Michelia × *alba* (*M. alba*)

Subjects: Plant Sciences

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Michelia × *alba* (*M. alba*) is a flowering tree best known for its essential oil, which has long been used as a fragrance ingredient for perfume and cosmetics.

Keywords: Magnolia alba ; therapeutic ; bioactive compounds

1. Introduction

Michelia × *alba* (*M. alba*), also known as *Magnolia* × *alba* (D.C.) Figlar, is a perennial plant commonly found in tropical regions including Thailand, Indonesia, Malaysia, and China. The plant is well known for its flower essential oil, which is commonly produced through steam distillation [1]. Its scent is often described as sugary, floral, champagne like with a slight herbal scent. *M. alba* essential oil is registered under the category of GRAS “generally recognized as safe” (FEMA Number: 3950, CAS: 92457-18-6) under Section 201(s) of the Federal Food, Drug, and Cosmetic Act by Flavor and Extract Manufacturers Association (FEMA). The essential oil is a common fragrance ingredient found in skin care, perfume, and cosmetics. In addition, it is also widely used as a flavoring agent in baked goods, beverages, condiments, frozen dairy, gelatins/pudding, meat products, and soft candy.

To date, there are about 200 patents reported on *M. alba* essential oil. In addition, there is an increasing trend in the number of *M. alba* research publications since 2001 (https://link.lens.org/3k1hpsF0pmc, accessed on 12 January 2022). There are accumulating studies reporting its potential bioactivities including tyrosinase inhibition, photoprotection, anti-stress, anti-diabetic, antioxidant, anti-gout, and antimicrobial activities. Some of the studies focused on bioactive ingredients found in *M. alba* such as linalool (72.8% in flower oil and 80.1% in leaf oil), α-terpineol (6.04% in flower oil), phenylethyl alcohol, β-pinene (2.39% in flower oil), and geraniol (1.23% of flower oil) [2]. Notably, linalool is the primary component found in *M. alba* which is also found in lavender and jasmine oils [2] Numerous studies on linalool have reported its anti-cancer, anti-inflammatory, neuroprotective activity, anti-hypertensive activity, anti-ulcer, anti-hypertriglyceridemia, anti-psoriasis, antidepressant, and anti-diarrheal activities. In 2018, a new compound named Michelaine ($C_{16}H_9NO_4$) was discovered from the flower of *M. alba* [3]. However, the bioactivities of Michelaine that are uniquely found in *M. alba* are not established. Taken together, the pharmacological potential of *M. alba* has not been fully uncovered.

2. Botanical Description

2.1. Taxonomic Classification and Nomenclature

M. alba is a hybrid of *Magnolia champaca* (L.) Baill. ex Pierre and *Magnolia montana* (Blume) Figlar (International Plant Names Index (IPNI) Life Sciences Identifier (LSID): urn:lsid:ipni.org:names:20011680-1) [4]. The taxonomic classification and nomenclature of *Michelia* × *alba* are as follows (**Table 1**):

Table 1: Taxonomic classification and nomenclature of *Michelia* × *alba*

Kingdom	**: Plantae**
Division	**: Magnoliophyta**
Class	**: Magnoliopsida**
Order	**: Magnoliales**
Family	**: Magnoliaceae**
Genus	**: *Michelia***

Species	**: *Michelia* × *alba***

2.2. Botanical Name

2.2.1. Synonyms

Michelia × *alba*, *Michelia alba* D.C., Figlar, *Magnolia* (D.C.) *Figlar* × *alba*, *Magnolia champaca* × *Magnolia montana*, *Magnolia longifolia* Blume, Verh. Bat. Gen., *Magnolia longifolia* var. racemosa Blume, Fl. Java Magnol., *Magnolia champaca* auct. non Linne, *Sampacca* × *longifolia* (Blume) Kuntze.

2.2.2. Common Name

Bailan (白兰), White Sandalwood, White Champaca, White Chempaka, Cempaka Putih, Chempaka Puteh, Cempaka Gading, Chempak, Chempaka, Pecari Putih, White Jade Orchid Tree, tjempaka bodas, tjampaka momero, tjempaka mawuro, tjampaka pote, tjempaka putih, Djeumpa gadeng, petjari putih, sampaka kulo, s. mopoesi, bunga edga kebo, patene, bunga edja mapute, tjapaka bobudo, tjapaka bobulo.

2.3. Distribution and Plant Morphology

M. alba belongs to the genus *Michelia* (Magnoliaceae) which consists of about 30 species [5]. *M. alba* is commonly cultivated in tropical and sub-tropical regions such as Southeast Asia, and it is widely cultivated in China, especially in southern regions such as Fujian, Guangdong, Hainan, Guangxi, and Yunnan [5][6][7]. The flowering plant is also native to Thailand, Indonesia, and Malaysia. In these countries, *M. alba* is widely cultivated as an ornamental plant [1].

M. alba is an annual flowering plant that can grow as high as 20 m in high humidity regions [5]. The morphological features and pictures of the *M. alba* plant (**Figure 1**) are shown in **Table 1**. The plant starts to produce flowers at a height ranging from 10 to 15 m and the flowering time usually begins in the evening (8–9 pm). The flower scent is said to spread quickly and widely which will be faded in the afternoon. Therefore, the harvesting activities for *M. alba* flowers are usually conducted in the evening and at dawn [1][5].

Figure 1. Photos of *M. alba*. (**a**) carpels, (**b**) flower, (**c**) leaves, and (**d**) *M. alba* plant (photo taken on *M. alba* planted in University Teknology Malaysia Pagoh Campus).

3. Bioactivities *M. alba* Extracts

To date, there are a number of reported bioactivities of *M. alba* extracts, including tyrosinase inhibition and photoprotective activities, antimicrobial, antidiabetic, anti-inflammatory, and antioxidant activities.

3.1. Tyrosinase Inhibition and Photoprotective Activities

Tyrosinase is an enzyme that catalyzes the production of melanin. Overexpression of tyrosinase can cause various dermatologic disorders including post-inflammatory hyperpigmentation [8]. This condition is not only aesthetically undesirable, but it may affect patients' emotions and quality of life [9]. It has been reported that (−)-N-formylanonaine, a purified compound isolated from *M. alba* inhibits in vitro mushroom tyrosinase activity in a dose-dependent manner with an IC_{50} value of 74.3 μM [10]. This inhibition activity is comparable to an established tyrosinase inhibitor, kojic acid with a recorded IC_{50} value of 69.4 μM. In addition, a molecular docking study suggests the tyrosinase inhibitory effect of (−)-N-formylanonaine may be due to its ability to chelate two copper ions in the active site of tyrosinase [10]. In an epidermal melanocytes cell culture study, (−)-N-formylanonaine was found to inhibit human tyrosinase activity at concentration ranges of 10–200 μM. Consequently, melanin content was also found reduced in cells treated with this compound at the same concentrations with an EC_{50} value of 90 μM [10]. On the other hand, a cell culture study showed the potential of α-terpineol as a skin whitening agent. Treatment of α-terpineol (at 100 and 200 μM) was reported to reduce melanin content and tyrosinase activity in B16 cells stimulated with α-melanocyte-stimulating hormone (α-MSH) [11]. Importantly, α-terpineol at concentrations of 100 and 200 μM did not affect B16 cell viability. In the same cell model, α-terpineol also prevented oxidative stress by reducing cellular malondialdehyde and increased cellular GSH levels. Tyrosinase inhibition activity of phenylethyl alcohol has been reported by [12] using in vitro mushroom tyrosinase assay. This compound was isolated from *Rosa rugosa* Thunb. var. plena Regal tea. Phenylethyl alcohol inhibits mushroom tyrosinase activity in a dose-dependent manner with an IC_{50} value of 315 ± 13 μg/mL. However, kojic acid (positive control) showed more potent inhibitory activity with an IC_{50} value of 80 ± 17 μg/mL.

Exposure to solar ultraviolet (UV) radiation on the skin leads to photoaging. This condition is characterized by the degradation of extracellular matrix (ECM) proteins which include type 1 collagen, elastin, proteoglycans, and fibronectin. This will then damage the connective tissue and reduce the elasticity of the dermis [13]. Irradiation of UV promotes the formation of reactive oxygen species, induces the expression of the mitogen-activated (MAP) kinase signaling pathway, and upregulates the expression of matrix metalloproteinase (MMP)-1, MMP-3, and MMP-9 [13]. *M. alba* extract inhibits the expression of the three matrix metalloproteinases in UVB-induced activation of p-JNK and p-ERK on cultured human fibroblasts cells and consequently restores total collagen synthesis [13].

3.2. Antimicrobial Activity

Natural products from microorganisms, plants, animals, and algae may serve as a good source of novel antimicrobial compounds [14]. A number of phytochemical extracts from flowers (including *M. alba*) or their essential oils have been reported to have potential antimicrobial activities for treating various diseases [15][16][17].

3.2.1. Antibacterial and Anti-Fungal Activities

The antimicrobial activity of the Magnolia family may be due to the presence of various bioactive constituents extracted from different parts of the plants. *M. alba* is rich in carbohydrates, alkaloids, terpenoids, flavonoids, tannins, steroids, and phenols. It has been used not only in traditional medicine but also as a potential antiseptic for the prevention and treatment of microbial infections [18]. *M. champaca* seed and flower extracts were reported to inhibit the microbial growth of *Aeromonas hydrophila*, *E. coli*, *Edwardsiella tarda*, *Flavobacterium spp.*, *Klebsiella pneumonia*, *Salmonella typhi*, *Vibrio alginolyticus*, *V. parahaemolyticus*, *V. cholerae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus subtilis*, and *Shigella dysenteriae* [17][19][20].

M. alba and *M. champaca* exhibited comparable effects on antibacterial inhibition of *S. aureus*, *E. coli*, and *Psedumonas aeuroginosa* (**Table 1**). Notably, the antimicrobial activity of leaf oil was found stronger than that of stem oil on growth inhibition of *S. aureus* ATCC 13709; *E. coli* ATCC 25922; *Candida albican* ATCC 10231 [21]. In addition, [22] reported the *M. alba* dichloromethane leaf extract with 76.6% linalool gave a better inhibitory effect on the growth of *Psedumonas aeuroginosa*, *C. albican*, and *Fusarium oxysporium* compared with the n-pentane flower extract (PF) with 63.2% linalool. The dichloromethane leaf extract was an efficient *C. albicans* growth inhibitor, while *F. oxysporium* was more susceptible to the dichloromethane flower extract [22].

The methanol extract of *M. alba* bark was reported to inhibit the growth of *C. Verruculosa*, which causes leaf spot disease on rice [23]. It was found that the antifungal activity of *M. alba* essential oil was strongly correlated with linalool and caryophyllene which are known to inhibit the growth of *Aspergillus flavus* [24]. In addition, the antifungal activity of *M. alba* oil against the growth of *Aspergillus niger*, *Aspergillus flavus*, *Penicillium sp.*, *Rhizopus sp.*, *Fusarium sp.*, and *Cladosporium sp.* was demonstrated through the application of the oil to the surface of bamboo paper packaging boxes [25].

3.2.2. Antiparasitics

Anti-parasitic agents have various applications including organic or conventional livestock production systems. Domestic animals such as cattle, pigs, dogs, and cats carry harmful parasites such as *Trypanosoma cruzi* [26]. *T. cruzi* can easily infest livestock animals and becomes an endemic that causes a devastating impact on the livestock industry worldwide. The trypanocidal constituents from the ethanol extract of the bark of *M. alba* (**Table 2**) showed good antiparasitic activity against *T. cruzi* [27]. In addition, the pharmacological activities of −anonaine from *M. alba* have been reviewed by Li and colleagues [28] which showed that the compound gives a significant inhibitory effect against *Plasmodium falciparum* that causes malaria in humans. The compound also protected red blood cells against *P. falciparum*. As the compound shows low cytotoxicity in the Chinese Ovarian cell line, it may be a potential phytochemical compound for the treatment of malaria (The Pharmacological Ac.).

Table 2. Antimicrobial activities screening from different part of *Michelia x alba* plant.

Plant Part	Types of Extract	Types of Antimicrobial Assay and Pathogens Test	References
Antibacterial and antifungal			
Flower	**Essential oil**	**Well diffusion—*A. flavus***	[24][29]
Leaves and stems	**Essential oil**	**Disc diffusion—*S. aureus* ATCC 13709; *E. coli* ATCC 25922; *Candida albican* ATCC 10231**	[21]
Bark	**Crude methanol extract**	**Well diffusion—*Curvularia verruculosa***	[23]
Leaf	**Essential oil extract in dichloromethane**	**Disc diffusion and in vitro assay—*Psedumonas aeuroginosa* and *C. albican*; disc diffusion and in vitro assay—*F. oxysporium***	[22]
Flower	**Extract**		
-	**Essential oil**	**In vitro assay: *A. niger*, *A. flavus*, *Penicillium* sp., *Rhizopus* sp., *Fusarium* sp. and *Cladosporium* sp.**	[25]
-	**Essential oil**	**Agar plate of spore and mycellium of *A. flavus* WU 1511**	[24]
Flower	**Essential oil**	**Disc diffusion: *S. aureus* and *E. coli***	[30]
Antiparasitics			
Bark	**Caryophyllene oxide, costunolide, dihydrocostunolide, parthenolide, dihydroparthenolide, 11,13-dehydrolanuginolide, santamarine, and dehydrolinalool oxide**	***Trypanosoma cruzi***	[27]
-	**Individual compound isolated from *M. alba*: (−)-anonaine**	***Plasmodium falciparum***	[28]

3.3. Anti-Diabetic Activity

The anti-diabetic potential of *M. alba* essential oil was demonstrated through the inhibition of α-amylase, a digestive enzyme found in saliva and pancreatic juice. This enzyme digests complex carbohydrates into oligosaccharides and disaccharides. α-amylase inhibitors delay the hydrolysis of carbohydrates in the intestines [31]. Therefore, inhibition of α-amylase may serve as a therapeutic target for the prevention and medical treatment of diabetes [32]. The essential oil from *M. alba* inhibits α-amylase activity with an IC_{50} value of 0.67 mg/mL. The inhibition activity is lower than the positive control, acarbose, which showed an IC_{50} value of 0.06 mg/mL. GC-MS analysis of essential oil indicated the presence of β-linalool (65.03%) as its major compound [33]. A molecular docking study suggests the β-linalool forms hydrogen bonds with His-299 and Asp-300 residues of α-amylase with a binding energy of − 5.20 kcal/mol [33]. On the other hand, aldose reductase is an enzyme that converts glucose into sorbitol in the presence of nicotinamide adenine dinucleotide phosphate (NADPH). Accumulation of sorbitol in the cells has been associated with the development of diabetic neuropathy. Aldose reductase inhibitor can be used as a target to reduce the concentration of sorbitol in the cells. Lee et al. [34] reported that *M. alba* flower extract dose-dependently inhibits aldose reductase activity with an IC_{50} value of 1.98 µg/mL.

3.4. Anti-Inflammatory Activity

Gout is an inflammatory arthritis characterized by the accumulation of uric acid in the blood and further deposited within visceral tissues and joints. Xanthine oxidase catalyzes the oxidation of hypoxanthine to xanthine and its further conversion to uric acid. A number of plant extracts and their metabolites showed inhibition against xanthine oxidase [35]. Leaves extract of *M. alba* inhibits in vitro xanthine oxidase activity by 22.49% at a concentration of 100 µg/mL. The observed inhibition activity is higher than *Gliricidia sepium* which showed 6.94% at the same concentration. However, the inhibition activity of *M. alba* extract was found lower than several medicinal plants such as *Antegonon leptopus* (59%), *Mimosa pudica* (62.36%), and *Vitex negundo* (38.4%) at 100 µg/mL [36].

3.5. Antioxidant Activity

Oxidative stress has been recognized as one of the classical risk factors for human diseases such as cardiovascular diseases, cancers, and neurodegenerative diseases [37]. In biological systems, macromolecules such as lipids, proteins, and nucleic acids are prone to oxidation upon exposure to free radicals. Excessive production of free radicals and a low antioxidant level collectively contribute to oxidative stress leading to a negative impact on physiological function.

In 2018, Zheng and colleagues reported antioxidant activity and phenolics profile of 65 edible flowers in China [38]). In the study, the *M. alba* flower was extracted using a mixture of acetone/water/acetic acid (70:29.5:0.5, *v*/*v*/*v*). Its 2,2-diphenyl-1-picrylhydrazyl (DPPH) results showed that the extract recorded 58.22 µmol Trolox equivalents (TE)/g sample) on a dry weight basis, higher than several other edible flowers including *Panax pseudoginseng* (15.18 µmol TE/g sample), *Prunella vulgaris* (21.39 µmol TE/g sample), and *Siraitia grosvenorii* (21.03 µmol TE/g sample) [38]. In the 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonate) (ABTS) and ferric reducing antioxidant power (FRAP) assays, the extract showed 111.54 µmol TE/g of dry weight sample and 15.51 mmol of Fe2+E/100 g sample, respectively [38]. In another study, petroleum ether extract of *M. alba* flower showed DPPH free radical scavenging activity with an IC_{50} value of 0.7155 mg/mL. This inhibition activity is higher than in several other aromatic plants such as *Plumeria alba* and *Cananga odorata* [39].

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