



(REVIEW ARTICLE)



Leucas zeylanica is a Bangladeshi plant with significant medicinal prospect: A review

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Abstract

Leucas zeylanica is one of the most precious gifts of nature to the entire civilization. It offers folkloric system a dependable option to heal numerous diseases like- burning urination, toothaches, common skin diseases, gout, inflammatory conditions, rheumatic diseases, abdominal pain, worms, anorexia, colic, flatulence, etc. Many of these ancient practices have got their scientific resemblances like- using as an agent for treating common pains, oxidative stresses, microbial infections, sleep disorders, inflammations, gout associated pains, thrombosis and sunlight related skin damages. Some researchers also isolated a huge bunch of vital phytochemicals like- torosaflavone A, drymariatin C, daidzein, luteolin 3',4'-dimethyl ether, apigenin, tricrin, chrysoeriol, linarigenin, β -sitosterol, stigmasterol, hexadecanoic acid, octadecanoic acid, 9,12,15- octadecatrienoic acid, farnesene, β -caryophyllene, caryophyllene oxide, phytol, β -cubebene, α -selinene, α -tocopherol etc. from different crude extracts of *Leucas zeylanica*. Making proper correlation between these phytoconstituents with the general utilizations of this plant will assist scientists to develop auspicious lead compounds. This review covers a summary of ethnomedicinal, phytochemical and biological studies of several crude preparations of *Leucas zeylanica*.

Keywords: *Leucas zeylanica*; Folkloric system; Phytoconstituents; Pharmacological activities; Lead compounds

1. Introduction

Nature provides humankind with an enormous and trustworthy source of medicinal plants that are comparatively safe and efficacious in many diseases in their usual forms or need to be chemically modified [1-3]. Before the advancement of medical sciences, plant parts were the only hope to get healed from a diseased condition. Researchers always attempt to verify and rationalize traditional practices of natural substances in scientific ways to develop new pharmaceuticals [4, 5]. Along with exploration of scientific rationale of traditional uses, unwanted and noxious substances are also marked in a herbal preparation [6]. Phytochemicals identified in a plant extract show scientists an optimistic path to develop novel lead compounds of medicinal importance [7]. The procedures of treatment with herbal products have been experiencing notable modifications that enable them to become stronger and more potent than earlier in human health management [8-11].

L. zeylanica, commonly recognized as Ceylon Slitwort, is an important species of the renowned genus *Leucas* that contains 80 species [12]. Usually these plants are highly distributed in East Africa and Asia including- India, Bangladesh, Nepal, Sri Lanka, Myanmar and China. *L. zeylanica* belongs to the well-known plant family- Lamiaceae and is an erect type annual herb with a height up to 50 cm [13]. Usually, it grows on dry and sunny areas like- sea beach, waste sites, paddy fields and, roadsides.

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2. Traditional Uses

Drug scientists are highly grateful to the traditional practitioners since they are continuously guiding to the probable sources of new medicines. *L. zeylanica* is one of the utmost popular plants of ethnomedicinal importance [14-16]. Generally, it is utilized as a reliable treatment choice for common skin diseases, burning urination, toothaches, gout, inflammatory conditions, rheumatic diseases, thrombus like conditions, abdominal pain, worms, cold, anorexia, colic, flatulence, malaria and abdominal skin tightening after delivery [17-19].

Different parts like- leaf, root and whole plant of *L. zeylanica* are reported to be utilized in different diseased conditions. Whole plants are chosen in headache, cold, scabies, and skin diseases [20]. Juice extracted from leaves is assumed to be helpful in snakebite [21]. Decoction of *L. zeylanica* leaves with seeds of *Nigella* or turmeric juice and rice is applied on nose ulcers as a lotion like preparation [22]. In India, leaf is used in jaundice, fever, and snake and scorpion bites [23]. Moreover, leaf paste is taken orally by Marma community in Bangladesh to treat burning urination [24]. Interestingly, a necklet type ornament made up of *L. zeylanica* roots is worn on legs and arms in Bangladesh with a belief to get healed from fever related convulsion [25].

A number of abovementioned local uses of *L. zeylanica* have already been verified while others are needed to be justified.

3. Phytochemical Properties

Leucas is the name of a genus of enormous potential phytoconstituents. Most probably, the first exploration on phytoconstituents of this genus started in 1947 [26]. Till now, a huge bunch of chemicals have been informed in this genus. Like other species, *L. zeylanica* is also a potential basis of many pharmaceutically important phytoconstituents. Some research groups found positive results for alkaloids, glycosides, tannins, flavonoids, carbohydrates, and steroids with conventional phytochemical screening procedures [27-30].

Analysis of dichloromethane whole plant extract of *L. zeylanica* with GC-MS identified fatty acids (9, 12, -octadecadienoic acid, hexadecanoic acid, octadecanoic acid, 9,12,5- octadecatrienoic acid), sesquiterpenes (farnesene, β -caryophyllene, caryophyllene oxide), phytol, neophytadiene, β -cubebene, α -selinene and, α -tocopherol [31]. GC-MS analysis of n-hexane extract (whole plants) reported caryophyllene oxide, (3, 7, 11, 15)-tetramethyl-2-hexadecen-1-ol, neophytadiene, hexadecanoic acid, octadecanoic acid, phytol, 4,8,12,16-tetramethylheptadecan-4-olide, stigmaterol, β -sitosterol and, α -tocopherol [31].

An investigation on *L. zeylanica* methanol extract (aerial parts) isolated three important chemicals- 12-O- β -D-glucopyranosyl-11, 16-dihydroxyabieta-8, 11, 13-triene, 12, 19-O- β -D-diglucoopyranosyl-11, 16-dihydroxyabieta-8, 11, 13-triene and, 19-O- β -D-carboxyglucopyranosyl-12-O- β -D-glucopyranosyl-11,16-dihydroxyabieta-8,11,13-triene [32].

Another work on ethanolic stem extract also reported three major components in *L. zeylanica*, namely- (-)-epiloliolide, leucriterpencoside and, (E)-4-((1S, 3R, 4R)-1-hydroxy-4,5,5-trimethyl-7-oxabicyclo [4.1.0] heptan-1-yl) but-1-en-3-one [33].

Moreover, GC-MS analysis of essential oil collected from *L. zeylanica* seeds confirmed a couple of components- oleic acid, hexadecanoic acid, 1-octene-3-ol, caryophyllene and, 2,4,6-trimethyl-1,3,6-heptatriene [34].

A recent study on ethanol extract of *L. zeylanica* (whole plants) explored a total of 30 compounds, with a completely new isomer of norditerpenoid [35]. Among all components, flavonoids and terpenoids were the major ones. The reported components include- three flavonoid glycosides (torosaflavone A, apigenin-7-O-(6''-E-p-coumaroyl)- β -D-glucopyranoside and, drymariatin C), six flavonoids (daidzein, luteolin 3',4'-dimethyl ether, apigenin, triclin, chrysoeriol and, linarigenin), two phytosterols (β -sitosterol and, stigmaterol), two phenylpropanoids (ethyl caffate and, evofolin B), two phthalate esters (dibutylphthalate and, dibutylterephthalate), two phenolic compounds (tyrosol and, catechol), five terpenoids (dehydrovomifoliol, cucumegastigmanes I, loliolide, isololiolide and, 4-hydroxyphthalide), one aliphatic glycoside (ethyl -D-galactopyranoside), one nucleobase (uracil), one amino acid (L-phenylalanine), two alkaloids (aurantiamide acetate and, 1H-indole-3-carbaldehyde), one cytochalasin (cytochalasin H) and, two norditerpenoids (6 β -Acetoxy-9 α ,13-epoxy-16-norlabd-13E-en-15-al and, unnamed new compound: C₂₁H₃₂O₄) [35].

4. Pharmacological Potential of *L. zeylanica*

4.1. Analgesic potential

Whole plant of *L. zeylanica* had been established to possess noteworthy analgesic properties [36]. A researcher group used methanolic extract and a number of soluble fractions to evaluate its efficacy in pain management. A well-known method (acetic acid induced writhing) was followed to settle the analgesic potential in peripheral area of mice [37]. Where the standard drug (Diclofenac sodium, 50 mg/kg) reported 66.67% inhibition, crude extract of methanol, soluble fraction of petroleum ether, chloroform and ethyl acetate ensured a dose dependent inhibition of 17.67-32.00% and 22.00-40.00% at 100 and 200 mg/kg dose, respectively [36]. Central pathway related pain management potential of *L. zeylanica* was also confirmed by following an established method where pain sensation in tail portion of mice was applied by a source of non-stop heat [38]. The highest activity was noticed at 60 min of administration of the test materials. They certified a quantity dependent elongation of tail flicking time of 5.53-17.40% (at 100 mg/kg) and 14.15-25.53% (at 200 mg/kg), where the standard drug (Morphine, 2 mg/kg) showed 82.28% elongation [36].

Peripheral pathway related pain controlling potential in mice was also reported by another research team [39]. They administered ethanolic extract of *L. zeylanica* plant at 250 and 500 mg/kg dose with Diclofenac as standard at 25 mg/kg. The test models yielded an inhibition of 54.8-65.6% ($p < 0.001$) where Diclofenac exhibited 55.2% inhibition of writhing [39].

4.2. Anti-oxidative potential

Leaves of *L. zeylanica* (extract of 100% methanol) had proven its significant potential against oxidative injury caused by hydrogen peroxide and ethanol in liver tissue of rats [40]. An established technique was followed to observe the variation of levels of common liver enzymes [41]. The extract reported a noteworthy reduction of alanine aminotransferase (~ 13-15%) and aspartate aminotransferase (~ 8-10%). This study also estimated two antioxidant phytoconstituents- flavonoids and polyphenols content as 15.69 ± 2.2 $\mu\text{g QE/mg}$ and 74.32 ± 4.6 $\mu\text{g of PE/mg}$ of extract, respectively by using previously defined procedures [40].

In another study, extract of methanol and different fractionates of *L. zeylanica* whole plants demonstrated significant antioxidative potential against a destructive free radical, DPPH (2,2-diphenyl-1-picrylhydrazyl [36, 42]. Crude extract, soluble fraction of petroleum ether, chloroform and ethyl acetate reported promising IC_{50} value of 28.46, 84.75, 97.09, and 65.61 $\mu\text{g/ml}$, respectively, where the result for standard drug (butylated hydroxytoluene) was 19.61 $\mu\text{g/ml}$ [36].

A hopeful outcome supporting the antioxidative property of *L. zeylanica* was also described where ascorbic acid was the standard treatment [39, 43]. Crude extract of ethanol and the standard agent (butylated hydroxytoluene) displayed an IC_{50} value of 62.9 and 14.9 $\mu\text{g/ml}$, respectively [39].

4.3. Anti-microbial potential

Globally, several studies had been conducted by following the well-established disc diffusion techniques with or without slight modifications to confirm the anti-microbial effect of *L. zeylanica* [44-47]. Abdullah *et al.* explored that the methanolic leaf extract (70 $\mu\text{g}/\mu\text{L}$ per well) gave a clear zone of 10.6 and 14.8 mm for *E. coli* and *S. aureus*, respectively. Here, Gentamicin formed 15.0 (*E. coli*) and 16.4 mm (*S. aureus*) clear zone [48]. Another study pronounced that ethanolic extract (600 $\mu\text{g}/\text{disc}$) of *L. zeylanica* yielded 10-21 mm inhibition zone against some bacteria [39]. This result reported *L. zeylanica* as possessing mild-moderate potential compared to the standard agent, Amikacin (30 $\mu\text{g}/\text{disc}$, 22-31 mm inhibition zone) [39].

Methanolic leaf extract (20 $\mu\text{g}/\mu\text{L}$ per well) was confirmed to have antifungal potential against *penicillium sp.*, *Trichophyton mentagrophytes*, *Candida albicans* and *Aspergillus flavus* producing 4.0-10.0 mm inhibition zone where Clotrimazole (20 $\mu\text{g}/\text{disc}$) created 9.0-10.5 mm clear zone [15].

Although the antimicrobial potential was well established by some studies, two research teams found insignificant or negligible activities of whole plants of *L. zeylanica* [31, 36].

4.4. Sedative-hypnotic potential

L. zeylanica showed its possible medicinal importance regarding neuropharmacological potential [39]. A research conducted by following previously recognized actions revealed that ethanol extract had substantial sedative-hypnotic potential [39, 49, 50]. 250 and 500 mg/kg dose confirmed sleeping in tested mice after 42.6 and 37.2 min of application

of the extract, respectively which could be measured as moderate action in comparison to the standard agent, Sodium phenobarbitone (25.8 min, 25 mg/kg dose) [39]. Tested preparations also ensured good sleeping time of 48.4 and 21.0 min at 250 and 500 mg/kg dose, respectively where the standard treatment presented a total sleeping period of 58.6 min [39].

4.5. Anti-inflammatory potential

Dichloromethane whole plant extract of *L. zeylanica* disclosed its anti-inflammatory potential by hindering the effect of 5-LO (5-lipoxygenase) and mPGES-1 (microsomal prostaglandin E₂ synthase-1) in a study undergoing some renowned procedures [31, 51-53]. The extract inhibited the activity of 5-LO in isolated human cells (neutrophils) with 5.5 µg/ml IC₅₀ value which was noteworthy compared to that of the reference control (Zileuton), 0.13 µg/ml (equivalent to 0.55 µM). This potential was rechecked by using the test preparations on recombinant 5-LO. In this case, Zileuton and the extract displayed an IC₅₀ value of 0.11 and 2.2 µg/ml, respectively [31]. Formation of PGE₂ (prostaglandin E₂), a pro-inflammatory substance, can be stopped by inhibiting mPGES-1 [54]. In a part of the aforementioned study, *L. zeylanica* presented its mPGES-1 blocking potential with 0.4 µg/ml IC₅₀ value where the reference inhibitor (MK-886) yielded an IC₅₀ value of 2.2 µM [31].

Table 1 Pharmacological potentials of *L. zeylanica*

Reported Pharmacological Effects	Type of Plant Samples	Preparations	Reference(s)
Analgesic activity (peripheral)	Whole plants	Methanol extract; soluble fraction of petroleum ether, chloroform and ethyl acetate	36
	Whole plants	Ethanol extract	39
Analgesic activity (central)	Whole plants	Methanol extract; soluble fraction of petroleum ether, chloroform and ethyl acetate	36
Antioxidative activity	Whole plants	Methanol extract; soluble fraction of petroleum ether, chloroform and ethyl acetate	36
	Whole plants	Ethanol extract	39
	Leaves	Methanol extract	40
Anti-microbial activity	Leaves	Methanol extract	15, 48
	Whole plants	Ethanol extract	39
Sedative-hypnotic activity	Whole plants	Ethanol extract	39
Anti-inflammatory activity	Whole plants	Dichloromethane extract	31
Anti-gout activity	Whole plants	Dichloromethane extract	31
Thrombolytic activity	Leaves	Ethanol extract	56
Photoprotective activity	Leaves	Methanol extract	58

4.6. Anti-gout potential

Dichloromethane extract of *L. zeylanica* whole plants unveiled its inhibitory potential against a major causative enzyme of gout, XO (xanthine oxidase) in a research work conducted by a formerly established method [31, 55]. IC₅₀ values for the extract and standard application (Allopurinol) were 47.5 and 16.8 µg/ml, respectively which specified moderate type anti-gout property of *L. zeylanica* [31].

4.7. Thrombolytic potential

For clot lysis, *L. zeylanica* leaf (extract of ethanol) had demonstrated its importance in an exploration led according to a previously established description [56, 57]. Where Streptokinase (standard) presented an ability of clot lysis in 85.77% cases, the experimental extract depicted that capability in 55.82% samples. This outcome established *L. zeylanica* as moderately effective in the lysis of thrombus [56].

4.8. Photoprotective potential

A study team explored sun protection potential of methanol extract of *L. zeylanica* leaf where Mansur equation was used to calculate SPF (sun protection factor) of the preparations [58, 59]. The crude extract displayed higher SPF value (39.8 ± 0.35) than that of two commercial sunscreen creams, SC1 (TiO₂+benzophenone-4, SPF 10.7 ± 0.07) and SC2 (*Aloe*+Sandlewood+*Ficus*, SPF 18.6 ± 0.01). Leaf extract of *Aloe vera* also reported less SPF value (28.86 ± 0.11) than the extract. All these outcomes strengthened the standing of *L. zeylanica* as a robust source of photoprotective agents [58].

5. Conclusion

Folkloric system always opens a new window for the discovery and establishment of new entities in existing therapeutic approaches. Usually, when an explorer team finds the authenticity of a traditional practice of any medicinal plant, it becomes more encouraged to isolate the phytochemicals responsible for that usage. This process results in new hopes for the patients resistant/less responsive to the current medicaments. For this reason, interest on natural plants are gradually increasing. *L. zeylanica* is a widely used plant in folkloric system. Some of its local practices have already been justified that confirm its enormous potential to manage pain, oxidative damage, microbial infections, inflammatory conditions, insomnia, anxiety, gout, blood clotting and UV (ultraviolet) rays related damages. A number of different carbohydrates, glycosides, flavonoids, steroids etc. have been traced in crude preparations of *L. zeylanica*. Proper linking of these substances with the reported pharmacological actions and local practices of *L. zeylanica* will draw a map to synthesize lead molecules. However, A substantial number of traditional uses are still to be verified and more advanced approaches are needed to recognize and isolate all the conceivable phytoconstituents of *L. zeylanica* for unveiling new grounds for the drug discoverers.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest.

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