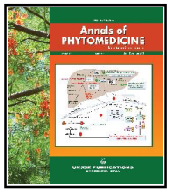
Annals of Phytomedicine 12(2): 327-338, 2023

DOI: http://dx.doi.org/10.54085/ap.2023.12.2.42

Annals of Phytomedicine: An International Journal
http://www.ukaazpublications.com/publications/index.php

Print ISSN : 2278-9839 Online ISSN : 2393-9885



Reveiw Article : Open Access

Review of phytochemical and pharmacological characteristics of some important species within the Litsea genus

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Article Info

Article history
Received 15 October 2023
Revised 5 December 2023
Accepted 6 December 2023
Published Online 30 December 2023

Keywords
Genus Litsea
Alkaloids
Flavanoids
Traditional use
Biodiversity

Abstract

The genus *Litsea*, consists of 392 tree species, is a diverse group of coniferous trees and shrubs within the Lauraceae family. These species are distributed across tropical and subtropical regions of Asia, North and South America, and other tropical areas. China has a total of 72 species belonging to this genus, with 47 indigenous to the nation, primarily found in mountainous regions above 1500 m above sea level. Over thousands of years, Litsea species have played a prominent role in traditional medicine across various countries, including China, Japan, Korea, India, Thailand, Myanmar, Bangladesh, Malaysia, Indonesia, the Philippines, Mexico, and Guatemala. Traditionally, they have been used to address a wide array of health conditions, such as influenza, gastric discomfort, inflammatory conditions, contusions, insect stings, *etc*. *Litsea* species exhibit various biological and pharmacological properties, including antitumor, antimicrobial, antioxidant, hypothermic, and anti-inflammatory effects. *Litsea* species has various alkaloids, flavonoids, terpenoids, *etc*., of pharmacological importance. This review aims to explore and document the ethnobotanical, phytochemical, and pharmacological (eight species) attributes of *Litsea* species to understand their potential benefits and applications in modern healthcare and industry as well as their historical and cultural significance.

1. Introduction

The genus *Litsea* is known for its remarkable diversity of evergreen trees and shrubs, and the group encompasses a diverse array of 392 tree species, distributed across extensive regions in tropical and subtropical areas in Asia, North and South America, and other tropical zones (Zhengyi and Peter, 1982). In China, the genus has a total of 72 distinct species, with 47 being native to the country and exhibiting growth mostly in the southern and southwestern regions, at an elevation of 1500 m above sea level (Kong *et al*., 2015).

Litsea plant has the potential to attain a height of approximately 8 meters and is primarily indigenous to regions in Southeast Asia, southern China, Japan, and Taiwan. Plants of the genus *Litsea* have been used in traditional medicine worldwide for thousands of years. Certain species of *Litsea* are highly regarded for their properties that reduce fever, alleviate pain, and treat diarrhoea in China, Japan, Korea, India, Thailand, Myanmar, Bangladesh, Malaysia, Indonesia, Philippines, Mexico, and Guatemala (Wang *et al*., 2016). The botanical, chemical, and pharmacological characteristics and the conventional use of *Litsea* species have been discussed in several ancient kinds of literature and monographs. These compounds find application in treating various medical conditions, including diarrhoea, vomiting, bone pain, infant colic, and central nervous system disorders. The *Litsea* genus exhibits various biological and pharmacological attributes, encompassing anticancer, antibacterial, antioxidant, hypothermic, and anti-inflammatory properties (Azhar and Salleh, 2020).

L. glutinosa is a moderately sized evergreen tree, with its roots used to treat sprains and bruises, while the oil derived from its seeds is employed to alleviate rheumatism. The bark and leaves of this plant are harnessed for their soothing and mildly astringent attributes, particularly in cases of diarrhoea and dysentery (Arunodaya *et al*., 2016). *L. glutinosa* species flourishes on elevated terrains in India at great heights. *L. verticillata* is a perennial small tree or shrub that may reach 2 to 5 meters high. It is dispersed over Kampuchea, Vietnam, and China. This species has a remarkable capacity for sprouting. Due to its considerable hardness, the wood is utilized as fuel. Rheumatism and menstruation cramps are treated using the roots and leaves. *L. pungens* is mostly found in northwest and eastern China. It has long been used in traditional Chinese medicine (TCM) to treat several illnesses, including flu, stomachaches, diarrhoea, and discomfort (Zhao, 2006; Xie, 1996). In TCM, evergreen bushes or small trees called *L. pedunculata* have long been used to treat rheumatoid arthritis, edema, and gastroenteralgia (Liang *et al*., 2011). *L. panamonja*, an evergreen tree is mostly located in the southern region of Asia, encompassing Vietnam, India, and southern China. *L.rotundifolia* is a perennial shrub tree that retains its leaves throughout the year and grows to a height of up to 3 m, where its

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roots are utilized to lessen rheumatic discomfort. The Xishuangbanna region of China has a rich historical tradition of *L. coreana* utilizing for both tea and medicinal properties. This tradition is notably widespread in the southwestern regions of China, encompassing Sichuan, Chongqing, and Guizhou. The tree is a perennial wood species that is dioecious and grows in tropical rain forests at elevations ranging from 500 to 1200 meters. It is commonly seen as a local canopy species. As an indigenous tree to China, *L. dilleniifolia* is an evergreen plant that grows 20-26 m tall. It grows at 500 m above sea level in Yunnan's rain forests in damp riverside locations (Song *et al*., 2022). It is also used in construction of buildings, furniture, and shipbuilding sectors. *L. hypophaea,* an evergreen tree that flourishes in broad-leaved environment woods and are native to Taiwan (Pan *et al*., 2010). *L. japonica* is found in southern Korea and Japan (Tran and Kim., 2023). In Korea, it is consumed as a vegetable. The extract obtained from the leaves of *L. japonica* using 80% ethanol (EtOH) has anti-inflammatory and antioxidant properties (Yoon *et al.,* 2010). Southeast Asia is home to the well-known tropical tree called *L. elliptica* (Jiwajinda *et al*., 2002). In order to treat headaches, certain *Litsea* species such as *L. elliptica* leaves are crushed and applied on the forehead (Grosvenor *et al*., 1995). These leaf extracts are used as an insect repellant, and in the realm of traditional indigenous herbal therapy, several ailments such as stomach ulcers and fever are commonly addressed. *L. garciae* is indigenous to Taiwan, Philippines, Kalimantan in Indonesia, the Sarawak and southwestern Sabah regions in Malaysia, as well as in the parts of Philippines, which share common geographic areas for this species (Lim, 2012). In Andhra Pradesh (India), *L. deccanensis* is widely used as medication to treat chest discomfort (Kumar *et al.,* 2011). The species *L.leefeana, c*ommonly called brown bollywood, belongs to the *Litsea* genus. This genus encompasses moderately sized trees native to the rainforests in the tropical region of Queensland, Australia and is usually planted as a garden plant. *L. glaucescens*, small trees and shrubs of the Kunth species are indigenous to Mexico and central America. Other names include laurel, aguarel, and laurelillo and it is frequently employed as a condiment. *L. glaucescens* may reach a height of 6 m and is found across Mexico, and grows in Tamaulipas through Veracruz and Chiapas, and Tepic extending north to central America. The leaves serve as a condiment and are utilized in gargling brews to alleviate colic and sore throats (Tucker *et al*., 1992).

2. Traditional uses of *Litsea* species

The genus *Litsea*, predominantly found in tropical and subtropical zones, holds significant importance in traditional and indigenous medicine systems. Renowned for its medicinal properties, it has historically been utilized to address a spectrum of ailments. Its applications span from alleviating diarrhoea, stomachache, and dyspepsia to combating gastroenteritis, diabetes, and edema. Moreover, *Litsea* is valued for its efficacy in treating colds, arthritis, asthma, and pain. Its therapeutic potential extends to aiding in the recovery from traumatic injuries. Across various cultures, *Litsea* stands as a versatile remedy, offering relief and support for a diverse array of health concerns. Some of the traditional use of *Litsea* species is tabulated below (Table 1).

Table 1: *Litsea* species in traditional use

Litsea species	Country	Parts of the plant	Traditional use	Reference
L. elliptica	Southeast Asia	Leaves	Migraine, Peptic ulcers, Hyperthermia, Insect repellent	Jiwajinda *et al.,* 2002
L. coreana	Jiangsu, Anhui, Zhejiang, Hubei, Henan, Jiangxi, Fujian, China	Roots leaves	Abdominal discomfort alleviation trauma recovery for injury treatment	Xie and Yu *et al.,*1996
L. deccanensis	Andhra Pradesh State, India	Leaves	Angina	Kumar *et al.,*2011.
L. chinensis	India	Stem, Fruit, Leaves	Fruit, Wood,Wood fuel	Ageel *et al.,*1994
L. glutinosa	Bangladesh, India, Sri Lanka, Guangxi, Fujiang, Myanmar, and Malaysia, Yunnan and Guangdong, China	Fruits, Leaves, Bark, Roots	Soothing agentfor joint discomfort, Ligament injuries	Mandal *et al.,*2000
L. hypophaea	Taiwan	Stems and leaves, Fruits	Mycobacterial inhibition, anti-retinopathy in diabetes	Pan *et al.,*2010
L. polyantha	India	Roots and barks	Aches, Injuries and abrasions, veterinary fractures, natural remedy for bowel irregularities	Ghosh and Sinha *et al.,*2010
L. monopetala	Burma, China, India, Bangladesh, Nepal	Roots, Trunk, Barks, Leaves	Herbal remedies for gonorrhea, Dermatological conditions, abscesses, *etc*. Leaves for rheumatic conditions Fresh leaves for gastrointestinal distress	Baul *et al.,*2011
L. pungens	Guangdong, Guangxi, Gansu, Xinan, Hubei, Hunan, Zhejiang, Shanxi, Tibet, China	Stems and roots, Leaves and fruits	Boosting spleen health gastric discomfort bowel irregularity Sun-related heat illness distended abdomen pain relief, Abdominal pain joint pain viral respiratory infection	Xie and Yu *et al.,*1996; Zhao, 2006

L. pedunculata	Yunnan, Jiangxi, Hunan, Sichun, Hubei, Guizhou, China	Stem and barks	Gastrointestinal pain fluid retention rheumatoid arthritis	Li *et al.*,2011
L. rotundifolia	China	Roots	Alleviating rheumatoid arthritis discomfort	Xie and Yu *et al.,* 1996
L. resinosa	Indonesia	Leaves	Anorexia	Roosita *et al.*,2008
L. rubescens	Sichun, Guizhou, Yunnan, Xizang, Shanxi, Hubei, Hunan, China	Roots and fruits, Stem and barks	Stomach discomfort gastroenteritis swelling rheumatoid arthritis, abdominal discomfort, Indigestion	Xie and Yu *et al.*,1996; Li *et al.*,2011
L. rotundifolia	Guangdong, Guangxi, Zhejiang, Jiangxi, Fujian, Hunan, Taiwan, China	Roots and barks, fruits and leaves	Swelling fluid retention rheumatoid arthritis gastrointestinal disorder	Xie and Yu *et al.,* 1996
L. salicifolia	Bangladesh, Bhutan, Guangxi, Guizhou, Guangdong, Hainan, Yunnan, China, India, Myanmar, Vietnam, Nepal	Fruits	Fractured bone, Gastrointestinal ailment	Kala, 2005
L. szemaois	Xishuangbanna, China	Seeds	Culinary essentials (aromatic oils and lauric acid), Fragrant essences	Li *et al.*,2004
L. verticillata	Guangxi, Yunnan, Vietnam, Kampuchea, China, Guangdong	Roots and leaves	Easing rheumatoid arthritis symptoms	Xie and Yu *et al.,* 1996
L. turfusa	Sarawak, Malaysia	Barks	Antifungal agent	Holloway and Scheinmann *et al.*,1973
L. populifolia	Tibet, Sichuan, China, Yunnan	Leaves, Fruits	Aromatherapy oils, Abdominal paindigestive discomfortmotion sickness	Xie and Yu *et al.,* 1996
L. petiolata	Thailand	Leaves	Disincentivized and Thwarted biting	Phukerd and Soonwera, 2014
L. zeylanica	Guangxi, Southeast Asia, China, Oceania	Roots	Alleviating air and soothing discomfort, Arthralgia	Padmakumari and Narayanan, 1992

3. Phytoconstituents

3.1 Alkaloids

Alkaloids from the genus *Litsea* have a broad spectrum of structural variations and biological activity. The initial alkaloid extracted from a particular species of *Litsea*, known as *L. chrysocoma*, was laurotetanine (Tomita *et al.,* 1965). Several alkaloids from *Litsea* were later discovered after a thorough study in this area. The bulk of the alkaloids recovered from the *Litsea* species are isoquinoline alkaloids. Several natural aporphine alkaloids' pharmacological properties include antioxidative, antiplatelet, anticancer, anticonvulsant, and antiplasmodial properties. These natural compounds and the artificial compounds derived from them are used as starting points for creating new treatments for various disorders (Thomford *et al.,* 2018). Some of the important alkaloids reported in various *Litsea* species is tabulated in Table 2.

Table 2: Alkaloids of reported *Litsea* species

***Litsea* species**	**Alkaloids**	**References**
L. deccanensis	Boldine, corytuberine, dicentrine, nordicentrine, laurolitsine, isocorydine, magnoflorine	Kumar *et al*., 2011
L. chrysocoma	Laurotetanine, (-) litcubine (2) and (-) litcubinine (3)	Lee *et al.,* 1996
L. lancifolia	Lancifoliaine, boldine, norboldine, actindaphnine.	Sulaiman *et al*., 2011
L. wightiana	Glaucine, boldine, norboldine, isoboldine, norcorydine and laurotetanine	Bhakuni and Gupta, 1983
L. gardneri	Laurotetanine, N-methyilaurotetanine	Bandara *et al*., 1989
L. elliptibacea	(+)-boldine and (+)-dehydrovomifoliol	Chuah *et al*.,1999
L.petiolata	β-carboline,aribine,norharman, reticuline,isoboldine,thalifoline	Omar *et al*., 2010
L. leefeana	Boldine, laurolitsine, l-benzyl1,2,3,4-tetrahydroisoquinoline and reticuline	Lamberton and Vashit, 1972
L. glutinosa	Isoboldine, laureliptine, Liriodenine, actinodaphnine, n-methylactinodaphnine, laurotetanine, n-methyllaurotetanine, laurolitsine, boldine, litseferine, litsine and glutinosine A	Yang *et al*., 2005; Jin *et al*., 2018
L.cubeba	(+)-N-(methoxycarbonyl)-N-norboldine (1) and (+)-isoboldine â-N-oxide	Sunyoung *et al*., 2002
L. lancifolia	litseferine, juziphine, phanostenine	Li *et al*., 2008

3.2 Terpenes

The genus *Litsea* has been determined to encompass many compounds, such as monoterpenes, sesquiterpenes, diterpenes, and triterpenoids. It is notable that sesquiterpenes are notably abundant in the majority of examined *Litsea* species. These metabolites have been identified in every part of the plant, although leaves and twigs contain most of them. Monoterpenes, comprising approximately 90% of essential oils, exhibit various structural variations (Duarte *et al.,* 2017). The *Litsea* genus contains three primary structural variations of monoterpenes; namely, acyclic, monocyclic, and bicyclic monoterpenes and their respective oxygenated derivatives. Menthane and cineole are the two varieties of these monoterpenes. All species of *Litsea*, except *L. coreana*, *L. mollis* and *L. lancilimaba* are abundant in cineole (Kamle *et al.,* 2019). The five essential skeletal structures of bicyclic monoterpenes (Figure 1) found in *Litsea* are thujane, carane, pinane, fenchane, and camphene (Zhao, 2006;Chen *et al.,* 2011).

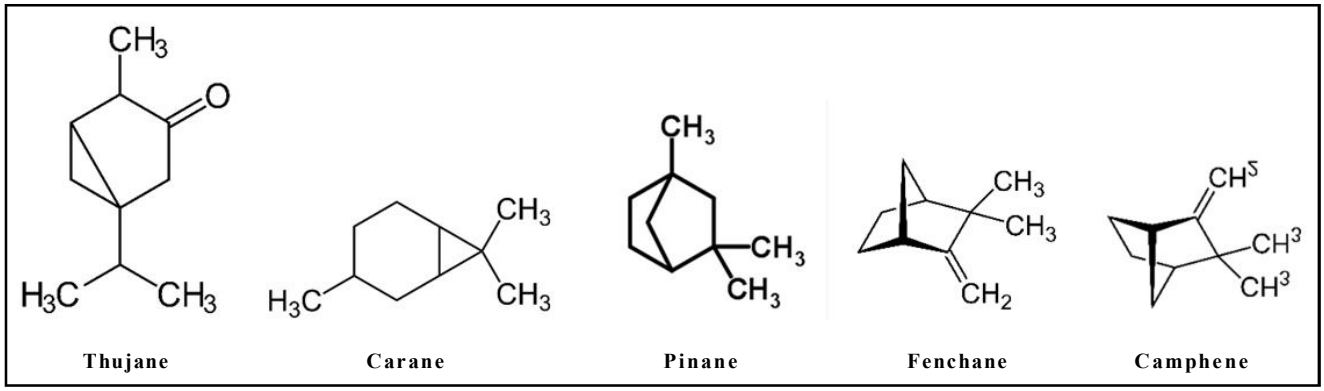

Figure 1: Bicyclic monoterpenes in *Litsea* species.

There have been reports of 73 naturally occurring sesquiterpenoids in *Litsea* species. Within the *Litsea* genus, a variety of sesquiterpene skeletons, encompassing monocyclic, bicyclic, and tricyclic sesquiterpenes, along with their oxygenated derivatives, as well as other sesquiterpenes, was also identified. Its carbon chains differ in terms of structure and bioactivity. Aliphatic sesquiterpenes, exclusive to the leaves and twigs of *L. mollis, L. lancilimaba, L. coreana, and L. verticillata*, were harnessed for the extraction of various potent *Litsean* sesquiterpenes. Among these, staphylionoside D, characterized as a sesquiterpenoid glucoside with a megastigmane type structure featuring an allenic side chain, was identified in the plant *L. szemaois* (Wang *et al.,* 2011). *Litsea* species, including *L. acutivena*, *L. consimilis, L. elliptica*, and *L. pedunculata*, possess eight triterpenoids (Agrawal *et al.,* 2011). The leaves and branches of *L. panamonja* have been traditionally utilized for the extraction of meroterpenoids, specifically panamonon A and B, which are natural compounds resulting from the combination of terpenoids (Wang *et al.,* 2016).

Table 3: Terpenoids phytoconstituents of reported *Litsea* species

Litsea species	Terpenoids	References
L. resinosa	Bulnesol, β-caryophyllene, γ-muurolene, β-selinene, α-eudesmol	Ahmad *et al*., 2005
L. grasilipes	Ledene, aromadendrene, α-copaene, calamenene, δ-cadinene, globulol and α-humulene	Ahmad *et al*., 2005
L. acutivena	δ-cadinene, trans-muurola-3,5-diene, and β-selinene	Ho *et al*., 2011
L.cubeba	Geranial, neral, limonene, β-myrcene, citronellal, linalool, 1,8-cineole, isoneral,	Zhao *et al*., 2023
L. lancilimba	Lancilimbnoid C	Muhammad *et al*., 2022
L. guatemalensis	1,8-cineole	Vallverdu*et al*., 2005
L. mollis	α-pinene, β-pinene, α-terpinene, α-terpinolene and 4-M-3-(1-M)-C, Caryophyllene	Liang *et al*., 2021
L. Coreana	*n*-decanal, 2E,6E-farnesol, β-eudesmol, τ-cadinol	Ho *et al*., 2010
L. pungens	Citral, Cis-verbenenol, D. Limonene, Linalool	Chen *et al*., 2011
L. glutinosa	β-Caryophyllene, Caryophyllene oxide and monoterpenes like (E)-β-Ocimene, (Z)-β-Ocimene	Azhar and Salleh, 2020
L. kostermansii	β-eudesmol, γ-eudesmol, δ-selinene, α-eudesmol, and γ-muurolene	Ho *et al*., 2009

3.3 Flavonoids

Flavanoids, a diverse group of phytonutrients found abundantly in various plant species, play a crucial role in the health benefits attributed to *Litsea* species. These bioactive compounds exhibit antioxidant properties, protecting cells from oxidative stress and reducing the risk of chronic diseases. Flavanoids were originally found in 1953 from immature leaves of *L. glauca* (Nakabayashi, 1953). Within *Litsea* plants, flavonoids contribute to their medicinal properties, including anti-inflammatory, antimicrobial, and anticancer effects. Chalcones, flavanoids, and their glycosides constituted a

part of isolated substances. From *L. glutinosa*, glutin, a new 2'-oxygenated flavone glycoside and pinocembrin chalcone, a rare flavonoid was also identified. Additionally, it was *L. fruticosa* that yielded the first isolates of the uncommon flavonoids pinocembrin chalcone and kaempferol (Yang *et al.,* 2010). Some of the flavanoids reported in various *Litsea* species is tabulated in Table 4.

Table 4 : Flavanoids phytoconstituents of reported *Litsea* species

Litsea species	Flavonoids	References
L. glutinosa	2',5,7-trihydroxy-6-methoxyflavone 2'-O-beta-D-glucopyranoside	Wang *et al*., 2010
L. japonica	Epicatechin, afzelin, quercitrin, and tiliroside	Lee *et al*., 2005
L. fruticosa	Pinocembrin chalcone and kaempferol 3,4-di-O-L-rhamnopyranoside	Liu *et al*., 2013
L.coreana	Quercetin-3 β-d-galactoside, quercetin-3 β-d-glucoside, kaempferol-3 β-d-glucoside, kaempferol-3 β-d-galactoside, (2R,3S)-catechin and (2R,3R)-epicatechin .	Wang *et al*., 2009
L. japonica	Epicatechin, afzelin, quercitrin and tiliroside	Lee *et al*., 2005
L. glutinosa	Pinocembrin chalcone and kaempferol	Yang *et al.,* 2010

3.4 Amides

The *Litsea* genus encompasses several distinct species, including *L. acutivena*, *L. hypophaea*, and *L. greenmaniana*, which served as the primary sources for amides. The initial exploration of lignanamides within the Lauraceae family entailed the identification of a compound known as 1,2-dihydro-6,8-dimethoxy-7-hydroxy-1-(3,5-dimethoxy-4-hydroxyxyphenyl), which is referred to as N^1,N^2-bis2-[(4-hydroxyphenyl) ethyl]. The compounds mentioned in this context encompass -2,3-naphthalene dicarboxamide and cannabisin D (Kamle *et al*., 2019). Some of the amides reported in various *Litsea* species is tabulated in Table 5.

Table 5 : Amides phytoconstituents of reported *Litsea* species

Litsea species	Amides	References
L. acutivena	N-Feruloyltyramine	Tsai *et al*., 2007
L. cubeba	cis-N-Feruloyl-3-methoxytyramine	Zhu and Yang, 2007
L. auriculata	N-Feruloyl-3-methoxytyramine	Tanaka *et al*., 2009
L. hypophaea	N-Sinapoyltyramine	Pan *et al*., 2010
L. cubeba	3-Methoxy-N-sinapoyltyramine	Guo *et al*., 2015
L. greenmaniana	N-trans-3,4-methylenecinnamoyl-3- methoxytyramine	Jiang *et al*., 2013
L. cubeba	Cubebamine A	Chen *et al*., 2011

3.5 Steroids

Steroids, a class of organic compounds, encompass various molecules vital for cellular functions in organisms. These compounds exhibit diverse biological activities, including hormonal regulation, inflammation control, and immune response modulation. The *Litsea* genus contributes to herbal remedies, fragrances, and serves as a source of potential therapeutic compounds, exemplifying nature's rich reservoir of beneficial botanical resources. At present, researchers have identified seven steroidal metabolites derived from *Litsea* plants. Among these compounds, β-sitosterol exists in both its unbound and glycosidic forms, and it is the most prevalent steroidal constituent found in *Litsea* species. Sitosterol was detected in the majority of *Litsea* species (Xiao *et al.,* 2005). Some of the steroids reported in various *Litsea* species is tabulated in Table 6.

Table 6: Steroidal phytoconstituents of reported *Litsea* species

Litsea species	Steroids	References
L. cubeba	β-sitostenone	Chen *et al*., 2013
L. acutivena	β-Sitosterol	Tsai *et al*., 2007
L. glutinosa	Stigmasterol	Yang *et al*., 2010
L. chingpingensis	Daucosterol	Yang *et al*., 2007
L. euosma	5,6-Epoxystigmastan-3-ol	Xiao *et al*., 2005

3.6 Essential oils

Essential oil stands out as a prominent chemosystematic character within *Litsea* species. Across most *Litsea* genus members, essential oil extraction is feasible from various plant parts, encompassing the fruit, leaf, stem, root, and flower, albeit with notable variations in composition and quantity. The essential oils derived from *Litsea* species, often referred to as LCEO or *Litsea* essential oil, predominantly comprise of oxygen-containing sesquiterpenes and monoterpenes. LCEO exhibits a transparent, oily texture with a faintly yellow hue and a zesty, citrus-like flavor, and it is obtained through the distillation process from the fresh fruits of the plant. It finds extensive application across the food, chemical, and pharmaceutical sectors. As per the standards outlined in GB 2760-2007, the Ministry of Health in China has granted approval for the incorporation of the essential oil of *Litsea cubeba* (EOLC) as a food additive. Their assessment focused on the essential oil compositions sourced from different parts of the *Litsea* species; namely, the fruits, leaves, and roots. Essential oils obtained from *Litsea cubeba* plants in Northeast India, specifically those derived from leaves and fruits, underwent analysis employing GC and GC-MS techniques. The primary component within *Litsea cubeba* essential oil (LCEO) was identified as sabinene, with notable companions such as 1,8-pinene, terpinen-4-terpineol, and myrcene, which play crucial roles in its composition

(Hammid and Ahmad, 2015). The fruit oils, in contrast, were primarily characterized by the presence of citronellol and citronellal. *L. glutinosa* contains lauric acid and natural phytols. The identification of essential oils in *L. glutinosa* leaves in China, both in their freshly harvested and dried states, was achieved through applying gas chromatography-mass spectrometry (GC-MS) (Zhao *et al.,* 2010). The analysis of oils derived from the fresh fruits, flowers, and bark of *L. monopetala* in northeast India was identified as the principal constituents within the essential oil of *L. rotundifolia's* leaves (Wang *et al.,* 2016). The chemical composition of essential oils extracted from the leaves and stems of *L. kostermanin* and *L. gerclae* displayed variations. Further examination focused on the hydrodistillate leaf essential oil of *L. kostermansii*, revealed two principal categories: Oxygenated sesquiterpenes and sesquiterpene hydrocarbons (Cheng, 1983). In 2009 study, hastings documented the major constituents present in the essential oil extracted from the leaves of *L. nakaii*. Their findings indicated that the primary components included β-humulene at 15.5%, β-cadinene at 9.2%, (E)-ocimene at 8.1%, and β-selinene at 7.1% (Hastings, 2010). The chemical makeup of the twig oil exhibited distinctions when compared to the essential oils derived from freshly harvested leaves of *L. acutivena*. The species *L. guatemalensis* originates from Mexico and central America (Vallverdú *et al.,* 2005). Some of the essential oils reported in various *Litsea* species is tabulated in Table 7.

Table 7: Flavanoid phytoconstituents of reported *Litsea* species

Litsea species	Essential oils	References
L. cubeba	Sabinene, 1,8-pinene, terpinen-4-terpineol, and myrcene, citral and limonene	Silinlin *et al.,* 2012
L. monopetala	Caryophyllene alcohol, pentacosane, caryophyllene oxide, humulene oxide, and tricosane	Wang *et al.,* 2016
L. pungens	1,8-cineole, Dodecanoic acid, myristic acid, n-undecanoic acid, and palmitic acid	Wang *et al.,* 2016
L. kostermansii	eudesmol, selinene, and murolene	Chen *et al.,* 2011
L. nakaii	β-humulene, β-cadinene, and β-selinene	Hastings, 2010
L. acutivena	tau-cadinol, selinene, trans-ocimene, and cadinol	Dai *et al.,* 2019
L. guatemalensis	1,8-cineole, terpineol and linalool	Vallverdú *et al.,* 2005
L. cubeba	Citral B (neral), β-phellandrene, and β-terpinene	Wang and Liu, 2010
L. helferi	Limonene, β-caryophyllene, bicyclogermacrene, bicycloelemene and α-phellandrene	Son *et al*., 2014
L. ferruginea	Sabinene, α-pinene, γ-terpinene, limonene and terpinen-4-ol	Son *et al*., 2014
L. verticillata	Linalool, α-pinene and β-pinene	Son *et al*., 2014
L. glutinosa	α-ocimene, along with α-pinene and β-pinene	Son *et al*., 2014

4. Pharmacological activities

Most *Litsea* species are recognized to be effective in treating various disorders, including normalizing body temperature, reducing pain, treating diarrhea, treating influenza infection, stomach ache, inflammatory diseases, bruising, and other disorders. Several ancient literatures, contemporary writings, and monographs have discussed the phytochemical, phytopharmacological, and traditional applications of *Litsea* species.

4.1 Pharmacological activity of *L. salicifolia*

According to an early report (Puppala *et al.,* 2023), the decoction of *L. salicifolia* stem bark is helpful for rheumatic-affiliated inflammation and bone disorders. An essential oil from the species *L. salicifolia* has insecticidal properties. Two essential oils, (E)-citral and (Z)-citral, were extracted from *L. salicifolia* by hydrodistillation, and they were identified by GC-MS. *Sitophilus zeamais* and *Tribolium castaneum* were the two bug species used in this experiment. The oil successfully repelled the insects even at low concentrations (0.16 g/cm^2). It has also demonstrated fumigant action against *Sitophilus zeamais*, contact toxicity towards *Sitophilus zeamais* and *Tribolium castaneum*, and antifeedant toxicity against *Tribolium castaneum* in addition to its repellent activity (Juntarajumnong and Chandrapatya, 2010). *L. salicifolia* leaves showed cytotoxicity and was investigated utilizing brine shrimp lethality bioassay. For extraction, dried leaves were employed which were thoroughly crushed, sifted, and subsequently, various extracts were obtained by employing solvents with varying polarity levels, spanning from low, such as hexane, to high, including ethyl acetate and methanol. Each of the extracts underwent a qualitative assessment for phytochemical constituents, revealing the existence of alkaloids, tannins, flavonoids, and carbohydrates. The LC_{50} value for the methanol extract, specifically 244.599 g/ml, significantly exceeded that of the other extracts when evaluated on brine prawns (Roy and Saraf, 2006). The study reported the antioxidant and antimicrobial attributes exhibited by various extracts derived from different species of *Litsea*, elucidating their research outcomes. The research revealed that the methanol extract of *L. salicifolia* demonstrated a significant phenol content, with 1021.414 mg/gm for gallic acid and 253.5714 mg/gm for tannic acid. LSE reduced RA *via* its antioxidant and anti-inflammatory characteristics by blocking TLR4-mediated NF-κB nuclear translocation and by triggering the signaling pathways (Papullaa *et al*., 2023).

4.2 Pharmacological activities of *L.coreana*

The methanolic extracts of *L. coreana* demonstrated significant hepatoprotective effects. In a rat model of nonalcoholic steatohepatitis (SREBP-1c transgenic mice), the administration of 200 mg/kg of total flavonoids from *L. coreana* (TFLC) led to a significant reduction in triglyceride and malondialdehyde levels in both blood and hepatic tissue, while also elevating superoxide dismutase (SOD)

activity. TFLC exhibited protective effects on alcoholic fatty liver in rats, as evidenced by a reduction in the expression of hepatic adipose differentiation-related protein and a decrease in serum levels of triglycerides, total cholesterol, low-density lipoprotein (LDL) cholesterol, TNF-α, glucose, and insulin when administered at a dose of 200 mg/kg. These findings suggest that TFLC derived from *L. coreana* may potentially lower blood sugar levels and alleviate hyperglycemia, as reported in previous studies (Zha, 2013). The oral administration of TFLC (400 mg/kg) led to an augmentation in high-density lipoprotein (HDL) cholesterol and an increase in SOD content in a rat model of type 2 diabetes induced by streptozocin. The assessment encompassed measurements of body weight and serum levels of free fatty acids, total cholesterol, triglycerides, LDL cholesterol, C-reactive protein, and MDA, all displaying antidiabetic activity. Furthermore, it caused a decrease in liver protein tyrosine phosphatase 1B expression. This resulted in a decrease in inflammatory cytokines and the suppression of MMP-9 expression, TFLC exhibited a therapeutic impact on rheumatid arthritic (RA) rats. *In vitro* tests reveal that *L. coreana* extracts and fractions have strong antioxidant properties. The 2,20-Azino-bis (3-ethyl-benzothiazoline-6-sulphonic acid) (ABTS), 2,2-diphenyl-1-picrylhydrazyl (DPPH), and hydroxyl radicals were present and effectively neutralized by the ethanol extracts of hawk tea, according to studies, with EC_{50} values of 1.09, 0.06, and 2.42 mg/ml, respectively.

It has been observed that *L. coreana* lowers blood sugar and treats hyperglycemia. Orally given 400 mg/kg elevated the quantity of high-density lipoprotein (HDL) cholesterol in a streptozocin-induced type 2 diabetics rodent model. It reduced the body's weight and serum levels of free fatty acids, total cholesterol, triglycerides, LDL cholesterol, C-reactive protein. Furthermore, it decreased liver protein tyrosine phosphatase 1B expression (Jia *et al*., 2017), lowered the expression of mTOR complex 1 and TNF-α in peritoneal macrophages, decreased secondary paw edema, and dropped serum levels of TNF-α and IL-1β (Zhong *et al*., 2014). *L. coreana* exhibited enhanced lowering and scavenging DPPH radical capacity, with EC_{50} values of 77.52 g/l and 18.17 g/l, respectively (Ji *et al*., 2011). Eight flavonoids subunits showed ABTS antioxidant activities which are hyperin, isoquercitrin, quercitrin, quercetin, kaempferol, catechins, chlorogenic acid, and epicatechin (Meng *et al*., 2012).

4.3 Pharmacological activities of *L. cubeba*

Gram-positive and Gram-negative microorganisms were tested for antibacterial efficacy using the oil from *L. cubeba* fruits (LCFO). *Escherichia coli* required a minimum bactericidal concentration (MBC) of LCFO of 0.38 µg/ml, while *Bacillus subtilis* required an MBC of 390.6 µg/ml. LCFO's MBC values varied depending on the pathogens that were tested. LCFO showed an LC_{50} The lethal concentration for 50% mortality is 31.62 µg/ml. Lethal concentration for 50% mortality in the brine shrimp was assessed using the brine-shrimp lethality assay, and the half maximal inhibitory concentration (IC_{50}) value in the 2, 2-diphenyl-1-picrylhydrazyl (DPPH) assay was determined to be 1628.85 µg/ml (Hammid *et al.,* 2015). LCFO contains potent antibacterial, anticarcinogenic, and antioxidant properties. After being derived from the plant *L. cubeba,* the fruit and leaf oils were tested for their capacity to kill human cancer cells (Bajracharya *et al.,* 2019). Unlike the leaf oil, which displayed a deficiency in antiproliferative capabilities against the examined cancer cells, the fruit oil demonstrated a dose-dependent anticancer effect on human oral (OEC-M1), liver (J5), and lung (A549) cancer cells. Furthermore, in murine models, LCFO exhibited anxiolytic and analgesic properties (Ho *et al*., 2010; Khan and Ahmad, 2021). The oral supplementation of LCFO considerably increased the time spent and quantity of mouse entry within the exposed section of the raised plus-shaped maze, as well as the duration of stay and sleep duration of pentobarbitone-induced mice. In the tail-flick test, adding 500 mg/kg of LCFO showed analgesic efficacy. LCFO displayed strong neuroprotective properties (Chen *et al.,* 2012)**.** LCFO was tested for its antioxidant and free radical scavenging abilities. Regarding hydroxyl and superoxide radical scavenging capabilities, LCFO had IC_{50} values of 0.19 and 0.45 mg/ml, respectively. LCFO successfully suppressed the process of peroxidation in linoleic acid. According to the GC-MS investigation of the composition of LCFO, the substance's high citral concentration may have contributed to its capacity to scavenge free radicals (Wang *et al.,* 2012).

L. cubeba's leaf oils, for their toxic potential against human cancer cells was evaluated. While the leaf oil showed no antiproliferative activity against tested cancer cells, the fruit oil demonstrated dose-dependent anticancer effects against human oral (OEC-M1), liver (J5), and lung (A549) cancer cells (Ho *et al*., 2010). *L. cubeba* seed volatile oils (VVO) vapor shown anti-proliferative and apoptotic properties against A549 non-small cell lung cancer cells. The VVO therapy causes apoptosis and inhibits cell growth in A549 cells (Seal *et al*., 2012), Solvent extraction was used to extract neral and geranial from the essential oil *of L. cubeba* fruits. Lower amounts of IL-6 and TNF-α were expressed by both geranial and neural macrophages after lipopolysaccharide (LPS) induction. Neral and geranial were shown to be potential anti-inflammatory drugs (Liao *et al*., 2015).

4.4 Pharmacological activities of *L. garciae*

Three different assay techniques were utilized, specifically the DPPH assay, the ferric reducing ability of plasma (FRAP) assay, and the ABTS (2,2-azino-bis-3-ethylbenzothiazoline-6-sulphonic acid) assay, to assess the antioxidant capacity of *L. garciae*. The obtained results were indicative of the antioxidant properties of this plant. The outcomes obtained from the FRAP and ABTS assays suggested that the inedible constituents of *L. garciae*, including the capsule, seed, and flesh, exhibited the highest levels of antioxidant activity compared to the edible parts. According to *L. garcia*, the plant serves as a valuable natural source of antioxidants and holds the potential for medicinal use in combating illnesses triggered by oxidative stress. The antibacterial attributes of *L. garciae's* branch, bark, and leaf were obtained using ethanol, n-hexane, and ethyl acetate as solvents at 1250, 625, and 312.5 ppm, respectively. Using a micro broth dilution technique to evaluate effectiveness against propionic bacterium acnes, every sample demonstrated inhibitory effects on bacterial development. The branch's n-hexane and extracts of ethanol, as well as the extracting leaves in ethyl acetate form, showed a minimal inhibitory concentration (MIC) of 312.5 mm (Wulandari *et al.,* 2018). Extraction with methanol demonstrated stronger fungicide effects against *C. capsici* compared to *C. gloeosporioides*. The isolated compound, specifically identified as 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium, was utilized as a means to investigate the prospective anticancer properties of *L. garciae* on human cell lines. The cytotoxic properties of *L. garciae* affected three different types of cell lines (Wang *et al.,* 2016). Alkaloids like boldine exhibited cytotoxicity and induces apoptosis in breast cancer cells, evidenced by increased lactate dehydrogenase release, membrane permeability,

and DNA fragmentation (Amit and Zinyin,2021). Hence, further exploration is necessary to assess the potential of various components of *L. garciae* as anticancer agents. Diverse components of *L.garciae* have been employed in traditional folk medicine for addressing various ailments, including muscle pains, injuries to the knees,wrists, skin problems, vaginal haemorrhage, boils, snakebites, and stinging caterpillars (Mirfat *et al.,* 2018). A study also demonstrated anti-inflammatory effects in the methanolic extracts obtained from the bark, leaves, and fruits of *L.garcia* in their raw form (Kutoi *et al.,* 2012).

4.5 Pharmacological activity of *L. cubeba*

Human lung, liver, and oral cancer cells exhibited cytotoxicity when exposed to the essential oil (EO) extracted from *L. cubeba* fruit. It was observed that the oil molecules derived from *L. cubeba* seeds induced apoptosis and caused cell cycle arrest in human non-small cell lung cancer cells (A549), leading to cellular damage. *In vitro* studies also revealed the cytotoxic effects of *L. cubeba* bark alkaloids on various types of human cancer cells, including gastric carcinoma (BGC-823), hepatocellular carcinoma (HepG2), breast cancer (MCF-7), and gastric adenocarcinoma (SGC-7901. Skin cancer in humans is represented by SK-MEL-2 represents melanoma, while SK-OV-389 represents ovarian cancer (Zhang *et al.,* 2012). The association between nuclear erythroid-2 related factor and the expression of antioxidant response element (ARE) genes has been established in scholarly research. *Litsea* species have successfully inhibited several pathogenic strains. The essential oil derived from the leaves and fruits of *L. cubeba*, has demonstrated its antibacterial properties by effectively inhibiting the growth of various microorganisms, including *S. aureus*, *L. monocytogenes*, *E. coli, P. aeruginosa, C. albicans,* and *A. niger*. Nevertheless, differences in the composition of chemicals found in *L.cubeba's* leaves and fruits were observed, potentially accounting for variations in their inhibitory effects. The study investigated the impact *L. coreana's* total flavonoids (TFLC) on blood glucose levels in diabetic rats. The results demonstrated that TFLC effectively lowered glucose and lipid levels and alleviated oxidative stress on the liver (Mounika and Hymavathi, 2021).

4.6 Pharmacological activity of *L.glutinosa*

Boldine, a phytoconstituent derived from *L.glutinosa* has been investigated for its impact on various cancer cell lines of several types such as leukemia, pancreatic, prostate, breast, and CNS as well as in normal cells, examining its kinase profile and inhibitory effect on 4J6G/9 (Khalipha *et al.,* 2019). *L. glutinosa* exhibited cytotoxicity against two leukemia cell lines, HL-60 and Molt-4, with GI45 values of 10 and 12 M, respectively. Additionally, the lung cancer A549 cell line is vulnerable to the cytotoxic effects of *L. glutinosa*, leading to increased ROS generation. Boldine, extracted from the fruits and leaves of *L. glutinosa*, exerted its influence on pro-inflammatory cytokines. To assess this impact, measurements of pro-inflammatory cytokine levels, specifically TNF-α, IL-1β, and IL-6, were conducted in human monocytic THP-1 cells. It displayed anti-inflammatory properties by significantly reducing TNF-a (40-51% inhibition) and IL-6 (80-90%) at concentrations of 4-12 mm. The phytochemical exhibited anti-inflammatory effects in J774A.1 macrophage cells stimulated with lipopolysaccharide (LPS) and inflammatory models in living organisms (Khalipha *et al*., 2009). In a rat model, oral administration of the isolated chemical boldine from *L. glutinosa* (15-35 mg/kg) demonstrated an impact on the gastrointestinal system.

4.7 Pharmacological activity of *L. lancilimba*

L. lancilimba, has antiflu effects, strong analgesic and anti-inflammatory characteristics. *Invitro* study signified that the oil of *L. lancilimba* has a notable inhibitory effect on beta-hemolytic streptococcus, *Staphylococcus albicans, staphylococcus aureus*, and dermatophyte on epidermidis. In cats with acute myocardial ischemia, *L. lancilimba* oil exhibited a protective effect. By ligating the coronary arteries in cats, *L. lancilimba* oil cured experimental myocardial ischemia, myocardial infarction, and posterior pituitary myocardial ischemia. Heart failure and moderate arrhythmias were treated with *L. lancilimba* in the form of herbal medications and dietary supplements. The impact of *L.lancilimba* oil on experimental arrhythmia was investigated and showed the potential to significantly raise the threshold for toxic potassium required to induce arrhythmia, and both delay and shorten the duration of ADR-induced arrhythmia in rabbits. Additionally, it exhibited a notable reduction in ventricular fibrillation induced by $CHCl_3$ in mice (Yu *et al.,* 2022). *L. lancilimba* oil hinders the contraction of isolated rabbit aortic strips triggered by elevated levels of K^+ and Norephenephrine. Furthermore, this oil demonstrates the ability to relax both the isolated normal tracheal smooth muscle of Guinea pigs and the spasmodic tracheal smooth muscle induced by histamine and Ach (Sun *et al.,* 2014).

4.8 Pharmacological activity of *L.elliptica*

The methanolic extract derived from its leaves has shown effectiveness in inhibiting the development of the bacteria *Helicobacter pylori* (*H. pylori*), which is associated with a number of stomach related issues that include intestinal cancer, peptic ulcer disease, and nausea (Srinivasan and Murali, 2022). The leaf of *L.elliptica* exhibited a minimum 100 mg/ml as the minimum inhibitory concentration (MIC) for *H. pylori*, a level comparable to that observed in the leaves of *Pouzolzia pentandra*, *Cycas siamensis*, and *Melaleuca quinquenervia* (Grosvenor *et al.,* 1995). The inhibitory activity observed in this study was comparatively lower than that of extracts from other plant species such as the aril of *Myristica fragrans* exhibiting an inhibitory activity of 12.5 mg/ml (Bhamarapravati *et al.,* 2003).

5. Toxicity of *Litsea* species

The toxicity of *Litsea* species has only been reported in a few articles. Normal hepatocyte survival was not significantly affected by *L.Coreana* pretreatment (100 mg/l) for 48 h. *L. elliptica* essential oil's acute toxicity, adverse reactions and mortality increased proportionally with the administered dose. However, in the subacute toxicity study, alterations in body weight, food intake, and water consumption were not evident (Budin *et al*., 2012). The effect on Sprague-Dawley rats' red blood cells (RBCs), by *L. elliptica* essential oil was reported. In this study, orally administered (via gavage), the *L. elliptica* essential oil was given to three treated groups at doses of 125, 250, and 500 mg/kg of body weight for five times per week over a three-week period. While significant variations were noted in hemoglobin, mean cell hemoglobin concentration (MCHC), mean cell volume (MCV), and mean cell hemoglobin (MCH) compared to the control group, but these values remained within normal ranges (Jiang *et al*., 2009). In an acute oral toxicity investigation, Sprague-Dawley rats were used to test the oral acute toxicity of *L. elliptica* essential oil over a period of 14 days and found to be safe at a dosage of 500 mg/kg/bw, according to the acute non-observed adverse effect

threshold study (Masran *et al*., 2011). Applied topically, the contact toxicity of *L. pungens* essential oils was evaluated against third-instar *Trichoplusia ni* larvae, demonstrating modest action against *Trichoplusia ni* larvae. The majority of the toxicity of the oils to *Trichoplusia ni* larvae was attributed to the phytoconstituent 1,8-cineole from the essential oil of *L. pungens*. The findings indicated that *L. pungens* essential oils may be developed into natural pesticides (Jiang *et al*., 2009). The toxicity of essential oil against the red blood cells (RBCs) of Sprague-Dawley rats was assessed. All groups given treatment exhibited considerably decreased amounts of RBC membrane phospholipids and cholesterol compared to the control group. There was not a significant distinction among the control and treated groups in terms of the RBC membrane's total proteins or osmotic fragility (Taib *et al*., 2009). The insecticidal toxicity of *L. cubeba* fruit extracts against *Sitophilus zeamais*, including contact toxicity, fumigant toxicity, and repellent action were reported. The most potent fumigant toxicity, contact toxicity, and repellent effect against *S. zeamais* were shown by the chloroform extracts of *L. cubeba* due to the presence chlorobutanol phytoconstituent. These results suggested the natural insecticide toxicity of *L. cubeba* fruit extracts against *S. zeamais* (Zhang *et al*., 2017). The generation of micronuclei in bone marrow cells and testing for chromosomal aberration in spermatocyte cells for acute toxicity determination of *L. cubeba* demonstrated negative genetic toxicity.

6. Conclusion

Litsea species emerge as a valuable and multifaceted resource, showcasing versatile applications and a broad spectrum of pharmacological activities. Despite significant strides in comprehending phytochemistry and pharmacology of the *Litsea* genus, a notable gap persists in our understanding of their potential health effects and clinical significance. Beyond the bioactive compounds discussed earlier, numerous secondary metabolites have been identified. Subjecting these metabolites to rigorous biological evaluation to unveil their potential benefits is crucial. Therefore, it is imperative that we embark on extensive, meticulously detailed research efforts, and clinical evaluations of *Litsea* species in the future. These endeavors are crucial for completely realizing the therapeutic potential of *Litsea* but also for ensuring the safety and efficacy of their applications across various fields, including medicine and natural remedies.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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Citation **Nidhya Govindarajan, Latha Somasundaram, Chamundeeswari Duraipandian and Alan Mathew Punnose (2023). Review of phytochemical and pharmacological characteristics of some important species within the Litsea genus. Ann. Phytomed., 12(2):327-338. http://dx.doi.org/10.54085/ap.2023.12.2.42.**