

Exploring the Medicinal Potential of *Leucaena leucocephala*: A Phytochemical and Pharmacological Analysis

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Abstract

Leucaena leucocephala, a perennial leguminous tree native to southern Mexico and northern Central America, has garnered significant scientific interest due to its diverse ecological, industrial, and pharmacological applications. Thriving in dry and semi-arid regions, this thornless, upright shrub or small tree remains an underutilized yet valuable species. Various bioactive compounds, including alkaloids, cardiac glycosides, tannins, flavonoids, saponins, and glycosides, have been identified in different plant parts, contributing to its extensive medicinal potential. Despite its rich phytochemical profile and adaptability, *L. leucocephala* remains overlooked in many regions. Recent advances highlight its expanding role as a sustainable raw material in the pulp and paper industry, as well as in biodegradable packaging solutions. This review comprehensively examines the global distribution, taxonomy, phytochemical composition, and pharmacological activities of *L. leucocephala*, they mainly involves anti-diabetic, anti-diarrheal, anti-microbial anti-bacterial and so on emphasizing its potential for pharmaceutical and industrial applications.

Key words: *Leucaena leucocephala*, Phytochemicals, Pharmacological activity, Medicinal plants, Leguminous tree, Flavonoids, Tannins.

1. Introduction

Leucaena leucocephala (Fabaceae) is a small, rapidly growing tree that goes by several popular names, including Jumbay, White Popinac, White Lead tree, and Wild Tamarind [1]. Originating in Southern Mexico and Northern Central America, it has spread to more than 35 nations on every continent except Antarctica [2].

Leucaena, which refers to the whitish blossoms, is derived from the Greek words "leuc" which means "white" and "caen" which means "new". The species name *leucocephala*, which combines the words "leu," which means white, and "cephala," which means "head," also alludes to the flowers. Because of its widespread popularity as a long-lived and incredibly nutrient-dense forage tree that can be utilized to create firewood, timber, human food, green manure, shade, and erosion control, *L. leucocephala* was dubbed a miracle tree. Globally, it is thought to encompass 2–5 million hectares [3-5].

Antimicrobial, anthelmintic, antibacterial, anti-proliferative and antidiabetic, anticancer, cancer preventive, diuretic, anti-inflammatory, and antioxidant properties have all been utilized in medicine. Its antitumor, antihistaminic, nematocide, pesticide, anti-androgenic, hypocholesterolemic, and hepatoprotective qualities have also been utilized [6]. It grows into dense thickets and spreads throughout the cleared regions as a shrub or small tree up to 10 m in height [7]. *Leucaena* species are evergreen, tiny trees or shrubs that can withstand dryness and have a profusion of flowers. Certain species of *Leucaena*, referred to as the Salvadorian type, can reach heights of up to 20 meters. Many regions of the world view those species as weeds[8]. *Leucaena* leaves resemble tamarind leaves in appearance, with long, flattened pods and white flowers with a hint of yellow. Dark brown seeds have a firm, glossy seed coat. Its heartwood is light reddish-brown, while its sapwood is pale yellow. Younger branches have smooth, grey-brown or salmon pink bark, while older branches have rougher, deeper grey-brown bark with deep red inner bark and shallow, rusty orange-brown vertical cracks [9].

2. Taxonomical classification

Kingdom	Plantae
Subkingdom	Tracheobionta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Rosidae
Order	Fabales
Family	Fabaceae-Pea family
Genus	<i>Leucaena</i> Benth-lead tree
Species	<i>Leucaena leucocephala</i>

3. Other names[10]

Common name	Countries
Kubabul, or subabul	India
Leucaena	Australia, United States
Lamtoro	Indonesia
Ipil ipil	Philippines
Katin	Thailand
Yin ho huan	China
Koa haole	Hawaii
Tangantangan	Some Pacific islands
Cassis	Vanuatu

4. Botanical description

The compound pinnate leaves of *L. leucocephala* have a pinnular rachis that is 5–10.2 cm long overall. They are bipinnate, with 6–8 pairs of pinnae that bear 9–20 pairs of leaflets. The leaves are linear-lanceolate, 8–15 mm long, 2–4.5 mm wide, slightly asymmetric, acute at the tip, linear-oblong to weakly elliptic, and glabrous except for the base of the margins, which are rounded to obtuse. The leaves of *L. leucocephala* fold up when it's hot, cold or dry [11].

Numerous blooms are produced, and the paired inflorescences of the axillary globose head have a diameter of 12 to 20 mm and a peduncle length of 2 to 3 cm. Each legume contains 15–20 hard, shiny, brown seeds that are flat and teardrop shaped. The axillaries are on long stalks that are white in color and have dense global heads that measure 1-2 cm across. The fruit pod has a raised border and is thin and flat. When it matures, it becomes dark brown and hard. It is 10–15 cm long and 1.6 2.5 cm wide. It is dehiscent at both sutures. This species has $2n = 104$ chromosomes, making it polyploidy [12-16].

Fig. 1. *Leucaena leucocephala* plant and parts



Pods are linear-oblong in shape, rounded at the apex, flat, 8 to 18 seeded, mid-to orange-brown, glabrous and faintly glossy in white silky hairs, papery, and open along both borders. They are 11 to 19 cm long, 15 to 21 mm wide, and 5 to 20 per each flower head. The hard, dark brown seeds have a hard, glossy testa that is transversely oriented in the pod and is 6.7 mm to 9.6 mm in length and 4 mm to 6.3 mm in width. The fruits start to grow in large quantities the first year. Small (8 mm long), glossy, teardrop-shaped, flat, and dark brown, the seeds have a thin but somewhat resilient seed coat. A kilogram of seeds contains roughly 17,000 to 21,000 seeds.

In pastures, ruminants, non-ruminants, wind, and legumes are the seed dispersers. While still on the tree, legumes have the ability to discharge their seeds. The seeds can travel a certain distance when carried by the wind. Legumes can be consumed by both ruminants and non-ruminants, which can then spread the seeds through their feces [17-18].

L. leucocephala's flowering phenology differs greatly between cultivars and depending on where they are grown. On the other hand, it can bloom throughout the year [16]. Within four to six months of seed germination, *L. leucocephala* begins to bloom. The blossoming season is typically twice a year or seasonal. They appear on young branches that are actively growing and have spherical, white flower heads that are 2 to 2.5 cm in diameter, with 100 to 180 blooms per head and 2 to 6 in leaf axils each group.

The flowers, which are carried on stalks 2 to 3 cm long at the ends or edges of twigs, can be white or pale cream-white in color [8-19].

5. Chemical Composition and Nutritional value

According to the nutritional composition analysis, *leucaena* seeds have the potential to be a source of both protein and energy. The seeds have an estimated metabolizable energy of 2573.26 kcal/kg and a protein content of 31.1%. 1.39% lysine, 0.36% methionine, 0.35% cystine, 2.62% arginine, 4.63% glutamic acid, 0.87% threonine, 1.38% glycine, 1.11% alanine, 1.11% valine, 0.93% isoleucine, 1.81% leucine, and 0.71% methionine + cystine were the amino acid profiles of *leucaena* seeds. The antinutritional factors (ANFs) were 697.50 mg/100g of phytate and 0.75% tannin [20].

The primary chemical components of the leaves of *L. leucocephala* were 3,7,11-Tridecatrienitrile, 4,8,12-trimethyl (25.64%), squalene (41.02%), phytol (33.80%), and 3,7,11,15-Tetramethyl-2-hexadecen-1-ol (30.86%). On the other hand, the primary chemical components of the leaf extracts of the same species from Mexico were pentadecanoic acid-14-methyl-methyl ester, 1,6-trimethyl-2-pentadecanone a ketone, and 2,6-benzofuranone-5,6,7,7a tetrahydro-4,4,7a-trimethyl [21].

Among the chemical components of Chinese whole plants of *L. leucocephala* were ficaprenol-11 (polyprenol), methyl-132-hydroxy-(132-S), squalene, lupeol, sitostenone, trans-coumaric acid, cis-coumaric acid, pheophytin-a, and pheophorbide a methyl ester. -pheophorbide-b coupled with aristophyll-C [22]. For many centuries, *L. leucocephala* was considered a high-potential fodder. Its high β -carotene content makes it as nutritious as or better than alfalfa (*Medicago sativa*) [23]. The most popular uses for *L. leucocephala* leaves are as feed for pigs and chickens and as a pellet for freshwater fish. *L. leucocephala* had a dry matter digestibility (DMD) of 57.7% and a crude protein content of 29.5% [24]. The composition of *L. leucocephala* leaves was 9.73% ash, 22.76% crude protein, 22.29% crude fiber, 4.60% fat, and 6.70% moisture [25]. For plants that were two and four years old, respectively, the highest percentages of minerals (12.5% and 14.0%) and crude protein (33.0% and 30.9%) were found in the leaves, the highest percentages of crude fiber (31.5 and 37%) and calcium (1.9% and 2.1%) were found in the twigs, and the highest percentages of crude fat (7.2% and 10.1%) and nitrogen-free extract (55.9% and 58.8%) were found in the dry seeds [26].

6. Phytochemical studies

The phytochemical screening of leaf extract of *L. leucocephala* revealed the presence of various secondary metabolites as alkaloid, cardiac glycosides, tannins, flavonoids, saponins and Glycosides [27]. Bioactivity studies on this plant revealed its anthelmintic, antibacterial, anti-proliferative and antidiabetic activities [28]. The *L. leucocephala* leaves possess many biological properties such as antimicrobial, anticancer, cancer preventive, diuretic, anti-inflammatory, antioxidant; antitumor, antihistaminic, nematicide, pesticide, antiandrogenic, hypocholesterolemic and hepatoprotective [29].

Table 1: Phytochemical compounds identified from the *L. leucocephala* leaf extracts and their therapeutic Activity [29].

Sl. no	Compound	Secondary metabolite	Therapeutic activity
1	Phytol	Diterpene	Antimicrobial, anticancer, cancer preventive, diuretic, anti-inflammatory
2	Squalene	Triterpene	Antibacterial, antioxidant, antitumor; cancer-Preventive, chemopreventive; immunostimulant, lipoxygenase-inhibitor, perfumery, pesticide, sunscreen
3	n-Hexadecanoic acid	Palmitic acid	Antioxidant, hypocholesterolemic nematicide, pesticide, antiandrogenic, flavor, hemolytic, 5-alpha reductase inhibitor

4	Hexadecanoic acid, 15-methyl-, methyl ester	Fatty acid ester	Antioxidant, nematocide, pesticide, flavor, antiandrogenic
5	Pentadecanoic acid, 14-methyl-, methyl ester	Palmitic acid methyl ester	Antioxidant.
6	9,12,15-Octadecatrienoic acid, methyl ester	Linolenic acid ester	Anti-inflammatory, insectifuge hypocholesterolemic, cancer preventive, nematocide, hepatoprotective, insectifuge, antihistaminic, antieczemic, antiacne, 5-alpha-reductase inhibitor, antiandrogenic, antiarthritic, anti-coronary
7	Oxalic acid, allyl hexadecyl ester	Dicarboxylic acid	Acaricide, antiseptic, CNS-paralytic, fatal, hemostatic, irritant, pesticide, renotoxic, varroacide.

7. Pharmacological activities

7.1 Antidiabetic activity

L. leucocephala has been reported to possess medicinal properties that control stomach diseases, facilitate abortion and provide contraception, and it is often used as an alternative, complementary treatment for diabetes

Antidiabetic activity testing was carried out by giving *L. leucocephala* seed extract at an oral dose of 250 mg/kg body weight to streptozotocin-induced diabetic rats daily for 6 wk. The results revealed that *L. leucocephala* seed extract significantly ($p < 0.05$) reduced the fasting blood glucose and the blood chemistry consisting of: albumin, alkaline phosphatase (ALP) and total protein and red blood cells in the diabetic-treated rats compared to those in diabetic-untreated rats. *L. leucocephala* seed extract slightly increased the serum insulin level in the diabetic-treated rats [30].

Among the three extract concentration levels used, 50% level was found to be most effective in reducing blood glucose levels (BGL) in the experimental animals, while the pure extract (100% concentration) was the least effective. Thus, it is clear that *Leucaena leucocephala* Linn has anti-diabetic potentials which are comparable to the commercial anti-hyperglycemic drug Metformin [31].

7.2 Anti-diarrheal

L. leucocephala seed of the ethanol extract decreased the onset of diarrhea, frequency of diarrhea, consistency, and weight of stool and duration of diarrhea in rats after induced by castor oil.

The *L. leucocephala* groups that received doses of 200 and 400 mg/kg BW decreased the duration of diarrhea, however there was no discernible difference between them and the loperamide group. *L. leucocephala* seed ethanol extract exhibits activity that decreased stool weight by altering stool consistency at a dose-dependent manner. The activity of 400 mg/kg BW in the dosage group was similar to that of loperamide [32].

7.3 Anti-microbial

Condensed Tannins showed inhibition against *S. epidermidis* which means that Condensed Tannins can be one of the new potential compound to produce antibiotics for skin disease infection [33].

The lotion formulation with an emulsifying ingredient had high medicinal qualities, and the *L. leucocephala* seed oil extract demonstrated concentration-dependent efficacy against both Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*) and Gram-negative (*Pseudomonas aeruginosa*, *Escherichia coli*) bacteria [34].

7.4 Anti-inflammatory

In a rat model in vivo study, the rich n-butanol and ethyl acetate fractions demonstrated a novel anti-inflammatory activity; the plant fractions were highly effective and exhibited robust activity when compared to the NSAID diclofenac sodium and the positive control.

The abundance of secondary metabolic substances, including flavonoids, stilbene, and phenolic acids (rutin, resveratrol, quercetin, isorhamnetin, luteolin, caffeic acid, and coumaric acid), that were identified and characterized to be present in plant n-butanol and ethyl acetate fractions using TLC and HPLC chromatographic analysis made the N-butanol and ethyl acetate fractions extremely valuable [35].

Chloroform, ethyl acetate and methanol extracts of *L. leucocephala* leaves have demonstrated highly distinctive anti-inflammatory properties [36].

7.5 Antibacterial activity

Leucaena leucocephala has been utilized as a medicinal plant for a long time, according to practical experience. This shrub's leaves are put to the wound after being finely pulverized, crushed, or chewed.

S. aureus and *S. epidermidis* can be inhibited by *L. leucocephala* leaf extract ointment when it is made with extract concentrations of at least 20% and 25%, respectively.

The powdered leaves of *L. leucocephala* were macerated in 70% ethanol at a 10% concentration to create the extract. The study samples comprised seven ointment formulae with different concentrations of *L. leucocephala* leaf extract (LLE): F1 (0%), F2 (5%), F3 (10%), F4 (15%), F5 (20%), F6 (25%), and F7 (100%). The antibiotic's ability to suppress the growth of *S. aureus* and *S. epidermidis* in nutrient agar medium was assessed by measuring the diameter of the inhibition zone that resulted.

The results showed that *L. leucocephala* extract inhibited the growth of *S. aureus* and *S. epidermidis* when prepared at concentrations of at least 20% (F5) and 25% (F6), respectively [37].

7.6 Anthelmintic activity

Helminthic infections are chronic illnesses both in human beings and cattles. The petroleum ether extract shows maximum activity at all the tested concentration. Thus, the wormicidal activities of the plant extract against earthworms suggest that it can be effective against parasitic helminths of humans and animals [38].

At the measured concentrations, some *Leucaena leucocephala* leaf extracts exhibit strong *in-vitro* anti-worm action. At every measured concentration, the petroleum ether extract exhibits the highest level of activity. Therefore, the plant extract's wormicidal properties against earthworms imply that it may also be useful against parasitic helminths that affect both humans and animals.

Exposure of *C. elegans* to different concentrations of *L. leucocephala* extract and mimosine significantly decreased the head thrashing, egg-laying and mean pump amplitude of pharyngeal pumping activity [39].

7.7 Anti-cancer

Leucaena leucocephala's root was ethanolicly extracted to reveal the presence of a number of phytochemicals, including tannins, terpenoids, steroids, glycosides, flavonoids, quinones, phenol, and carbohydrates [40]. Compounds derived from the plant *Leucaena leucocephala* have been shown to have anti-cancer properties on human cell lines from stomach, colon, liver, tongue, lung, prostate, melanoma, and chronic myelogenous leukemia. Fourteen substances that belong to phenols, sterol, flavonoids,

coumarins, and triterpene derivatives have been identified based on the results from the chemical studies. Pheophorbide a methyl ester, pyropheophorbide, and pheophytin-a had IC₅₀ values of 2.6, 3.69, and 1.89 μ M in the AGS cell line, respectively [41].

7.8 Analgesic activity

Methanolic extract of *L.leucocephala* has given promising results in the management of nociception action. Tail immersion method performed in albino rats was found to be significant by the administration of methanolic extract of *L.leucocephala*. The standard drug used was diclofenac sodium, test dose (300mg/kg) has produced significant effect same as that of standard drug but during course of time the reaction time for tail withdrawal has gradually decreased.

The phytochemical constituents like terpenoids may contribute to the anti-nociceptive activity terpenoids inhibits both peripheral and centrally mediated analgesia [42].

7.9. Other Pharmacological activities

7.9.1 Anti – Lipidemic activity

The leaf extract of *Leucaena Leucocephala* exhibited a moderate hypolipidemic effect in diabetic induced rats and this can be attributed to the triterpenoids, which is the phytochemical constituent in this plant. Thus, it may be considered one of the major constituents causing hyperlipidemia [43].

7.9.2 Reproductive activity

The findings indicated that the poisonous substance in *L. leucocephala*, possibly mimosine, induced infertility in the rats by causing reduced food consumption; when food intake was sufficient for reproductive performance, the toxic material caused an increased incidence of foetal death and resorption [44].

7.9.3 Anti-Proliferative

The research shows that the ethanolic extract from *Leucaena leucocephala* (LL) has notable antioxidant, anti-proliferative and anti-migration capabilities against the human cervical cancer cell line, HeLa. The ethyl acetate fraction of *Leucaena leucocephala* had the highest total phenolic and flavonoid content, which was associated with the strong antioxidant activity reported - 319.289 ± 10.934 μ g GAE/mg extract (phenolics) and 399.572 ± 10.905 μ g QE/mg extract (flavonoids). Cell viability analysis showed that LL extract was effective in reducing the viability of HeLa cells in a dose-dependent manner (cytotoxic effects observed at 250–500 μ g/ml). The *Leucaena leucocephala* extract also effectively reduced the migration rate of HeLa cells suggesting potential cancer metastasis inhibition. Overall, these data suggest that *Leucaena leucocephala* may be used as a source of natural chemotherapeutic agents [45].

7.9.4 Effects on the Estrous cycle

The investigation of the effects of *Leucaena leucocephala* leaf extract suggests it may act as a natural phytoestrogen with notable results on the estrous cycle and uterine weight of ovariectomized rats. *Leucaena leucocephala* leaf extract not only increased uterine weights but also helped to modulate the estrous cycle implying that the extract may have the potential to restore the reproductive function of females experiencing estrogen deficiency. This can contribute to the proposed application of *Leucaena leucocephala* leaf extract as a less hazardous and economical alternative to synthetic hormone replacement therapy (HRT),

attributing decreased risks of cancers and cardiovascular risks associated to the chronic use of estrogens, as well as reduced costs and medical evaluations required for HRT [46].

8. Conclusion

Leucaena leucocephala is a highly versatile leguminous tree with significant ecological, pharmacological, and industrial applications. Despite its widespread adaptability to diverse climatic conditions, this species remains underutilized in many regions. The plant is a rich source of bioactive compounds, including alkaloids, flavonoids, saponins, tannins, and glycosides, which contribute to its broad pharmacological activities, such as antimicrobial, anticancer, antidiabetic, anti-inflammatory, and anthelmintic properties. Additionally, its high nutritional value and sustainable biomass production make it an important resource for animal feed, biofuel, and the pulp and paper industries.

Given its multifaceted applications, further research should focus on optimizing its cultivation, enhancing its medicinal utilization, and exploring innovative industrial applications. Advances in biotechnological interventions and sustainable harvesting practices could unlock its full potential, paving the way for its integration into modern pharmacological and agro-industrial sectors. Recognizing and promoting *L. leucocephala* as a valuable natural resource could contribute to environmental sustainability, economic development, and public health.

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CRediT authorship contribution statement

Rakesh S P conceptualized, investigated, collected data and wrote the original draft. Prakash Dabadi reviewed and edited the manuscript. A M Krupanidhi supervised the manuscript. All author reviewed and finalized the manuscript for submission.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

This is a review paper, all data in this paper are available from references used.

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