REVIEW: POTENTIAL PHARMACOLOGICAL ACTIVITY OF KALANGKALA PLANT (*Litsea angulata*)

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ABSTRACT

Kalangkala plants are native to Kalimantan and belong to the genus Litsea, family Lauraceae. Traditionally, it is used to treat diarrhea, boils, dyspepsia, diabetes, pain, asthma, fever, arthritis, traumatic injuries, gastroenteritis, edema, and stomachaches. This review article aims to explain the phytochemical components and pharmacological activities of the kalangkala plant. Databases from Google Scholar, ScienceDirect, and PubMed were searched for articles published from 2016 to 2024. The keywords used were Kalangkala, Litsea, *and Litsea angulata*. The results showed that *Litsea angulata* contains phytochemical compounds including saponins, alkaloids, flavonoids, tannins, steroids, triterpenoids, terpenoids, carotenoids, coumarin, β-pinene, (S)-cis-verbenol and β-sitosterol. The pharmacological activity of *Litsea angulata* includes antioxidant, antibacterial, antidiabetic, and spermacidal activities and is toxic. Antioxidant activity of kalangkala plant from various parts of the plant, namely branches, bark, leaves, seeds, fruits, leaves, and fruit seeds. Antibacterial activity in plant parts, namely branches, bark, leaves, seeds, and essential oils from leaves, and antidiabetic activity in the fruit seeds of the kalangkala plant. *Litsea angulata* is the most widely reported phytochemical component for its pharmacological activity, namely flavonoids. Flavonoids are found in various parts of plants, including the seeds, bark, and leaves. Pharmacological activity as an antioxidant, antibacterial, and antidiabetic. Further research is needed to identify the phytochemical components responsible for the pharmacological activity in the discovery of new drugs.

Keywords: Kalangkala, Litsea, *Litsea angulata*

INTRODUCTION

Kalangkala plants are native to Kalimantan and belong to the genus Litsea, family Lauraceae. The Litsea genus is often found in several areas in East Kalimantan, including *Litsea firma, Litsea elliptica, Litsea garciae, Litsea angulata, Litsea resinosa*. The distribution of Litsea is in the districts of Kutai Kartanegara, East Kutai, West Kutai, Paser, Bulungan and the city of Balikpapan, there are 38 types of the Litsea genus. Litsea plants have several benefits, including medicinal use, production of essential oils, insecticides, and production of natural dyes (Kusparadini et al., 2018).

Ethanol extracted from the Litsea genus generally contains alkaloids, flavonoids, tannins, terpenoids, carbohydrates, and coumarins (Wulandari et al., 2018). Many studies have reported that members of the Litsea genus have antioxidant activity (Hawa et al., 2013). Flavonoids are phytochemical compounds with the potential to act as antioxidants (Rizki et al., 2023;Rohama et al., 2023). Flavonoid compounds have many hydroxyl

groups (OH), which make them polar (Ramadhani et al., 2022). The antioxidant activity of *Litsea angulata*, an antidiabetic, has been reported to reduce and prevent oxidative stress due to hyperglycemia (Susiani & Saputri, 2020;Ilmia, 2024). Flavonoids have also been reported to possess antibacterial potential (Amalia et al., 2022). Flavonoids are bioactive polyphenolic compounds with low molecular weights in various plant parts. Activity as an antibacterial is demonstrated by the mechanism of becoming a complex compound by binding to extracellular proteins, damage bacterial cell walls, lysosomes and microsomes which are a form of flavonoid interaction with bacterial DNA and become soluble, resulting in phospholipids not being able to protect the structure of the cell membrane and causing leaks, thereby blocking bacterial growth and causing death, this bioactive compound is always active to inhibit bacterial growth (Villiya & Maimunah, 2021).

Litsea angulata is also called kalangkala with another (Aryadi, M dan Fauzi, 2013) name *Tetranthera angulata* Blume Ness as a producer of red dye (Efendi et al., 2016). Traditionally, it has been used to treat diarrhea, boils, dyspepsia, diabetes (Amalia et al., 2022), pain, asthma, fever, arthritis, traumatic injury, gastroenteritis, edema, and abdominal pain (Kong et al., 2015). People in the Sebelat National Park area of Kerinci use the leaves and flowers of *Litsea angulata* BI to treat joints and rheumatism (Frankistoro, 2006).

The antioxidant activity of various test samples was determined in vitro, one of which used free radicals (2,2-diphenyl-1-picridirazyl-(DPPH) with UV-Vis spectrophotometry at an inhibitor concentration of 50 (IC_{50}); If the IC_{50} value was smaller, the antioxidant activity was greater (Wulandari et al., 2021). The 70% ethanol extract of *Litsea angulata* leaves was analyzed using UV-Vis spectrophotometry with a total flavonoid content of 0.395% w/w and had antioxidant activity with an IC_{50} value of 302.80 ppm, classified as weak activity (Rizki et al., 2023). Another study reported that the antioxidant activity of 96% ethanol extract of *Litsea angulata* leaves obtained an IC_{50} value of 152.39 ppm. Relatively strong antioxidant activity was observed in the stem bark of *Litsea angulata*, with an IC_{50} value of 85.33 ppm (Susiani & Saputri, 2020). Another study reported that antioxidant activity was very strong in *Litsea angulata* fruit seeds with an IC_{50} value of 48.78 ppm (Saputri & Susiani, 2018). *Litsea angulata* stem bark with an ethyl acetate fraction was reported to have the strongest antioxidant activity with an IC_{50} value of 2.41 ppm (Wulandari et al., 2018). UV-Vis spectrophotometry is the most widely used instrument to detect bioactive components, one of which is flavonoids, based on light absorption. Fractionation is used to separate bioactive components based on their polarity. Differences in polarity reflect differences in the extraction results and antioxidant activity (Mardlatillah et al., 2023).

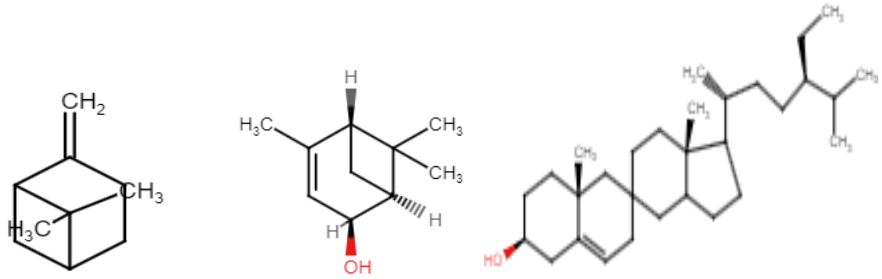
In this review article, the aim is to explain the phytochemical components and pharmacological activities of the Kalangkala plant, so it can provide very helpful information for further research in the discovery of new drugs.

Phytochemical Compound

The seeds of the *Litsea angulata* plant extracted using methanol as a solvent have been reported to contain alkaloids and tannins (Mustikasari & Ariyani, 2010). The 95% ethanol extract of the stem bark shown in **Table I** contains phytochemicals, including alkaloids, tannins, terpenoids, carotenoids, and coumarin. The stems contain alkaloids, tannins, coumarins, carbohydrates, and carotenoids. The leaves contain flavonoids, tannins, carotenoids, and coumarins (Wulandari et al. 2018). The 70% ethanol extract of *Litsea angulata* seeds contains flavonoids, alkaloids, saponins, and tannins (Ramadhan et al., 2020). The essential oil components of *Litsea angulata* leaves analyzed using Gas Chromatography-mass spectrophotometry (GC-MS) have been reported to contain monoterpenoids (85.28%), β-pinene, and (S)-cis-verbenol (Figure 1) (Kuspradini et al., 2020). *Litsea angulata* stem bark containing n-hexane has been reported to contain

steroid and triterpenoid compounds. Ethanol extract has been reported to contain flavonoids, saponins, steroids, and triterpenoids (Ramadhan et al., 2021). The total flavonoids of the ethyl acetate fraction of kalangkala leaves with the eluent ethylacetate:hexane (3:7) were reported by UV-Vis spectrophotometry to be 0.9 mg QE/g (Mardlatillah et al., 2023). The chromatographic profile of the total flavonoid content with the eluent n-hexane: ethyl acetate (8:12) was reported as 8.367 mg QE/g (Astuti et al., 2023).

The ethanol extract of *Litsea angulata* stem bark has been reported to contain flavonoids, saponins, tannins, and alkaloids (Fitriyanti et al., 2020). The seeds of *L. angulata* fruit were extracted, fractionated, and isolated using flash chromatography techniques. Molecular structure determination using nuclear magnetic resonance (NMR), 1H-NMR, 13C-NMR, and confirmed as the active compound β-sitosterol (C29H50O) is shown in **Figure 1** (Ilmia, 2024).



(1) (2) (3)

Figure 1. ***Compounds found in kalangkala plants include (1) β-pinene, (2) (S)-cis-veratronol, and (3) β-sitosterol (Kuspradini et al., 2020;Kurniawan et al., 2021).***

Table I. Phytochemical Compounds of Kalangkala Plants (Litsea angulate)

No	Source	Solvent	Analytical method	Analytes of interest	Reference(s)
1.	Fruit seed	Methanol	Qualitative with TLC	Alkaloids and tannins	(Mustikasari & Ariyani, 2010)
2.	Fruit seed	Ethanol 70%	Qualitative with TLC	Flavonoids, alkaloids, saponin dan tannins	(Ramadhan et al., 2020)
3.	Bark	Ethanol 95%	Qualitative with TLC	Alkaloids, tannins, terpenoids, karetenoids, kumarin	(Wulandari et al., 2018)
4.	Bark	n-hexane	Qualitative with TLC	Steroid dan triterpenoid	(Ramadhan et al., 2021)
5.	Bark	Ethanol		Flavonoids, saponins, steroid, triterpenoid	(Ramadhan et al., 2021)
6.	Stem	Ethanol 95%	Qualitative with TLC	Alkaloids, tannins, terpenoid, carbohidrat, caretenoids, coumarins	(Wulandari et al., 2018)
7.	Leaf	Ethanol	Qualitative with	Flavonoids,	(Wulandari et

		95%	TLC	tannins, carotenoids and coumarins	al., 2018)
8.	Leaf	Aquadest fraction (aquadest (butanol: acetic acid: distilled water (4:1:5))	Thin Layer Chromatography and UV-Vis Spectrophotometry	Flavonoids	(Amalia et al., 2022)
9.	Leaf	Ethyl acetate fraction ethylacetate: hexane (3:7)	Thin Layer Chromatography and UV-Vis Spectrophotometry	Flavonoids	(Mardlatillah et al., 2023)
10.	Essential oil from leaves	Distillation	Gas Chromatography-mass spectrophotometry (GC-MS)	β-pinene and (S)-cis-verbenol	(Kuspradini et al., 2020)
11.	Fruit seed	Ethanol, n-hexane, ethyl acetate and methanol fractions	Flash chromatography determines molecular structure using Nuclear Magentic Resonance (NMR), 1H-NMR, 13C-NMR,	confirmed isolate of the active compound β-sitosterol (C29H50O)	(Oswari, L. D, 2021)

Antioxidant Activity

The antioxidant activity of *Litsea angulata* from branches, bark, and leaves using n-hexane, ethyl acetate, and ethanol fractions is shown in **Table II** with varying concentrations of 12.5, 25, 50, and 100 ppm through inhibition of DPPH free radicals. The results showed that the IC_{50} value for each n-hexane fraction was best obtained from the stem bark, with an IC_{50} value of 17.12 ppm. The ethyl acetate fraction of stem bark had the strongest antioxidant activity with an IC_{50} value of 2.41 ppm. The ethanol fraction had the highest antioxidant activity, with an IC_{50} value of 14.58 ppm (Kusparadini et al., 2018;Kuspradini et al., 2019).

The antioxidant activity of the 96% ethanol extract of *Litsea angulata* seeds and fruit qualitatively, using the DPPH color degradation parameter from purple to yellow, was proven on a thin layer chromatography plate showing yellow spots on a purple background. Quantitative research on *Litsea angulata* seeds had an IC_{50} value of 48.78 ppm. For *Litsea angulata* fruit, the IC_{50} value was 243.14 ppm. Antioxidant activity was stronger in *Litsea angulata* seeds than in fruits (Saputri & Susiani, 2018). The antioxidant activity of the 96% ethanol extract of *Litsea angulata* leaves and stem bark qualitatively with DPPH showed a yellow color with a purple background on a thin layer

chromatography plate. Quantitative research on *Litsea angulata* leaves had an IC_{50} value of 152.39 ppm. The IC50 value of the stem bark was 85.33 ppm, indicating that *L. angulata* stem bark has stronger antioxidant activity (Susiani & Saputri, 2020).

Litsea angulata leaf essential oil is reported to have antioxidant activity by inhibiting DPPH at a concentration of 0-50 µg/ml (Kuspradini et al., 2020). A 96% ethanol extract of *Litsea angulata* leaves was formulated into effervescent tablets using the simplex lattice design (LSD) method. The test parameters were friability, hardness, and dissolution time. The results showed that the optimal tablet formula was formula 3 with a dose of 53 mg citric acid and 75 mg sodium bicarbonate with a desirability value of 0.516. The optimal granule evaluation is given by Formula 2. Leaf ethanol extract effervescent tablets showed antioxidant activity using the DPPH method in the strong category with an IC_{50} value of 52.21 ppm. Antioxidant activity is thought to originate from secondary metabolites of flavonoids (Rohama et al., 2022).

The methanol fraction of *L. angulata* fruit seeds has antioxidant activity by inhibiting DPPH free radicals, with an IC50 value of 7.36 ± 0.47ppm (Ilmia, 2024). The 80% methanol extract of Litsea garciae fruit seeds was reported to have antioxidant activity by inhibiting DPPH, FRAP and ABTS free radicals with EC_{50} values of 17.32 mg/ml, 1,910 mg/ml, 19.4 mg/ml. Water extract of Litsea garciae fruit seeds showed antioxidant activity of 22.7 mg/ml, 6.90 mg.ml, 6.86 mg/ml (Hawa et al., 2013).

Table II. Antioxidant Activity of Kalangkala Plant (*Litsea angulata*)

No	Source	Solvent	IC_{50} value (ppm)	Reference
1.	Branches	n-hexsane	117.92	(Kusparadini et al., 2018)
		Ethyl acetate	52.75	(Kuspradini et al., 2019)
		Ethanol 96%	26.81	
2.	Bark	n-hexsane	76.12	(Kusparadini et al., 2018)(Kuspradini et al., 2019)
		Ethyl acetate	2.41	
		Ethanol 96%	14.69	(Kusparadini et al., 2018)(Kuspradini et al., 2019)
3.	Leaf	n-hexsane	113.51	
		Ethyl acetate	127.14	
		Ethanol 96%	14.58	
4.	Seed	Ethanol 96%	48,78	(Saputri & Susiani, 2018)
5.	Fruit	Ethanol 96%	243.14	
6.	Leaf	Ethanol 96%	152.39	(Susiani & Saputri, 2020)
7.	Bark	Ethanol 96%	85.33	
8.	Leaf	Ethanol 96%	52.21	(Rohama et al., 2022)
9.	Fruit seed	Methanol	7.36	(Oswari, L. D, 2021)

Antibacterial Activity

The antibacterial activity of *Litsea angulata* branches, bark, and leaves with n-hexane, ethyl acetate, and ethanol fractions against the growth of Staphylococcus aureus and mutant Streptococcus is shown in **Table III** using 96-well microdilution of liquid media, with various concentrations of 1250, 625, 312.5, 156.25 ppm. The results showed that all fractions from various parts of the plant inhibited bacterial growth at a concentration of 156.25 ppm. The minimum kill concentration in all parts of the plant could not be detected at a concentration of 156.25 ppm – 1250 ppm, which requires

higher concentrations (Kuspradini et al., 2019). The ethanol extract of 70% *Litsea angulata* seeds was reported to have antibacterial activity using the well diffusion method with varying doses of 100%, 50%, 25%, 12.5%, 6.25%, and 3.125%. The results of this study showed an MIC value of 25% and an average diameter of drinking resistance of 8.667 mm in Propionibacterium acnes bacteria in the medium category (Ramadhan et al., 2020).

The antibacterial activity of *Litsea angulata* leaf essential oil has been reported to inhibit the growth of *Streptococcus mutans, Staphylococcus aureus, Streptococcus sobrinus,* and *Candida albicans* using the diffusion method, with an inhibitory power of 11.44 – 50 mm. The MIC was obtained at a concentration of 1%. The highest inhibitory activity was on *Streptococcus mutans* and *Streptococcus sobrinus* (Kuspradini et al., 2020). The 96% ethanol extract of *Litsea angulata* leaves in the mouthwash preparation formula was reported to have antibacterial activity at varying doses of 2%, 2.5%, and 3% in each formula using the agar diffusion method. It was reported that 3 doses of the 3% formulation were able to inhibit the growth of mutant Streptococcus bacteria (Rohama & Melviani, 2021). Antibacterial activity of 96% ethanol extract of *Litsea angulata* leaves in capsule formula using various doses of 100, 200, and 300 mg using the positive control ciprofloxacin dilution method. The results showed that all formulas inhibited the growth of Escherichia coli but did not kill bacteria (Wulandari et al., 2023).

Table III. ***Antibacterial Activity of Kalangkala Plant (Litsea angulata) extract from various parts of plants was expressed in MIC (minimum inhibitory concentration (MIC).***

No.	Source	Solvent	Type of bacteria	Method	MIC	Reference
1.	Branches	n-hexsane Ethyl acetate Ethanol 96%	*S. aureus* and *S. mutans*	96-well microdilution of liquid media	156.25 ppm 156.25 ppm 156.25 ppm	(Kuspradini et al., 2019)
2.	Bark	n-hexsane Ethyl acetate Ethanol 96%	*S. aureus* and *S. mutans*	96-well microdilution of liquid media	156.25 ppm 156.25 ppm 156.25 ppm	(Kuspradini et al., 2019)
3.	Leaf	n-hexsane Ethyl acetate Ethanol 96%	*S. aureus* and *S. mutans*	96-well microdilution of liquid media	156.25 ppm 156.25 ppm 156.25 ppm	
4.	Seed	Ethanol 70%	*Propioni bacterium acnes*	Well diffusion	25%	(Ramadhan et al., 2020)
5.	Essential oil from leaves		*S.mutan*, *S.aureus*, *S.sobrinus*, dan *Candida albican*	Agar diffusion	1%	(Kuspradini et al., 2020)
6.	Leaf	Ethanol 96%	*S. mutan*	Agar diffusion	3%	(Rohama & Melviani, 2021)

Antidiabetic Activity

The antidiabetic activity of *Litsea angulata* fruit seeds in vivo is shown in **Table IV**, using varying doses of 100 mg, 200 mg, and 400 mg/kg BW with 6 groups of 5 test animals each, with induction of alloxan 150 mg/kg BW, positive control metformin 45 mg/kg BB. The research results were reported on the 3rd day after induction, and all mice had diabetes with blood sugar levels > 200 mg/dl on the glucometer, except the normal group. The increase in blood sugar levels in mice after being induced by alloxan induction is thought to be caused by damage to cell membrane permeability, which causes damage to pancreatic β-cells that produce insulin (Irdalisa et al., 2021). Observation of the 7th and 14th days of all rats treated with Litsea angulata fruit seed extract at doses of 100 mg, 200 mg, and 400 mg/kg body weight showed a decrease in blood sugar levels, as did the group of mice administered metformin, but this was significantly different from the negative group (Adawiyah, 2024). This incident is thought to be due to the possible presence of bioactive content in Litsea angulata fruit seeds, namely polyphenols and other bioactive components that play a role (Amalia et al., 2022). Polyphenols play an important role in blocking the activity of the α-glucosidase enzyme, which accelerates the absorption of glucose into the intestine, resulting in a decrease in blood sugar levels (Oswari, 2021).

The methanol fraction of *Litsea angulata* fruit seeds has antidiabetic activity with the best enzyme activity/concentration value in inhibiting the α-glucosidase enzyme at 4.88 ± 10.69 U/L. If the enzyme activity/concentration is small, the enzyme's ability to degrade the substrate is higher, causing more products to be produced. This event is thought to play an important role in the bioactive components that cause low α-glucosidase enzyme activity, resulting in reduced glucose production and glucose absorption in the blood. Flavonoids are thought to be the bioactive compounds that play a role (Ilmia, 2024). The ethanol extract of *Litsea angulata* fruit seeds is reported to have nephroprotective activity at doses of 100, 200, and 400 mg, capable of reducing creatinine, urea, and SGPT levels. Doses of 200 mg and 400 mg reduced SGPT and were hepatoprotective in alloxan-induced rats. Flavonoids are thought to play an important role in this process (Daipadli, 2024).

Table IV. ***Antidiabetic activity of Litsea angulata plant.***

No	Plant parts	Method	Parameter	Results	Reference
1.	Fruit Seed	in vivo with animal models of diabetes with alloxan induction, positive control metformin, extract doses of 100 mg, 200 mg and 400 mg	Decreased blood sugar levels on days 3, 7, 14 with a glucometer	All rats treated with *Litsea angulata* fruit seed extract with dose variations of 100 mg, 200 mg, and 400 mg / kg body weight showed a decrease in blood sugar levels	(Adawiyah, 2024)
2.	Fruit Seed	in vitro α-glucosidase inhibitor	Measurement of absorbance at a wavelength of 450 nm at 0 minutes and	Value in inhibiting the α-glucosidase enzyme of 4.88 ± 10.69 U/L	(Ilmia, 2024)

			20 minutes		
3.	Fruit Seed	in vivo using animal models of diabetes induced by alloxan 150 mg/kgBW, metformin 45 mg/kgBW, ethanol extract of fruit seeds 100 mg, 200 mg and 400 mg, using blood serum to determine nephroprotective activity by spectrophotometry, hepatoprotective by hematoxylin eosin staining	Creatinine, urea, SGPT and SGOT activity and liver hispathology	Ethanol extract of kalangkala fruit seeds at doses of 100 mg, 200, 400 mg can reduce levels of reatinine, urea, SGPT activity. doses of 200 mg and 400 mg reduce SGOT activity and improve the histopathological appearance of the liver in test animals.	(Daipadli, 2024)

Toxicity Activity

The toxicity of *Litsea angulata* tree bark using the Brine Shrimp Lethality (BST) method has been reported to kill A. salina Leach shrimp larvae. A higher level of toxicity was observed for the extract with an LC_{50} value of 21.96 ppm at a concentration of 0.00394 mg. The n-hexane fraction had an LC_{50} value of 32.89 ppm at a concentration of 0.00327 mg. A lower LC_{50} value indicates a greater level of toxicity (Ramadhan et al., 2021). This was thought to be due to the presence of different phytochemical components in the two fractions. The n-hexane fraction of *L. angulata* tree bark contains steroids and triterpenoids. The ethanol extract of *L. angulata* tree bark contains more phytochemical compounds, including flavonoids, saponins, steroids, and triterpenoids, which have the potential for toxicity (Ramadhan et al., 2021).

Spermicide Activity

Spermicide activity of methanol extract of *Litsea angulata* seeds in vitro against spermatozoa taken from the secret cauda epididymis of 25 male mice of the Balb/c strain in a completely randomized manner in 5 groups. The results reported that a concentration of 0.5% methanol extract of *L. angulata* seeds reduced the motility parameters and movement speed of spermatozoa until they reached zero. This decrease in motility is likely due to secondary metabolites contained in *Litsea angulata*, including tannins, which are cytotoxic, causing a decrease in the quality of spermatozoa (Akmal et al., 2016).

CONCLUSION

This review article concludes that the kalakala plant (Litsea angulata) has pharmacological activity as an antioxidant, antibacterial, spermicide, and antidiabetic properties. Further research is needed to determine the pharmacological potential of Kalakala plants in the discovery of new drugs using various methods.

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