



REVIEW

# Theoretical Evaluation of *Michelia* Species' Bioactive Compounds and Therapeutic Potential: A Literature Review

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## Abstract

*Michelia alba* is a multifunctional plant found in Indonesia and is also called magnolia. *Michelia alba* is a tree known for its essential oil, which has long been used as a fragrance ingredient in perfumes and cosmetics. The potential of *M. alba* is immense for use in the prevention and treatment of disease as well as the management of human health and wellness. To date, there have been few publications regarding the biological activities of *M. alba*, focusing on tyrosinase inhibitory, antibacterial, antidiabetic, anti-inflammatory and antioxidant activities. However, *M. alba* may have additional undiscovered biological activities associated with its bioactive compounds. The purpose of this literature review research is to find out the bioactive compounds and therapeutic potential of the *M. alba* plant through literature searches that can be a reference for further research. The literature review method is carried out by searching and collecting data from literature sources obtained from several national and international journals that review bioactive compounds and the therapeutic potential of *M. alba* plants. Based on the literature review, it was found that *M. alba* has bioactive compounds namely linalool (72.8 flower oil and 80.1% leaf oil),  $\alpha$ -terpineol (6.04% flower oil), phenylethyl alcohol (2.58% flower oil),  $\beta$ -pinene (2.39% flower oil) and geraniol (1, 23%) which have therapeutic activities such as mental health disorders, anticancer, anti-inflammatory, antihypertensive, antidiabetic, antihyperlipidemia, antimaagic, antidiarrheal, anti-asthma, and antihyperpigmentation. In traditional medicine it is used to treat fever, syphilis, gonorrhoea and malaria, bronchitis, prostatitis, cancer, headache, sinusitis, cough, inflammation of the respiratory tract, chest fullness, flatulence, nausea, body and underarm odor, and vaginal discharge.

## Introduction

Indonesia is a country rich in various types of plants, both from low to high levels [1,2]. Plant diversity has so many benefits for human life, one of which is as a traditional medicine [3,4]. Plants that are used as medicines get great attention in addition to providing beneficial physiological and pharmacological effects as well as to avoid the use of synthetic drugs that tend to have more side effects. Plants that are rich in medicinal benefits that have been widely used by the community, one of which is the white champaca plant (*Michelia alba* DC).

*Michelia alba* (*M. alba*) is a multifunctional plant found in Indonesia and is also called magnolia. *M. alba* tree can produce a powerful distinctive aroma, mainly during the night [5]. The potential of *M. alba* recognized for its essential oil, has a significant role in preventing and treating diseases, and also in maintaining human health and well-being. This tree's essential oil has been a traditional component in perfumes and cosmetics due to its enduring popularity. Moreover, extensively utilized as flavor-boosting elements of food and beverage [6]. The plant is employed

in traditional medicine for the treatment of treat malaria, fever, gonorrhea, and syphilis [7,8], cancer, prostatitis, bronchitis, [7]. sinusitis, headache, inflammation of the respiratory tract, cough, flatulence, chest fullness, body and underarm odor, vaginal discharge, and nausea [9].

*M. alba*'s utilization in traditional medicine is associated with its bioactivity and the content of secondary metabolites, particularly essential oils [10]. Essential oils are generated by all parts of *M. alba*, albeit with variations in types and concentrations. Generally, the production of linalool (is a terpene alcohol) is more pronounced in flower organs when compared to other parts. The compound 1,10-di-epi-cubenol is exclusively present in the stem, copaene, ethyl 2-phenylhexanoate, borneol, and selinene are solely detected in the leaves [11]. *M. alba* has bioactive compounds namely Linalool (72.8% in flower oil and 80.1% in leaf oil),  $\alpha$ -terpineol (6.04% in flower oil), phenylethyl alcohol (2.58% in flower oil),  $\beta$ -pinene (2.39% in flower oil), and geraniol (1.23%), which have therapeutic activities such as mental health disorders, anticancer, anti-inflammatory, antihypertensive, antidiabetic, and antihyperlipidemia [6].  $11\alpha,13$ -dihydroparthenolide,  $11\alpha,13$ -dihydro- $\beta$ -cyclocostunolide, costunolide,  $9\beta$ -hydroxy-dihydroparthenolide, (-)-bisparthenolidine, cadinol, parthenolide, and magnograndiolide are exclusively present in the bark and roots [12].

The purpose of this study is to comprehensively explore the bioactive compounds of *M. alba*. Through a literature review, the research seeks to identify and analyze the specific compounds present in different plant organs, elucidating their therapeutic potential. By highlighting *M. alba*'s historical use in traditional medicine to address diverse health conditions, the study aims to provide insights for the avoidance and treatment illness. Ultimately, which find aspire to contribute valuable information for researchers and healthcare practitioners, guiding future investigations and promoting the utilization of *M. alba* in herbal medicine.

## Taxonomic Insights and Morphological Features of *Michelia alba*

### Taxonomy and Naming

*M. alba* plants are taxonomically categorized within the Kingdom Plantae, Division Magnoliophyta, Class Magnoliopsida, falling under the Order Magnoliales, Family Magnoliaceae, and the Genus *Michelia*, with the specific species being *Michelia alba*.

*M. alba* is typically grown in tropical and subtropical areas, such as those found in Southeast Asia [8]. *Michelia alba* is indigenous to Indonesia, Thailand, and Malaysia. Within these nations, this flowering plant is extensively grown for decorative purposes [13]. *M. alba*, a yearly blooming plant, attains a maximum height of 20 meters in regions with high humidity during its life cycle [8]. Picture of the *M. alba* plant can be seen in Figure 1. Green leaves are elliptical to oblong-ovate, Measuring 15 to 35 cm in length and 5.5 to 11 cm in width. Leaf blade is cuboidal, hairless on top. The flowers emit a fragrant scent, particularly in the evening, boasting a 5 cm diameter. Petals come in white or cream hues, measuring 30-55 mm. Lanceolate in shape, they span  $3-5.5 \times 0.3-0.5$  mm. The stamens are sized at 8-10 mm [6].



**Figure 1.** White champaka plant (a) tree, (b) leaf, (c) flower (photo taken on *M. alba* planted in Kerkhoff Poetjoet Banda Aceh).

### Botanical Name

White champaca, scientifically known as *Michelia* × *alba* D.C., Figlar, is also referred to by various names such as *Michelia alba*, *Magnolia* (D.C.), *Magnolia longifolia* blume, Verh. Bat. Gen., *Figlar* × *alba*, *Michelia champaca* × *Magnolia montana*, *Magnolia longifolia* var. *racemosa* blume, Fl. java magnol., *Sampacca* × *longifolia* (blume) kuntze. Other common names include tjampaka momero, bailan, sampaka kulo, white sandalwood, white chempaka, tjempaka putih, white champaca, tjempaka mawuro, cempaka putih, tjapaka bobudo, chempak, chempaka puteh, bunga edga kebo, white jade orchid tree, tjapaka bobulo, chempaka, pecari putih, cempaka gading, tjempaka bodas, *Michelia champaca* auct. non linne, tjampaka pote, s. mopoulosi, petjari putih, patene, djeumpa gadeng, bunga edja mapute [6].

### Distribution Plant and Morphology

The *Magnoliaceae* family comprises approximately 240 species, with the majority (160 species) found within the *Michelia* genera, *Magnolia*, and *Manglietia*. *Michelia* sp. is the specific species utilized for essential oil production and stands as the second-largest genus within the *Magnoliaceae* family [14,15]. Currently, the taxonomic classification of *Michelia* L. remains uncertain, however findings from phylogenetic analysis indicate a close relationship between *M. alba* and *M. odora*. [16]. *M. alba* is common in tropical and subtropical areas like Southeast Asia and is extensively grown in China, particularly in the southern provinces of Yunnan, Guangdong, Fujian, Guangxi, and Hainan [8,17,18]. *M. alba* is indigenous to Thailand, Indonesia, and Malaysia. In these nations, this flowering plant is commonly grown for ornamental purposes [13].

*M. alba* is a yearly blooming plant that has the potential to reach a height of 20 meters in regions characterized by elevated humidity [8]. The morphological characteristics of *M. alba* are shown in Table 1. Flowering in the plant commences at a height ranging from 10 to 15 meters, and typically, the blossoming period initiates during the night, around 8-9 pm. The fragrance of the flowers disperses rapidly and extensively but diminishes in the afternoon. Consequently, the harvesting of *M. alba* flowers is commonly conducted during the night and early morning [8,13].

**Table 1.** The morphological characteristics encompassing the leaves, stems, flowers, fruits, and seeds of *Michelia alba* [6].

Plant Part	Morphological Features
Tree	Elevation: 10-30 meters Bark color: Gray
Leaves	Hue: Green Structuring: leathery, smooth on the upper side, with sparse hair on the lower side, elliptical to obovate-elliptical Dimensions: 15-35 cm in length and 5.5-11 cm in width. Tip: acuminate Acumen length: 0.7-30 mm Form: simple and elliptical
Twigs/ petiole	Twigs color: Grayish Twigs length: 15-50 mm Structuring: Sparingly appressed puberulent to smooth
Flowers	Odor: aromatic, particularly in the evening Width: 5 cm Lanceolate: 3–5.5 mm in length and 0.3–0.5 mm in width Stamens: 8–10 mm Filaments: 1–1.5 mm Flower Color: white/cream
Carpels	The plant does not yield fruit and is propagated through grafting. Carpels: mostly sterile, with few reaching maturity. Mature carpels: Oval to ellipsoidal. Size: 5 mm

## Bioactive Compounds of *Michelia alba*

*M. alba* is renowned for its valuable essential oil. Arabs pioneered the steam distillation method to extract essential oils during the Middle Ages, and these oils are distinguished by their potent fragrance. The volatile compounds originate from secondary metabolites derived from aromatic plants [19]. Extracting essential oils from *M. alba* is possible using its flowers, leaves, or stems [20]. Various extraction techniques such as solvent extraction, steam distillation, and enfleurage are frequently employed for obtaining essential oil from *M. alba*. Among these methods, steam distillation is a prevalent choice for commercial extraction due to its simplicity and cost-effectiveness [13,21].

The primary volatile compound found in *M. alba* leaves is linalool, and its concentration differs between leaves that are fresh and those that are dried, particularly concerning  $\beta$ -elemene, caryophyllene, and selinene. The leaves of *M. alba* also comprise various compounds such as (-)-N-Formylanonaine, lysicamine, (+)-epi-yangambine, pheophytin a, (+)-nornuciferine, aristophylla C, (+)-cyperone, (-)-oliveroline, michephyl A, and ficaprenol-10 [22]. Linalool constitutes the primary component of the leaf, with  $\beta$ -caryophyllene, nerolidol, caryophyllene oxide, and  $\beta$ -elemene present as minor constituents [23], (E)- $\beta$ -ocimene, (Z)- $\beta$ -ocimene,  $\beta$ -caryophyllene, cis- $\beta$ -elemene, caryophyllene oxide, and (E)-nerolidol humulene [11]. In 1982, a study identified 24 components in the essential oil extracted from the flowers of *M. alba*. These include  $\delta$ -cadinene, methyl,  $\beta$ -myrcene,  $\alpha$ -ylangene, camphene,  $\alpha$ -cubebene,  $\beta$ -cubebene,  $\beta$ -bisabolene, o-cymene, trans-carveol, methyl isoeugenol,  $\Delta^3$ -carene,  $\beta$ -selinene, trans-linalool oxide, methyl-2-methylbutyrate, eugenol, isoaristolene, limonene, cis-caryophyllene, linalool, ocimene, cis-linalool oxide,  $\beta$ -pinene, and  $\alpha$ -phellandrene [24]. Studies investigating the chemical composition of essential oils derived from the leaves, flowers, and stems of *M. alba* have revealed a collective count of 168 constituents. Among these, 102 constituents were identified in flowers, 101 in leaves, and 77 in stems [25,26]. Notably, in 2018, a novel compound called michelaine ( $C_{16}H_{19}NO_4$ ) was identified in *M. alba* flowers [27]. However, the biological effects of michelaine, a compound exclusive to *M. alba*, remain undisclosed.

Terpenoids play a crucial role in the growth and development of plants as essential secondary metabolites, contributing significantly to the aroma, taste, and color of plants. Additionally, these compounds serve as a defense mechanism, safeguarding plants against environmental stress, pests, and microorganisms [28]. The majority of identified chemical components are sourced from monoterpenes and sesquiterpenes. The principal constituents in *M. alba* oil include linalool,  $\beta$ -cubebene, eugenol methyl ether, caryophyllene,  $\alpha$ -fenchene, germacrene D,  $\alpha$ -humulene, eucalyptol, nerolidol, (E)-ocimene, isoeugenyl methyl ether, and 2,4-diisopropenyl-1-methyl-1-vinylcyclohexane [20,25,26,28]. *M. alba* exhibits a notable linalool content across various plant parts. The linalool concentration in leaves ranges from approximately 0.21% to 0.65%, in flowers from 1.63% to 4.89%, and in young twigs at around 0.43% [18]. Linalool is notably abundant in young flowers of *M. alba*, reported concentrations are ten times higher in flowers compared to leaves and stems. Moreover, linalool concentrations are also heightened in fallen leaves of *M. alba* [18].

## Therapeutic Potential of *Michelia alba*

To date, the number of reports on the bioactivity of *M. alba* plants is still very limited, The therapeutic effects of *M. alba* are attributed to the presence of bioactive compounds, so this suggests that *M. alba* has additional bioactivities that have not been reported. In this section can be seen in Table 2 regarding bioactive compounds from *M. alba* that can be used as additional therapeutic potential. Multiple studies have suggested the effectiveness of *M. alba* and its bioactive compounds in treating various diseases. These diseases were categorized based on different body systems, and a comparative analysis of the pathological mechanisms involved

was conducted. The impact of *M. alba* and its extracts on these diseases was summarized. Drawing from these results, a comprehensive review was undertaken to assess the influence of *M. alba* on systemic diseases and explore potential underlying mechanisms.

**Table 2.** Bioactive compounds of *M. alba* that can be used as potential therapeutics.

Active Compounds	Therapeutic Potential	Mechanism of Action	References
Linalool and (-)-anonaine	Anticancer	<ul style="list-style-type: none"> <li>Stimulator of the p53/CDKI pathway, hindering the proliferation of several leukemia cells possessing wild-type p53, such as Kasumi-1, HL-60, Molt-4, and Raji cells</li> <li>Preferential suppression of the proliferation of human melanoma cells (RPMI 7931), with no impact on normal keratinocytes cell lines (NCTC 2544)</li> <li>Suppressed cellular growth and induced anti-migratory and DNA-damaging effects in H1299 human lung carcinoma cells.</li> <li>induce DNA damage and reduce viability in HeLa cells</li> </ul>	[27,29–32]
(-)-linalool and geraniol	Antiinflammatory	<ul style="list-style-type: none"> <li>Hindered the generation and release of nitric oxide (NO) in lipopolysaccharide-activated J774.A1 macrophages.</li> <li>Reduced the expression of proinflammatory markers (such as iNOS, COX-2, PGE2, NO release, TNF-<math>\alpha</math>, and IL-6) in IL-1<math>\beta</math>-activated mouse chondrocytes.</li> </ul>	[33–35]
Linalool, $\alpha$ -terpineol, and $\beta$ -pinene	Mental Health Disorders	<ul style="list-style-type: none"> <li>Reduced the concentrations of dopamine, 3,4-dihydroxyphenylacetic acid, and homovanillic acid (HVA)</li> <li>Decreased lipid peroxidation levels in the hippocampus</li> </ul>	[36–38]
Linalool	Antihypertensive, Antidiabetic and Antihypertriglyceridemia	<ul style="list-style-type: none"> <li>Enhanced cardiovascular parameters by reducing cardiac hypertrophy, improving vasodilation, and decreasing vasoconstriction.</li> <li>Decreased levels of triglycerides</li> </ul>	[39]
Linalool and geraniol	Antiulcer	<ul style="list-style-type: none"> <li>Diminished the area of gastric lesions</li> <li>Elevated GSH levels and lowered MPO activity and gastric secretion</li> </ul>	[40,41]
$\alpha$ -terpineol	Antidiarrheal	<ul style="list-style-type: none"> <li>Diminished fluid formation and chloride ion loss through interaction with GM1 receptors and cholera toxin</li> </ul>	[42]
$\alpha$ -terpineol	Antiasthmatic	<ul style="list-style-type: none"> <li>Provoked relaxation in the smooth muscle of the trachea</li> <li>Reducing airway resistance (RL) and improving the dynamic compliance of the airway</li> </ul>	[43]
Nerolidol, $\alpha$ -humulene, and $\beta$ -elemene	Antihyperpigmentation	<ul style="list-style-type: none"> <li>Suppresses the activity of the enzyme tyrosinase</li> </ul>	[44]
(-)-N-formylanonaine	Skin protection	<ul style="list-style-type: none"> <li>Reduces both tyrosinase activity and total melanin content without causing adverse effects.</li> <li>Decreases the UVB-induced expression of matrix metalloproteinases, elastase, hyaluronic acid, and type I procollagen in human dermal fibroblasts</li> </ul>	[8,45]

## Toxicological Aspect of *Michelia alba*

Toxicity tests are tests intended to identify the toxic effects of a substance on biological systems to obtain data on the prevalent dose response of the test preparation. Toxicity testing of a compound in vitro and in vivo can be done. In vitro toxicity tests are tests conducted outside living organisms, such as isolated cells, bacteria, organs. In vivo toxicity test is a test conducted on the inside of living organisms, such as test animals [46]. Generally, toxicity parameters include LC<sub>50</sub> and LD<sub>50</sub>. LC<sub>50</sub> is the concentration of the test preparation in water that kills 50% of the test animals within a certain period of exposure [47]. Meanwhile, LD<sub>50</sub> is a single dose of the test preparation that causes 50% mortality of test animals due to oral administration [46].

In a 2022 study, the toxicity assessment of *M. alba* plants was carried out on shrimp larvae (*Artemia salina* Leach) using the Brine Shrimp Lethal Test (BSLT) method, which is determined by the LC<sub>50</sub> value. The data regarding shrimp larvae mortality were subjected to probit analysis to ascertain the LC<sub>50</sub> value. The findings of this research revealed that ethanol extracts from the flowers and leaves of *M. alba* exhibited LC<sub>50</sub> values of 831.76 ppm and 398.10 ppm, respectively [48]. Therefore, it can be concluded that the ethanol extract of *M. alba* demonstrates potential toxicity to shrimp larvae (*Artemia salina* Leach), as evidenced by an LC<sub>50</sub> value below 1000 ppm [49].

In contrast to the above study, toxicity test research by [40] states that all compounds in *M. alba* leaves are not mutagenic and not carcinogenic based on the Ames toxicity test using bacterial samples. Oral acute toxicity test against rodents (LD<sub>50</sub>) was used to evaluate the toxicity of all compounds. The LD<sub>50</sub> of all compounds in *M. alba* leaves was 1,535 to 1,917 mg/kg and belonged to the moderately safe group as per the guidelines of the United States Environmental Protection Agency [50].

## Conclusions

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This study demonstrated that *M. alba* plant has a lot of content in it, one of which is the linalool compound which is the main component of the *M. alba* plant which is mostly contained in the flowers and leaves. Bioactive compounds from *M. alba* plants have therapeutic effects that are very useful and diverse. *M. alba* plants have been reported to have bioactivities as tyrosinase inhibitors and photoprotectors, antimicrobials, antidiabetics, anti-inflammatories, and antioxidants. The plant is employed in traditional medicine for the treatment of prostatitis, syphilis, fever, cancer, gonorrhoea and malaria, headache, sinusitis, bronchitis, cough, inflammation of the respiratory tract, chest fullness, flatulence, nausea, body and underarm odor, and vaginal discharge. A number of reports on the bioactivity of *M. alba* plants are still very limited, so the development of its bioactive compounds as potential therapies really needs to be developed again in the future.

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