive screenings to identify therapeutic agents. Hence, imperative assess the anti-microbial efficacy of *Leucas aspera*. This study was employed of the disk diffusion method to assess the antibacterial efficacy of various components of *Leucas aspera*. The selected microorganisms for investigation included Gram(+) microbes such as Staphylococcus aureus and Gram(-) microbes such as Escherichia coli, Pseudomonas Aeruginosa, Salmonella Typhimurium, Salmonella Choleraesuis, and Shigella Flexneri. These bacterias for study was based on their significance as important pathogens and their rapid development of antibiotic resistance, a phenomenon observed in response to increasing antibiotic usage. In this research, the average zone of inhibition resulting from the use of the commercially available antibiotic, chloramphenicol, exceeded the sizes observed with all methanol extracts. The observed phenomenon could be attributed to the crude form of the plant extracts, which inherently possess lower concentrations of bioactive compounds. Generally, in categorizing antimicrobial activity, a higher number of substances are anticipated the efficient in opposition to Gram (+) bacteria contrasted to Gram (-) bacteria. Nevertheless, in this investigation, the plant extracted from the roots, stems, and flowers demonstrated efficacy against both Gram (+) and Gram (-) microbes. The ability to act opposing each other types of microbes are suggest the existence a broad spectrum of antibiotic combinations or potentially overall metabolous toxins.[11]

The antibacterial properties of *Leucas aspera* extend to Staphylococcus epidermidis, Bacillus subtilis, Bacillus megaterium, Klebsiella pneumoniae, Pseudomonas aeruginosa, Vibrio cholera, and Shigella dysentriae. Upon evaluation of the plant's antibacterial efficacy against these pathogens, it is evident that Gram-positive bacteria exhibit higher sensitivity compared to Gram-negative bacteria. The ethanol extracts obtained from the plant showed an impressive antibacterial effectiveness of 80% against both Staphylococcus aureus and Bacillus subtilis. Furthermore, these extracts displayed significant activity against Escherichia coli, Pseudomonas aeruginosa, and Shigella dysenteriae.[48]

Table 4: Example of bacteria.

Gram (-) bacteria	Escherichia Coli
	Pseudomonas Aeruginosa
	Salmonella Paratyphi
	Salmonellac Dysenteriae
	Shigella Dysenteriaes
	Shigella Sonnei
	Staphylococcus Aureus
	Vibrio Choleraes
Gram (+) bacteria	Bacillus Aspera
	Bacillus Megaterium
	Bacillus Subtilis

The activity 0f anti-Bacterial all three extract are assessed usually the disc methods diffusion against eleven pathogenic bacteria, comprising four Gram-positive and seven Gram (-) strain. In the analysis, clear zones with diameters exceeding 15mm were categorized as highly susceptible, those ranging from 8 to 15mm were deemed moderately susceptible, and less than 8mm were considered as resistant. The investigated pathogens exhibited a moderate susceptibility to the ME extract, showcasing a range of 8 to 15mm for the of inhibition. The most significant activity was observed against P. aeruginosa, with area of inhibition measuring 15mm. The anti-bacterials potential are EA extract of evident, showing zone activity against all bacteria except E. coli and V. cholera. The most notable activity was observed against S. dysenteriae, exhibiting a zone of inhibition measuring 15mm.[38]

Larvicidal Activity

The larvicidal efficacy of plant leaf crude methanolic decoctions was assessed against Quinquefasciatus Culex, Aedes Aegypti, and Anopheles Stephensi. These assessments were conducted on the phases of the fourth instar. One isolated plant ingredient is called catechin, exhibited significant Larvicidal activity even at a less concentration. The larvicidal impact of methanolic flower decoctions on Anopheles subpictus was evident, with LC50 as well as LC90 value recorded at 53.16 ± 3.64 and 233.18 ± 25.68 ppm, respectively. Hexane decoctions displayed highly effective larvicidals properties againsts these vector when compar to ethanolic and chloroform decoctions.[18]

$$\text{Corrected mortality} = \frac{\text{Percentage of mortality in treatment} - \text{percentage of mortality in control}}{100 - \%\ \text{mortality in control}} \times 100$$ [4]

The toxicity of *Leucas aspera* was evaluated in the present study against four different Aedes aegypti and Culex quinquefasciatus larval stages. After recording the data, statistical calculations were conducted to determine the LC50, 95% confidence limit, LC99, and Chi-square values. The LC50 values for *Leucas aspera* against first, second, third, and fourth instar larvae of Culex quinquefasciatus were determined to be 122.50, 149.97, 193.43, and 230.71 ppm. Correspondingly,

For Aedes aegypties, the LC50 values were 77.40, 144.00, 199.72, and 257.17 ppm, Corresponding. No mortalities were observed in the control group, and Tween-80 did not induce any adverse effects. The greatest larvicidal activities are show with the significant death pace, Specifically throughout the Transmuting procedure or the following stages of darkening and tan. Murugas and Jayabalans recorded that a 4 percent focus of leaf excerpt from *Leucas aspera* resulted in a larval mortality rate of 90% in opposition to 4th initial stage larvicidal of Anopheles stephensi. Sakthivadivel and Daniel noted that the fossil fuels ethers extract derived from *Leucas aspera* exhibited an LC50 value ranging between hundred to two hundred ppm in opposition to the larvae of Culex Quinquefasciatused, Anopheles stephensi, and Aedes aegypti. The results from the present study confirm the potent larvicidal properties of *Leucas aspera*.[49] The evaluation was conducted using the World Health Organization method with minor adjustments. Twenty-five larvaes from each instar (1st, 2nd, 3rd, and 4th) are placed in a Five hundred millilitre glass jar including Two hundred forty-nine millilitres of removed the chlorination from water and 1.0 millilitre of the mentioned focus of the plant extracts. Four replicates were simultaneously performed for each concentration. The dying and survival rates were noted twenty-four hours subsequent to the being exposed time frame Moribund and departed larvae from the four replicates were combined and expressed as a percentage to represent larval mortalited at each focus. departed larvae were recognized as those displaying no motion when examined with a needle in the cervical region. Moribund larvae were also known as those not able to attain the surface within a sensible moment the typical plunging reaction when the water was uneasy.[49]

Central Nervous System Activity

According to previous scientific findings, the root of *Leucas aspera* has demonstrated properties that act as central nervous system depressants. For this reason, the current research aimed to explore the central nervous system are depressant effects the Methane excerpts obtained from the leaf of *Leucas aspera* (MELA) using mice models. Nevertheless, additional investigations are required to assess the potential application of these

findings in treating diseases associated with central nervous system depression.[50] In this research, *Leucas aspera* exhibited a notable reduction in open field and whole cross test locomotor activities, along with a significant extension in the length of time spent motionless observed in testing for tail suspension and force swimming. In the sleeping time test produced by thiopental sodium, the Methane extract from the leaf of *Leucas aspera* shown a noteworthy induction of sleep at the initial stage, accompanied by a prolonged duration of sleeping time. The findings of the study lead to the concluded the methanol leaf extracts of *Leucas aspera* possesses central nervous system depressant activity.[8]

Antivenomous activity

The Methane extracts of *Leucas aspera* was chosen for a thorough investigation, which involved purifying, isolating, and characterizing the active compound responsible for its antagonistic effect in opposition to cobra poison. This compound demonstrated substantial antivenom activity.[14] Traditional medicinal practices often involve the use of crude plant extracts for treating various ailments, including snakebite envenomations. In this current investigation, we assessed the effectiveness of the methanolic extract derived from *Leucas aspera*, a herbal plant commonly employed as an antidote in various rural communities.The goal of this research was to evaluate the effectiveness the methanol extracts of *Leucas aspera* in preventing venom-induced inhibition of caseinolytic activity. Snake venom proteases primarily affect blood clotting and cause widespread bleeding. It is believed that plant extracts can inhibit these proteases due to the chelating properties of their phenolic components. Previous research has shown that phenolic compounds can form hydrogen bonds and effectively bind to histidine residues found in the Zn2+ binding motifs of metalloproteases, thereby reducing their ability to degrade molecules. This suggests that plant extracts may contained compound capable of bind to differencing metallic ion, which are essential for enzyme-based actions. These hydrolytic activity are metalloproteases relies on the proper coordination of metal ions, and any metabolite capable of diminishing the interaction between the protease-metal ions will lead to the inhibition of proteolytic activity.[51]

Cytotoxic Activity

The cytotoxic effect of *Leucas aspera* root were looked into using the brine shrimp lethal assay. Additionally, the whole parts of plant showed cytotoxic effects in Swiss Albino mice with Dalton's Ascitic Lymphoma as observed in vitro through MTT and Trypan blue assays. Compared to other extracts, the 80% ethanolic extract from the root demonstrated higher cytotoxic effect in the brina shrimps nauplii biological assay. The LC50 worth for this extract are determined to be 52.8 micrograms /millilitres. The crude methanolic extract from the leaves of the Indian plant exhibited cytotoxic activity in the brina shrimps deadly biological assay with an LC50 value of 30 micrograms /millilitres, while vincristine sulfate had an LC50 value of 10.44 micrograms /millilitres.[48] The cytotoxic effect of plants is primarily given credit the presence of secondary metabolite, such as Alkaloids, Glycosides, Steroids, Tannins, Phlobatannin, Terpenoid, and Flavonoids, in their extracts.[52] After a 24-hour period, the LC50 Worth for the *Leucas aspera* extract was determined to be (181.68±2.15) µg/mL, with a 95% confidence interval. The decrease and higher limits were recorded as 125.12 µg/mL and 265.96 micrograms /millilitres, correspondingly. When comparing this result to the standard vincristine sulfate, which had a lethality value of (0.76±0.04) µg/mL, the *Leucas aspera* extracted exhibited in terms of statistics noteworthy lethality. This suggests that the extract has significant clinical importance in addressing issues related to tumor cells, pesticides, and similar concerns. The brina shrimps assays is commonly used as a easy to use tool for the initial evaluation of harmfulness, identification of fungal toxin, evaluation of insecticidal and antitumor effects, and other pharmacologically effect.[12] Recent studies have shown that the ethyl acetate extract obtained from the entire *Leucas aspera* plant possesses larvicidal, pupicidal, and cytotoxic effects on the HeLa cell line.[53][54] Moreover, the LC50 worth of the extract was discovered to be below 1000 micrograms /millilitres, which is the recognized threshold for identifying cytotoxicity. This highlights the significant relevance of the extract in relation to the aforementioned objectives. Additionally, the extract's "Chi square" value, measuring at 0.76, rejects the null hypothesis and thus enhances the statistical significance of the results. This helps to eliminate any inconsistencies between the expected and observed mortality rates of newly hatched Artemia salina. These findings align with previous research conducted on the alcoholic root extract of *Leucas aspera*.[12] The brines shrimp lethality biological assay was usually to identify cytotoxicity compound, usually the zoological organism Artemia salina for convenient monitoring. The brine shrimp egg was hatching in synthetic seawater for 48 hours, allowing the development of mature shrimp known as nauplii. The cytotoxic evaluation was executed on the brine shrimp nauplii following a specific method. Vincristine sulfates was used as the positive control. The fully developed nauplii were introduced into each of the experimental vials, as well as the control vial. After a 24-hour period, the vials were examined using a magnifying glass, and the count of surviving nauplii every one vial was recorded.

Percentage of brine shrimps mortality for each focused attention was determined usually a specific formula:

$$\text{Percentage of Mortality} = N1/ N0 \times 100$$

Where, Nt = No. of kill nauplii after twenty-four hours of incubation,

N0 = No.of overall nauplii transferred[55]

Antinociceptive Activity

The methanolic extract derived from the entire *Leucas aspera* plant exhibited superior anti-nociceptive effects in the test for stomach pain caused by acetic acid. Even so, at a minimal dosage of 50 milligram per kilogram body weight, the extracts resulted in a 50.1% reduction in the number of writhing, a level of efficacy that was roughly comparable to that of aspirin.[9] The assessment of the extract involved in a mice model with acetic acid-induced writhing. The test animals were chosen at random allocated into four division, each comprising 8 individuals. Control group one received a 1% volume per volume solution of Tween-eight in water, while collective two, serving as the collective favorable standard, received Diclofenac sodium at a dose of 25 milligram per kilogram. Test groups three and four were administered the extract at dose of 250 and 500 milligram per kilogram, correspondingly. For thirty minutes, the extracts, standard medication, and control vehicle were all taken orally before the injection of acetic acid (0.7%). After a 15-minute interval, the count number of writhing was conducted over a 5-minute duration.[27]

Antimicrobial Activity

The methanolic extract, fractions, alkaloid remnants, and expressed flowers juices of *Leucas aspera* exhibited noteworthy antibacterial activity. Notably, the alkaloidal residue demonstrated the greatest antibacterial effect in comparison to the methane extract and methanol fraction.[6] The evaluation of antimicrobial efficacy is conducted through the agar well diffusion method targeting wound pathogens. The microorganisms were evenly distributed on Muller Hinton agar, and wells were created using a cork borer.[56] Current researchers are highly focused on discovering antimicrobial agents from various origins to counteract microbial resistance. Antimicrobial susceptibility testing finds broad utility in drug exploration, epidemiological studies, and forecasting therapeutic results. Numerous researchers have investigated and deliberated upon the antimicrobial attributes of *Leucas aspera*. Their findings indicate that the antimicrobial action of *Leucas aspera* involves a mechanism where in it induces the formation of pores in bacterial membranes, leading to the subsequent leakage of cellular contents. That are proposed that the bactericidal impact of *Leucas aspera* is attributed to the detergent like characteristics of its phenols and flavonoids. They suggested that the damage to bacterial membranes occurs depending on one's focus and amount of time. The phytochemical analysis revealed that ethanol extraction is more effective in extracting active components from the plant compared to water, enhancing the antimicrobial activity. claimed that *Leucas aspera* petroleum ether extract was more efficient. Biofilm is formed when bacterial communities create a self-generated matrix of extracellular polymeric substances (EPS). This development of biofilm. 15 in challenging environments serves as a survival strategy for bacteria and fungi, enabling them to adapt to their surroundings. Managing biofilm infections clinically poses challenges due to the inherent tolerance and resistance of microbes within biofilms to antibiotics and immune responses. The extracts from *Leucas aspera*, specifically methanol and ethyl acetate extracts, have been observed to inhibit the formation of biofilm by Streptococcus pyogenes.[3]

The extract's antimicrobial efficacy was assessed using the disk diffusion technique.[57] Microorganisms were collected from the broth culture using an inoculating loop and then transferred to test tubes containing 5.0 millilitre of pure distilled water. Inoculum were added until reaching a turbidity equivalent to 0.5 McFarland standards. The suspension in the test tube was then spread on the surface of a Muller Hinton agar plate usually a cotton fabric swab, and the plate was left to dried. What man paper disks with a diameter of 6 mm, which had been sterilized, were soaked with a specified concentration of an ethanol extract solution using a micropipette. Subsequently, the treated disks were air dried under aseptic conditions and positioned at equal distances in a circular arrangement on the inoculated plate. The extract concentration was 2 milligram per disk. The plates were incubated for a duration of 4-6 hours at a minimal temperature, allowing the test substances to diffuse from the discs into the encompassing medium during this period. This process was replicated for both ethanol and tetracycline. The experiment was carried out in triplicate. The plates were placed in an incubator at 37 °C for 24 hours. Following this period, the inhibition zone produced by the plant extract against each microorganism was measured. The analysis involved utilizing one-way Analysis of variance, followed by Tukey's post hoc test for several analogies, employing descriptive statistics in Statistical package for social science 18.0.[12]

Antipyretic Activity

The anti-pyretic activities of ethanolic extracts from *Leucas aspera* and Glycosmis pentaphylla were investigated in rats employing the Brewer yeast induce pyrexia prototype. The antipyretical effect was most prominent throughout the 6-hour test period in the collective executed with the *Leucas aspera* excerpt (at a dosage of 200mg/kg) and the standard paracetamol group. This effect is likely attributed to the suppressive of prostaglandin amalgamation in the hypothalamus.[29] Antipyretics are medications employed to reduce elevated body temperature. Their targeted impact on body temperature is a result of their influence on the heat regulating nervous mechanism in the hypothalamic center. Primarily, these drugs are utilized to alleviate neuralgic pain, headaches, and overall discomfort. The anti-pyretic possible of the 50% watery extracted of *Leucas Aspera* was examined using an experimentally induced pyrexia model in rats. The protocol outlined by Gopalakrishnan et al. (1980) was adhered to. Eighteen healthy albino rats, irrespective of gender, with an average weight of approximately 100 grams, were

chosen and categorized into three groups, each consisting of 6 animals. In Group one, a 0.5% CMC suspension was executed at a dose of 1 millilitre /100 milligram, serving as the solvent control. In Group two, the test sample received the aqueous extract at a dose of 1000 mg/kg body weight, while in Group Three, the standard drug, paracetamol, was administered at a dose of 500 mg/kg body weight. All drugs were administered intraperitoneally.[58]

BIOCOMPOUNDS OF *LEUCAS ASPERA*

The initial chemical analysis of *Leucas aspera* indicated the existence of triterpenoids throughout the entire plant. Oleanolic acid, ursolic acid, and 3-sitosterol have been identified in the entire plant. The aerial parts of the plant are documented to contain nicotine, along with two novel alkaloids (compound A with a melting point of 61-2°C, α-sitosterol, and β-sitosterol) (with a melting point of 183-4°C). Reducing sugars, specifically (galactose) ,glucoside (melting point 230-1°C) in *Leucas aspera*. The plant also contains diterpenes, including leucasperones A and B, leucasperols A and B, and isopimarane glycosides (leucasperosides A, B, C). In the leaf volatiles, u-farnesene (26.4%), x-thujene (12.6%), and menthol (11.3%) were identified as the predominant constituents among the 25 compounds. Analysis of the flower revealed ten compounds with amyl propionate (15.2%) as well as isoamyl propionate.[54]

The seed is documented to possess palmitic acid (6.25%), stearic acid (2.84%), oleic acid (42.07%), linoleic acid (48.11%), and linolenic acid (0.65%). The unsaponifiable fraction contained 3-sitosterol and ceryl alcohol. The shoot comprised novel phenolic compounds, including 4-(24-hydroxy-1-oxo-5-n-propyltetracosanyl)-phenol, aliphatic ketols like 28-hydroxypentatriacontan-7-one and 7-hydroxydotriacontan-2-one, long-chain compounds such as 1-hydroxytetratriacontan-4-one, 32-methyltetratriacontan-8-ol, aswellas nonatriacontane, 5-acetoxytriacontane, β-sitosterol, and dotriacontanol. Leucolactone (I), derived from the root of *Leucas aspera*, has been identified as 3,3,16c-dihydroxyoleanan28-1,3-olide.[16]

Table 5: Therapeutic Activities of *Leucas aspera.*

Sr. No.	Bioactive Compounds	Activities	Secondary Metabolites	Reference
1.	Terpenes and Terpenoid compounds	Anticancerous, Anti-inflammatory, Antimicrobial, Anxiolytic and Bronchodilator activity	Oleanolic acid, Ursolic acid, Squalene, □-Caryophyllene,α-humulene,α-pinene, epia-α-bisabolol, Limonene, Terpinen -four-ol, X-thujene, Menthol, Leucasperone A, Band C	[48]
2.	Sterols and Fatty compounds	Cardiovascular activity, inflammatory activity	3-sitosterol,9,12,15-Octadecatrienoic acid methyl ester, Linoleic acid, n-Hexadecanoic acid, Oleic acid, stearic acid, Ceryl alcohol, Dotriacontanol	[14]
3.	Glycoside compound	Anti-inflammatory,Antioxidant and Antimicrobial effect	Linifolioside, Glucoside, Leucasperosides A, Leucasperoside B, Leucasperoside C.	[48]
4.	Flavonoid compound	Antioxidant, Anti-inflammatory, Antiviral, and Anticancer	Apigenin, Chrysoeriol, Acacetin, Catechin, Luteolin, Quercetin	[48]
5.	Lignane compound	Antioxidant and Anti-inflammatory	Nectandrin B, *meso*-Dihydroguaiaretic acid, Macelignan, (-)-Chicanine, Licarin A,*erythro*-2-(4-aallyl-2,6-dihydroguaiarectic-1-(4-hydroxy-3-methoxyphenyl)propan-1-ol, Myristargenol B, Machilin.	[47]

MEDICINAL IMPORTANCE OF *LEUCAS ASPERA*

A significant portion in global number of people relies conventional medicine derived from medicine plants to meet their medical care requirements.[9] The local application of the juice extracted from the leaf of *Leucas aspera* is usually in skin condition and persistent skin eruptions. Additionally, in rural areas, the leaves of *Leucas aspera* serve as both an insecticide and a mosquito repellent. The complete plant is utilized as an insecticide and is recommended in conventional medical care for conditions such as coughing, colds, unpleasant edema, and persistent skin eruptions. *Leucas aspera* is employed in the treatment of inflammatory and allergic conditions. *Leucas aspera* flowers, when combined with honey, are administered to alleviate coughs and colds in children. Furthermore, the leaves of the *Leucas aspera* are used applied to bites from snakes, poisonous insects, and scorpion stings. The plant has healing of wounds properties and is usually to treat poisoned by cobra

venom. The extract of the plant is used with honey to treat stomach discomfort and aid with digestion.[59][60]

Analysis of Dynamic Trajectories Against COVID-19 Spike Protein

Approximately 20 significant bioactive compounds found in *Leucas aspera* were exposed to the CDOCKER procedure, utilizing the CHARMM based algorithm. This process led to the successful generation of 17 phytoconstituents with proper conformations within the chemical space of the binding site of the spike protein domain. This enhanced affinity was attributed to the molecule fully penetrating the cavity within the space of both the spike protein domain and the response protein. This has the potential to inhibit the formation of protein-protein complexes. The molecule achieved a noteworthy configuration within the chemical space of the spike protein binding site, facilitated by conventional hydrogen bonds. Six additional phytoconstituents exhibited improved interactions within the binding site of the spike protein, with binding energies ranging from -33.945 kcal/mol to -30.498 kcal/mol.[61]

FUTURE PROSPECTIVE

Traditional medicine often relies on crude plant extracts for treating various diseases, with the methanolic extract of *Leucas aspera*. This herbal plant is widely acknowledged and utilized as an antidote in numerous rural communities. *Leucas aspera* is a usual field weed that are usually a quick remedy of poisoning. This Compound are derived from the extract of *Leucas aspera* exhibit phytotoxic properties, making them valuable as natural herbicides. The ongoing exploration of medicinal plants for drug discovery continues to yield novel and significant lead compounds targeting various pharmacological objectives, including cancer. The application of computational and molecular modeling studies can utilize these phytochemicals for the design and discovery of novel drugs targeting specific objectives. Examining the chemical composition of the plant may unveil unique compounds with possible used in the pharmaceutical industry, cosmetics or various industries. The review on pharmacological activities in this study can guide researchers in exploring the plant's potential to a greater extent. Testing its application in various diseases and evaluating its toxicity is essential. Therefore, establishing clinical trials as a standard is crucial for ensuring the safe therapeutic use of this species. *Leucas aspera* serves as a rich a source of substances that are bioactive with pharmacological and therapeutic significance, exerting diverse physiological and pharmacological effects; Consequently, exploring new therapeutic applications for this drug is encouraged. Future directions will involve conducting pharmacological studies utilizing animal models and isolated bioactive compounds to further understand its potential. Biotechnological progress may present opportunities for genetically modifying or enhancing *Leucas aspera* for distinct objectives, such as amplifying its medicinal efficacy or adapting it to various climates. Sustained investigation into this plant is crucial for revealing further significant, necessary, and undiscovered advantages. Special attention is given to mosquito vector-borne diseases like dengue, malaria, chikungunya, zika, and yellow fever. The majority of the phytoconstituents present in *Leucas aspera* exhibited higher activity against COVID-19 compared to HCQ and Remdesivir.

CONCLUSION

The exploration of the efficacy of bioactive compounds from *Leucas aspera* has unveiled a rich reservoir of potential applications in various fields, including medicine, agriculture, and nutrition. The comprehensive analysis of the current development in research has shed light on the diverse pharmacological activities exhibited by these compounds, ranging from anti-inflammatory and antioxidant properties to antimicrobial and anticancer effects. The multifaceted nature of *Leucas aspera* bioactive compounds opens up avenues for their utilization in the development of novel pharmaceuticals, nutraceuticals, and agrochemicals. The continuous advancements in technology and research methodologies have enabled a deeper understanding of the mechanisms underlying the bioactivity of these compounds. This knowledge serves as a foundation for further investigations, allowing researchers to optimize extraction processes, identify specific bioactive molecules, and explore synergistic interactions. Moreover, the potential synergies between bioactive compounds from *Leucas aspera* and existing therapeutic agents present opportunities for the development of combination therapies with enhanced efficacy and reduced side effects. Looking ahead, the prospects of *Leucas aspera* bioactive compounds appear promising. Continued research efforts should focus on elucidating the molecular pathways involved in their therapeutic effects, conducting clinical trials to validate their safety and efficacy, and optimizing cultivation practices to ensure a sustainable and reliable supply. Collaborations between researchers, pharmaceutical industries, and agricultural stakeholders will be pivotal in translating scientific discoveries into practical applications, ultimately benefiting human health, agriculture, and environmental sustainability. The journey from understanding the bioactivity of *Leucas aspera* compounds to their widespread application holds immense potential for addressing contemporary challenges and improving the overall well-being of society.

REFERNCES

1. C. B. Rao, “Reproductive ecology of leucas aspera (wild) link (Lamiaceae),” August, 2014; 5674: 1332–1338.
2. A. Kurian, H. Van Doan, W. Tapingkae, and P. Elumalai, “Fish and Shellfish Immunology Modulation of mucosal parameters, innate immunity, growth and resistance against Streptococcus agalactiae by enrichment of Nile

tilapia (Oreochromis niloticus) diet with Leucas aspera," December 2019; 97: 165–172.
3. K. Agnes Nirmala and M. Kanchana, "Leucas aspera – A Review of its Biological activity," *Syst. Rev. Pharm.*, 2018; 9(1): 41–44, doi: 10.5530/srp.2018.1.8.
4. C. Xu, "Trends in phytochemical research," *J. Food Biochem.*, 2019; 43(6). doi: 10.1111/jfbc.12913.
5. K. Ilango, S. Ramya, and G. Gopinath, "Antibacterial Activity of Leucas Aspera Spreng," March 2008; 6(2007): 526–530.
6. R. Srinivasan, B. Ravali, P. Suvarchala, A. Honey, A. Tejaswini, and P. Neeraja, "Leucas aspera - Medicinal plant: A review," *Int. J. Pharma Bio Sci.*, 2011; 2(2): 153–159.
7. Mani prakash, "Therapeutic potentiality assessment of Leucas aspera as an effective phyotochemical, neuro-pharmacological, anti-helminthic, analgesic and selective lethal agent Academia ," *J. Pharm. Pharmacol.*, February, 2018; 6(2): 024–031, doi: 10.15413/ajpp.2017.0112.
8. S. Hiremath, Pradeep, and A. Jeerankalagi, "Leucas aspera Spreng (Dronapushpi): A Review," *J. Ayurvedic Herb. Med.*, 2022; 8(1): 48–54, doi: 10.31254/jahm.2022.8111.
9. S. Kundu *et al.*, "An Update on the Medicinal uses, Phytochemistry and Pharmacology of Leucas Aspera, A Medicinally Important Species," *Int. J. Agric. Innov. Res.*, 2018; 6(4): 2319–1473, [Online]. Available: https://www.researchgate.net/publication/322644223
10. N. Products, "SHORT REPORTS LONG-CHAIN COMPOUNDS I-Docriacontanol," 1992; 31(5): 1809–1810.
11. A. L. Chew, J. James, A. Jessica, and S. Sasidharan, "Antioxidant and antibacterial activity of different parts of Leucas aspera," *Asian Pac. J. Trop. Biomed.*, 2012; 2(3): 176–180, doi: 10.1016/S2221-1691(12)60037-9.
12. A. Rahman and S. Islam, "antibacterial and cytotoxic effects of the phytochemicals of whole Leucas aspera extract A ntioxidant ," *Asian Pac. J. Trop. Biomed.*, 2013; 3(4): 273–279, doi: 10.1016/S2221-1691(13)60062-3.
13. U. Sharma, S. Bhadauria, and N. Pathak, "A REVIEW ON MEDICINAL VALUES OF LEUCAS ASPERA (L.)," 2023. [Online]. Available: www.wjpls.org
14. A. M. Krupanidhi, A. Ali, K.; Amulya, S. A. Siddaika, and A. Kalal, "A Comprehensive Review on: The Efficacy of Biocompounds of Leucas Aspera," *Austin Biomol Open Access*, 2022; 4(1): 1–5, [Online]. Available: www.austinpublishinggroup.com
15. H. S. Chouhan and S. K. Singh, "A review of plants of genus Leucas," *J. Pharmacogn. Phyther.*, 2011; 3(2): 13–26.
16. M. Prajapati, J. Patel, K. Modi, and M. Shah, "Leucas aspera: A review," *Pharmacogn. Rev.*, 2010; 4(7): 85–87, doi: 10.4103/0973-7847.65330.
17. V. K. Enjamoori, A. Nampalli, B. Vasudha, K. Gangarapu, and N. Boggula, "A Review on Leucas aspera for Phytopharmacological Studies," *INNOSC Theranostics Pharmacol. Sci.*, 2018; 2(1): 3–7, doi: 10.26689/itps.v2i1.436.
18. S. Choudhury, P. Ghosh, T. Sarkar, S. Poddar, and A. Sarkar, "Morphological Features , Phytochemical , and Pharmacological Study of Leucas aspera (Lamiaceae): A Brief Review," 2020; 1–6, doi: 10.25258/phyto.12.3.2.
19. D. P. Chemica, "Hepatoprotection by Leucas Aspera," 2010; 2(5): 458–462.
20. S. Manonmani, R. Madhavan, P. Shanmugapriya, V. Manjari, S. Murugesan, and V. Banumathi, "INTERNATIONAL JOURNAL OF CURRENT RESEARCH IN BIOLOGY AND MEDICINE A Review of beneficial effects of Siddha medicinal herbs on Snake bite," 2016; 1: 27–35, doi: 10.22192/ijcrbm.
21. C. Venkatesan *et al.*, "Human & Experimental Toxicology," 2014, doi: 10.1177/0960327113494901.
22. G. C. Madhu, J. Kannaiyan, B. Paulraj, and V. Veeramani, "RESEARCH ARTICLE CODEN (USA): IJPSPP Anti-diabetic, Anti-cancer Activity and Associated Toxicity of Leucas aspera Extract in Wistar Albino Rats," 2019; 11(6): 387–392, doi: 10.25004/IJPSDR.2019.110617.
23. I. Diabetic and W. Albino, "Induced Diabetic Wistar Albino Rats," 2019; 9: 105–110.
24. D. Hyperlipidemia, "Antihyperlipidemic Activity of Leaf,"2016; 3: 408–413.
25. M. S. Latha, "Chemopreventive Potential of Methanolic Extract of Leucas aspera Against N-Nitrosodiethyl Amine (NDEA) Induced Hepatotoxicity in Rats," no. January 2013, 2015.
26. R. Ramani, B. M. Boddupalli, S. Kandati, N. Anisetti, N. Malothu, and R. R. Proddoku, "I S S N 2278 – 4357 ANTIPARKINSON ' S STUDIES OF ETHANOLIC EXTRACT OF LEUCAS ASPERA IN MICE," 2015; 3(6): 1226–1235.
27. M. S. Rahman, S. K. Sadhu, and C. M. Hasan, "Preliminary antinociceptive, antioxidant and cytotoxic activities of Leucas aspera root," 2007; 78: 552–555, doi: 10.1016/j.fitote.2006.06.018.
28. R. Ramu, "Evaluation of anticancer activity of ethanol extract of Leucas aspera flower," no. October, 2020; 1–9.
29. S. K. Jha, "Journal of Chemical and Pharmaceutical Research," January 2011, 2015.
30. K. R. A. J. Kiran, "WHOLE PLANT ON BLOOD GLUCOSE LEVELS OF STREPTOZOTOCIN-INDUCED DIABETIC RATS," 2013; 5: 5–7.
31. T. J. Hasmukhlal, S. D. Das, P. C. Amrutlal, and J. G. Kantilal, "Evaluation of antimutagenic potential of Lagenaria siceraria , Desmodium gangeticum and Leucas aspera," 2016; 2(3): 56–60, doi: 10.5530/PTB.2016.2.9.
32. A. I. Journal, "Natural Products," 2010; 6(1).
33. S. K. Singh, H. S. Chouhan, A. N. Sahu, and G.

Narayan, "Assessment of in vitro antipsoriatic activity of selected Indian medicinal plants," 2015; 53(9): 1295–1301, doi: 10.3109/13880209.2014.976713.
34. D. Bharathi, L. Subbiah, P. Thangavelu, and S. Palanisamy, "Assessment of anti-psoriatic activity of ethanolic extract of Justicia tranquebariensis Linn . on amelioration of IMQ-induced hyperkeratosis in Balb / C mice," 2020; 10(12): 83–89, doi: 10.7324/JAPS.2020.101211.
35. P. Review, "protective effect of L eucas aspera in various experimental ulcer models U lcer," 2014; 4(1), doi: 10.1016/S2222-1808(14)60477-1.
36. J. L. Rios and A. Villaw, "Paper SCREENING METHODS FOR NATURAL PRODUCTS WITH ANTIMICROBIAL ACTIVITY: A REVIEW OF THE LITERATURE," 1988; 23: 127–149.
37. G. Sabri and Y. Vimala, "Antibacterial and antioxidant activity of leucas aspera flowers from Bihar, India," *Asian J. Pharm. Clin. Res.*, 2018; 11(2): 223–226, doi: 10.22159/ajpcr.2018.v11i2.21976.
38. "In vitro studies on antibacterial, antifungal, and cytotoxic properties of Leucas aspera Biology and Medicine," 2012; 4(4): 183–187.
39. A. Muthumanickkam, S. Subramanian, S. Dharani, Y. A. H. H. Sudhan, S. Karthick, and K. R. Rajgowdam, "Development of Mosquito Repellent Cotton Fabric using Leucas aspera and Ocimum americanum," 2018; 3(7): 145–148.
40. D. Elumalai, M. Hemavathi, P. Hemalatha, C. V. Deepaa, and P. K. Kaleena, "Larvicidal activity of catechin isolated from Leucas aspera against Aedes aegypti, Anopheles stephensi, and Culex quinquefasciatus (Diptera : Culicidae)," 2015, doi: 10.1007/s00436-015-4856-6.
41. M. A. Olszewska, "IN VITRO ANTIOXIDANT ACTIVITY AND TOTAL PHENOLIC CONTENT OF THE INFLORESCENCES, LEAVES AND FRUITS OF SORBUS TORMINALIS (L.) CRANTZ," 2011; 68(6): 945–953.
42. G. Manikandan and S. D. Noel, "Antioxidant Activity and Phytochemical Analysis of Methanolic Leaf Extract of Leucas aspera (Wild) Link .," 2019; 9: 320–325.
43. V. N. Kalpana and V. D. Rajeswari, "Phytochemical and Pharmacological investigation of an indigenous medicinal plant Leucas aspera," 2016; 9(8): 399–407.
44. A. Borah, R. Narayan, S. Yadav, and B. G. Unni, "Research Article ANTIOXIDANT AND FREE RADICAL SCAVENGING ACTIVITY OF," 2011; 9(2): 46–49.
45. B. S. Archive, "EVALUATION OF ANTI ULCER ACTIVITY OF HYDROALCOHOLIC LEAVES," 2021; 7–13.
46. M. Suruthi, S. Sivabalakrishnan, G. Yuvasri, R. Ragunathan, and J. Johney, "ANTIOXIDANT ANTICANCER ACTIVITY OF Leucas aspera PLANT EXTRACT AND ITS DNA DAMAGE STUDY ON He-La CELL LINES," *Life Sci. Informatics Publ.*, 2016; 1(7): 1–9, [Online]. Available: www.rjlbpcs.com
47. G. V. Kumar and N. Devanna, "An update of Leucas aspera – a medicinal plant," *Int. J. Sci. Res. Methodol.*, 2016; 5(1): 485–503.
48. L. Leucas, R. Priya, M. Nirmala, T. Shankar, and A. Malarvizhi, "Leucas aspera," 2018; 19–35.
49. L. Aedes, "Larvicidal activity of Leucas aspera (Willd.) against the larvae of Culex Larvicidal activity of Leucas aspera (Willd .) against the larvae of," May, 2014.
50. R. Reza, A. Mannan, S. Hosen, and M. N. Parvin, "Neuropharmacological Profile of Methanolic Extract of Leucas aspera Leaves in Swiss Albino Mice," 2018; 1–8, doi: 10.15226/2374-6866/5/4/00186.
51. K. Gopi, K. Renu, and G. Jayaraman, "Inhibition of Naja naja venom enzymes by the methanolic extract of Leucas aspera and its chemical profile by GC – MS," *Toxicol. Reports*, 2014; 1: 667–673, doi: 10.1016/j.toxrep.2014.08.012.
52. B. Özçelik, M. Kartal, and I. Orhan, "Cytotoxicity , antiviral and antimicrobial activities of alkaloids , flavonoids , and phenolic acids," December 2009; 49: 396–402, 2011, doi: 10.3109/13880209.2010.519390.
53. C. Kamaraj *et al.*, "Antimalarial activities of medicinal plants traditionally used in the villages of Dharmapuri regions of South India," *J. Ethnopharmacol.*, 2012; 141(3): 796–802, doi: 10.1016/j.jep.2012.03.003.
54. K. Kovendan, K. Murugan, S. Vincent, and D. R. Barnard, "Studies on larvicidal and pupicidal activity of Leucas aspera Willd. (Lamiaceae) and bacterial insecticide, Bacillus sphaericus, against malarial vector, Anopheles stephensi Liston. (Diptera : Culicidae)," 2012; 195–203, doi: 10.1007/s00436-011-2469-2.
55. S. Ali, M. A. Sayeed, M. Nabi, and A. A. Rahman, "In vitro Antioxidant and Cytotoxic Activities of Methanol Extract of Leucas aspera Leaves," 2004; 2(1): 8–13.
56. K. Mangathayaru, J. Lakshmikant, N. Shyam Sundar, R. Swapna, X. F. Grace, and J. Vasantha, "Antimicrobial activity of Leucas aspera flowers," *Fitoterapia*, 2005; 76(7–8): 752–754, doi: 10.1016/j.fitote.2005.08.009.
57. "M07: Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically, 11th Edition".
58. R. Srinivasan, G. Lakshmana, D. Rajesh Kumar, B. Anjaneyulu, K. Shaleem Raju, and D. A. Kumar, "Analgesic, antipyretic, antimicrobial activity of whole Leucas aspera ethanolic extract," *Pharmanest*, 2014; 5(2): 1980–1986.
59. L. Pharmacy and M. Bharti, "Leucas aspera a perfect poor man remedy," 2017; 6(1): 275–277.
60. S. K. U. Deshmukh, "Use of Aromatic Plant Leucas aspera in Cosmetic Industry," 2020; 7(2): 341–347.

61. I. Navabshan, B. Sakthivel, R. Pandiyan, and M. Gover, "Computational Lock and Key and Dynamic Trajectory Analysis of Natural Biophors Against COVID‐19 Spike Protein to Identify Effective Lead Molecules," *Mol. Biotechnol.*, 2021; 0123456789, doi: 10.1007/s12033-021-00358-z.