ABSTRACT

Leucaena leucocephala trees are commonly known as White Lead tree. It is native to Southern Mexico and Northern Central America and spread across many tropical and subtropical locations. It has multipurpose uses, such as generation of firewood, timber, greens, fodder, and green manure, as well as to provide shade and control soil erosion. It has been used for medicinal purposes because of possessing multiple pharmacological properties. Studies have shown the presence of various secondary metabolites such as alkaloid, cardiac glycosides, tannins, flavonoids, saponins, and glycosides in this species. In traditional medicine, it is used to control stomach ache and as contraception and abortifacient. In the present study, the global distribution, taxonomy, chemical composition, pharmacological activities, and potential uses of Leucaena leucocephala are discussed.

Keywords: Leucaena leucocephala, Medicinally, Multipurpose, Pharmacological activities, Traditional medicine

INTRODUCTION

Leucaena leucocephala (Family: Fabaceae) is a small, fast-growing tree, and has multiple common names by which it is known such as White Lead tree, White Popinac, Jambay, and Wild Tamarind [1]. It is native to Southern Mexico and Northern Central America and diffused in over 35 countries across all continents, except Antarctica (table 1) [2].

Table 1: The global distribution of Leucaena leucocephala [2]

| Region       | Countries                                                                 |
|--------------|---------------------------------------------------------------------------|
| Africa       | Angola, Burundi, Cape Verde Is, Cameroon, Chad, Djibouti, Egypt, Equatorial Guinea, Ethiopia, Ghana, Guinea, Guinea-Bissau, Ivory Coast, Kenya, Liberia, Malawi, Mali, Mozambique, Niger, Nigeria, Sao Tome and Principe, Senegal, Sierra Leone, Somalia, South Africa, Sudan, Tanzania, Togo, Uganda, Zaire and Zimbabwe |
| Asia         | Bhutan, Cambodia, India, Indonesia, Iraq, Iran, Laos, Malaysia, Pakistan, Philippines, Sri Lanka, Taiwan, Thailand, Vietnam and Japan |
| Australasia  | Australia, Papua New Guinea (New Guinea, New Britain and Bismarck Archipelago) |
| Caribbean    | Bahamas, Bermuda, Cayman Is, Cuba, Dominican Republic, Grenada, Haiti, Jamaica, Puerto Rico |
| Central America | Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, and Panama. |
| Europe       | Spain                                                                      |
| Indian Ocean | Aldabra, Chagos, Archipelago, Madagascar, Mauritius, Reunion Is. (Rodrigues Is., Seychelles, and Christmas Island. |
| Middle East  | Saudi Arabia and Yemen.                                                   |
| North America | United States in Arizona, Georgia, Virgin Islands, Texas, Florida and Hawaii |
| Pacific Ocean | Caroline outer islands (Fiji), Polynesia (Tahiti, Moorea).                   |
| South America | Argentina, Bolivia, Brazil, Chile, Colombia, Guyana, Peru, Venezuela         |

Leucaena originated from the Greek words “leuc,” which means “white,” and “caen,” which means “new,” referring to the whitish flowers. The species name also refers to the flowers: leucocephala from “leu,” meaning white, and “cephala,” meaning “head.” L. leucocephala was known as a miracle tree because of its worldwide success as a long-lived and highly nutritious forage tree used to produce firewood, timber, human food, green manure, shade and also to control erosion. It is estimated to cover 2-5 million ha worldwide [3-5].

Medicinally it has been used for its antimicrobial, antihelmintic, antibacterial, anti-proliferative and anti-diabetic, anticancer, cancer preventative, diuretic, anti-inflammatory, antioxidant; antitumor, antihistaminic, nematicide, pesticide, anti-androgenic, hypolipolemic, and hepatoprotective properties [6]. It spreads as a shrub or small tree growing up to 10 m in height throughout the cleared areas and forms dense thickets [7]. Leucaena species is an evergreen, drought-tolerant shrub or small tree, which grows abundantly. Some species of Leucaena can grow up to 20 m in height and those are known as the Salvadorian type. Those species are considered as weeds in many parts of the world [8]. Leucaena leaves appear similar to those of tamarind, having white flowers tinged with yellow, and having long flattened pods. Seeds are dark brown with the hard shining seed coat. It has hard heavy wood (about 800 kg/m), with a pale yellow sapwood and light reddish-brown heartwood. Bark on young branches is smooth and grey-brown, and rough with shallow, rusty orange-brown vertical fissures, and deep red inner bark [9].

Taxonomic classification

| Kingdom      | Plantae                   |
|--------------|---------------------------|
| Subkingdom   | Tracheobionta             |
| Superdivision| Spermatophyta             |
| Division     | Magnoliophyta             |
| Class        | Magnoliopsida             |
| Subclass     | Rosidae                   |
| Order        | Fabales                   |
| Family       | Fabaceae-Peа family       |
| Genus        | Leucaena                  |
| Species      | Leucaena benthamiifolium  |
beating the dried legumes in cloth bags. Sun-dried after harvest and then threshed to release seeds by changes their color to dark brown before dehiscence. The fruits are harvested and then disperse the seeds through their fecal matters, and the seeds can then be stored as un-scarified or scarified seeds. Unscarified seeds can be stored for more than one year under dry conditions. The harvested seeds of *L. leucocephala* should be decontaminated from larvae using fumigation by exposing the seeds to 32 g/m³ methyl bromide for 2 h at 27 °C. Although seeds can be sown directly after harvest without pre-sowing treatment, the seed germination, in that scenario becomes very low. Therefore, to increase the rate of germination, one of the pre-sowing treatments such as scarification, hot water treatment and/or sulfuric acid treatment should be used. Soaking *L. leucocephala* seeds in 100 °C water for 20 s and subsequently in water at room temperature for 48 h had the highest seed germination rate, higher cumulative germination (CGP) and seedling establishment. Soaking *L. leucocephala* seeds in hot water at 80 °C for 3–4 min followed by soaking in the water at room temperature for 12 h or soaking *L. leucocephala* seeds in concentrated sulfuric acid for 15–30 min are the best pre-sowing treatments that can be used to increase the seed germination of *L. leucocephala*. However, scarification is the most effective treatment that can be used as pre-sowing inoculation of seeds as it facilitates good field establishment of nitrogen-fixing rhizobium bacteria in soil devoid of rhizobia strains.

Germination percentage of *L. leucocephala* seeds are 50% to 98% for fresh seeds [8, 19]. The complete dormancy period for scarified seeds is 6 to 10 days after sowing and for unscarified seeds are 6 to 60 days after sowing [20]. The sowing of *L. leucocephala* seeds should be on or near the soil surface, but not any deeper than 2 cm. For growth in the nursery, the growth medium should be well drained, have proper nutrients and water holding capacity, and have a pH between 5.5 and 7.5 [16]. Light shade is recommended during the seedling development and full sun thereafter [16]. In young seedlings, taproot development is rapid and seedlings reach plantable size of 20 cm height in 2 to 3 mo [16, 22]. Weeding in plantations, until the seedlings outgrow competing grasses or herbaceous competitors in plant biomass, is recommended [16]. Direct seeding by planting container seedlings, bare root seedlings and stem cuttings of 2 to 5 cm in diameter can be used as a method of plantation development [23]. It grows moderately rapid but not as fast as the giant variety for which most of the data are available [24].

### Chemical composition and nutritive value

The chemical composition analysis of the leaves of *L. leucocephala* from Malaysia revealed the presence of 30 compounds: tetratetracontane, oxalic acid, allyl hexadecyl ester, squalene, Octacosane, hexatriacontane, 5-octadecene, 1-octadecyne, 3,7,11,15-tetramethyl-2-hexadec-1-ol, pentadecanoic acid, 14-methyl, methyl ester, 9,12-octadecadienoic acid, methyl ester, hexadecanoic acid, 15-methyl, methanethiol ester, 12,15-octadecadienonic acid, methyl ester and 3,7,11-tridecanetrienienitrile, 4,8,12-trimethyl, 2-dodecane, 7-hexadecene, 5-ecosenoic, 9,12,15-octadecatrienonic acid, methyl ester, 1-docosenoic, heptacosanoic acid, methyl ester, n-hexadecanoic acid, phytol and squalene [6]. The major chemical constituents of the leaves of *L. leucocephala* from Malaysia were Squalene (41.02%), Phytol (33.80%), 3, 7, 11,15-Tetramethyl-2-hexadec-1-ol (30.86%) and 3,7,11- Tridecanetrieni eni nitrile, 4,8,12-trimethyl (25.64%) [6], whereas the principal chemical constituents of the leaf extracts of the same species from Mexico were 2(R)-benzofuranone-5,6,7,7a-tetrahydro-4,4,7a-trimethyl, pentadecanoic acid-14-methyl ester, 12,15-octadecadienonic acid, methyl ester and 6,10,14-trimethyl-2-pentadecanone a ketone [25]. For whole plants of *L. leucocephala* from China the chemical composition were fcaprenol-11 (polyprenol), squalene, lupeol, sitostanol, trans-coumaric acid, cis-coumaric acid, pheophytin-a, pheophorbide a methyl ester, methyl-132-hydroxy-(132-S)-pherophorbide-b and aristophyll-C [26].

### Harvested fruits and germination requirements

*Leucaena leucocephala* fruits are harvested from branches when they change their color to dark brown before dehiscence. The fruits are sun-dried after harvest and then threshed to release seeds by beating the dried legumes in cloth bags [16]. *L. leucocephala* seeds can then be stored as un-scarified or scarified seeds. Unscarified seeds can be stored for more than one year under dry conditions at ambient temperature and up to 5 y when stored at 2 °C to 6 °C, dried. In contrast, scarified seeds can be stored for 6 mo to a year [16, 19, 20].

The harvested seeds of *L. leucocephala* should be decontaminated from larvae using fumigation by exposing the seeds to 32 g/m³ methyl bromide for 2 h at 27 °C. Although seeds can be sown directly after harvest without pre-sowing treatment, the seed germination, in that scenario becomes very low. Therefore, to increase the rate of germination, one of the pre-sowing treatments such as scarification, hot water treatment and/or sulfuric acid treatment should be used. Soaking *L. leucocephala* seeds in 100 °C water for 20 s and subsequently in water at room temperature for 48 h had the highest seed germination rate, higher cumulative germination (CGP) and shortened period of complete dormancy (CDP), when compared to the germination rate when seeds were soaked for only 24 h or untreated seeds [21].

Soaking *L. leucocephala* seeds in hot water at 80 °C for 3–4 min followed by soaking in the water at room temperature for 12 h or soaking *L. leucocephala* seeds in concentrated sulfuric acid for 15–30 min are the best pre-sowing treatments that can be used to increase the seed germination of *L. leucocephala*. However, scarification is the most effective treatment that can be used as pre-sowing inoculation of seeds as it facilitates good field establishment of nitrogen-fixing rhizobium bacteria in soil devoid of rhizobia strains [20].
and pigs and processed as a pellet for freshwater fish. The dry matter digestibility (DMD) of L. leucocephala was 57.7% and crude protein based on the dry matter was 29.5% [28].

Forage quality of L. leucocephala is higher than other Leucaena species such as L. pallida and L. diversifolia as stated by Castillo et al. [29]. Leaves of L. leucocephala contained 6.70% moisture, 22.76% crude protein, 22.29% crude fibre, 4.60% fat, and 9.73% ash content [30]. In another study by El-Baha [31], leaves were reported to contain the highest percentage of minerals (12.5% and 14.0%), pods the highest percentage of crude protein (33.0% and 30.9%), twigs contained the highest percentage of crude fiber (31.5% and 37%) and calcium (1.9% and 2.1%), and dry seeds possessed the highest percentage of crude fat (7.2% and 10.1%) and nitrogen free extract (55.9% and 58.8%) for the 2-4-years-old plants, respectively.

**Use of Leucaena leucocephala as ruminant feeds**

Forage containing 40% to 60% L. leucocephala leaves gave a maximum gain in weight in rabbits, goats, sheep, and cows. Rushkin [32] reported that "L. leucocephala is palatable forage, digestible and serves to increase milk output in both the humid and the monsoonal tropics for ruminants and non-ruminants. However, when L. leucocephala is fed at levels above 7.5% (dry mass) of the diet, non-ruminants lost weight and had general health problems due to the mimosine toxicity." When using L. leucocephala leaves in a rationed manner for fattening cattle, it is equivalent to cottonseed cake [33] and superior to groundnut cake [34]. In Queensland, Australia, a very high live weight gain was recorded using L. leucocephala leaves [32, 34-35] and the same is done as well in several other places [36].

Several reports showed that L. leucocephala could be a substitute for the imported protein supplements fed to dairy cows [32]. Dairy cattle produce well when fed with L. leucocephala [32, 37]. Henke and Morita [38] reported that dairy cows produce milk with higher fat content when they are fed with L. leucocephala compared to similar cows fed on pasture and concentrates or ammoniated straw in the grass-based diet. In Australia, Hawaii and Indonesia, annual milk production of 5,000 to 9,700 L/ha was recorded [32]. Feeding cows and buffaloes on L. leucocephala foliage at 10% of their diets produce higher milk yield by 20% than that of the control group [39]. Jones [40] reported that feeding dairy cows on L. leucocephala foliage increases milk fat and protein contents and also increases milk production by 14% on average. Feeding dairy cows on grazing Brachiaria decumbens with L. leucocephala produce higher milk yield than cows fed only with grass. However, the use of L. leucocephala for cattle feedings has problems, due to mimosine toxicity. Symptoms of mimosine toxicity include infertility, decreased weight gain, goiter, cataract in young animals, and loss of hair [41]. Cattle fed completely on L. leucocephala will not die but may lose some of their coarse hairs. However, newborn calves have shown signs of enlarged thyroids, which may result in death within a few days if their mothers have signs of toxicity [42]. In addition, thyroidine levels were accounted to be higher in the group (10-month age) fed on an L. leucocephala diet [32].

Feeding rabbits on fresh or dried L. leucocephala or leaf meal improve animal performance. The inclusion of 24% to 40% of fresh L. leucocephala leaves is recommended for growing or fattening rabbits [76-81]. L. leucocephala can replace concentrate alfalfa (Medicago sativa) in the diet of rabbits [82]. L. leucocephala is more palatable than Arachis pintoi. 25% of L. leucocephala leaf meal can be included in supplementing a diet with cassava peels and Gliricidia sepium and 30% to 40% with Arachis pintoi [83]. However, when more than 10% to 15% dried L. leucocephala was included in the diet and replaced with wheat bran resulted in a decrease in growth in rabbits. [84]. 20% to 25% of fresh L. leucocephala leaves in diet resulted up to 55% mortality of female and young rabbits [85-86].

For fish, a few studies have been used with L. leucocephala leaf meal as a protein source in fish feeds and the data obtained are conflicting. Hossain et al. [87] revealed improved growth responses of Clarias gariepinus (African catfish) on diets containing 30% L. leucocephala leaf meal. Sant et al. [88] found that the slow growth rate of C. macrocephala (Asian catfish) on diets in which 30% of the fish meal was replaced by L. leucocephala leaf meal.

**Leucaena leucocephala as human food**

Almost every part of the L. leucocephala species is consumed as human food since the era of the Mayans [6]. In Indonesia, Thailand, and Central America, people eat the young leaves, flowers, and young pods in soups [6]. In the Philippine Islands, the young pods are cooked as a vegetable and roasted seeds are used as a substitute for coffee. The young dry seeds are popped like popcorn [6]. In Indonesia, Thailand, Mexico and Central America people also eat the young leaves, flowers, and young pods as an ingredient for soups and salads. Seeds are being considered as non-conventional sources of protein, together with other leguminous seeds [6]. In addition, it is one of the medicinal plants used to control stomach ache, as contraception and abortifacient.

**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 [3].

Bioactivity studies on this plant revealed its anthelmintic, antibacterial, anti-proliferative and anti diabetic activities [8]. The L. leucocephala leaves possess many biological properties such as antimicrobial, anticancer, cancer preventive, diuretic, anti-inflammatory, antioxidant; antitumor, antithrombinic, nematocide, pesticide, antiandrogenic, hypocholesterolemic and hepatoprotective (table 2) [6].
Antidiabetic activity

The seed extract from L. leucocephala leaves exhibits antidiabetic activity [90]. An aqueous extract derived from boiling the seeds of L. leucocephala is taken orally to treat type-2 (NIDDM) diabetes and is claimed to be efficacious [94]. Moreover, the seed extract from L. leucocephala inhibits the development of type-2 diabetes [92]. The seed gum used in tablet formulation and the extracts of the seeds used as anthelmintic, antidiabetic and has a broad spectrum antibacterial activity [1].

Recent studies revealed the presence of various secondary metabolites as alkaloid, cardiac glycosides, tannins, flavonoids, saponins and Glycosides. Its seeds have great medicinal properties and are used to control stomachache, as contraception and abortifacient. The seed gum used as a binder in tablet formulation and the extracts of the seeds used as anthelmintic, antidiabetic and has a broad spectrum antibacterial activity [1].

Pharmacological activities

Antioxidant activity

L. leucocephala seeds have great medicinal properties and are used to control stomachache, as contraception and abortifacient. The seed gum used as a binder in tablet formulation [6]. A sulfated glycosylated form of polysaccharides from the seeds was reported to possess significant cancer chemo-preventive and antiproliferative activities [1]. The extracts of the seeds have been reported as anthelmintic, anti-diabetic and have a broad spectrum antibacterial activity [1]. Recently, the seed oil was used in engineering as a novel bio-device useful in biomembrane modelling in lipopolysaccharide determination of drugs and xenobiotics [1]. The plant is reported to be a worm repellent.

Table 2: Phytochemical compounds identified from the L. leucocephala leaf extracts and their therapeutic Activity [6]

| No | Compound                           | Secondary metabolite | Therapeutic activity                                                                 |
|----|------------------------------------|----------------------|-------------------------------------------------------------------------------------|
| 1  | Phytol                             | Diterpene            | Antimicrobial, anticancer, cancer preventive, diuretic, anti-inflammatory              |
| 2  | Squalene                           | Triterpene           | Antibacterial, antioxidant, antioxidant; cancer-Preventive, chemopreventive; immunostimulant, lipooxygenase-inhibitor, perfumery, pesticide, sunscreen |
| 3  | n-Hexadecanoic acid                | Palmitic acid        | Antioxidant, hypcholesteremic nematicide, pesticide, antiandrogenic, flavor, hemolytic, 5-alpha reductase inhibitor |
| 4  | Pentadecanoic acid, 14-methyl-, methyl ester | Palmitic acid methyl ester | Antioxidant; nematicide, pesticide, flavor, antiandrogenic                           |
| 5  | Hexadecanoic acid, 15-methyl-, methyl ester | Fatty acid ester | Anti-inflammatory, nematicide, pesticide, flavor, antiandrogenic                       |
| 6  | 3,7,11,15-Tetramethyl-2-hexadec-1-ol | Terpene alcohol     | Antimicrobial                                                                      |
| 7  | 9,12,15-Octadecatrienoic acid, methyl ester | Linolenic acid ester | Anti-inflammatory, insectifuge hypcholesteremic, cancer preventive, nematicide, hepatoprotective, insectifuge, antihaemostatic, antieczemic, antiancine, 5-alpha-reductase inhibitor, antiandrogenic, antiarthritis, anti-cancer |
| 8  | 9,12-Octadecadienoic acid, methyl ester | Linolenic acid ester | Anti-inflammatory, nematicide, insectifuge hypcholesteremic, cancer preventive, hepatoprotective, antieczemic, antiancine, antiarthritis, anti-eczemic |
| 9  | Oxalic acid, allyl hexadecyl ester | Dicarboxylic acid | Acaricide, antiseptic, CNS-paralytic, fatal, hemostatic, irritant, pesticide, renotoxic, varroxicide |

(Modified from Dr. Duke’s: phytochemical and ethnobotanical databases)

Antidiabetic activity

L. leucocephala leaves and seed extracts have antioxidant activity [89]. The seed gum contains a principal constituent, 2-(H)-benzofurane-5, 6, 7, 7a-tetrahydro-4, 4, 7a-trimethyl [25] and phenolic compounds and flavonoid quercitin was also isolated from the leaves extracts [90].

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 [25]. Leaf and seed extracts also have antidiabetic activity [90]. An aqueous extract derived from its boiled seeds was taken orally to treat type-2 diabetes [92].

The seed gum used as a binder in tablet formulation and the extracts of the seeds used as anthelmintic, antidiabetic and has a broad spectrum antibacterial activity. To date, no information is available about the pharmacological activities of flower, fruit, bark, wood branch, stem and root of L. leucocephala which need further studies.

CONFLICT OF INTERESTS

Declared none

AUTHORS CONTRIBUTIONS

All the author have contributed equally

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Pharmacological activities

Antioxidant activity

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