

The Utilization and Bioactivity of *Murraya paniculata* (L.) Jack

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Abstract

Kemuning (*Murraya paniculata*) is a plant easily found in Indonesian home garden and has been long used as a traditional medicine. This study aims to explain the botany, utilization, and bioactivity of *M. paniculata*. The research method was conducted through online library research on Google Scholar using words such as: *M. paniculata*, *M. paniculata* bioactivity, and *M. paniculata* uses. The information found was then synthesized to obtain comprehensive information regarding the botany, utilization, and bioactivity of *M. paniculata*. The *M. paniculata* has a shrubby habit, scattered leaves, clustered flowers, white corollas, and produces a fragrant aroma. In traditional medicine, *M. paniculata* is used to treat stomach ache, diarrhea, headache, edema, thrombosis, fever reducer, astringent, anti-dysenteric, and tonic. The use of *M. paniculata* as a traditional medicine is related to its bioactivity as an antidepressant, anti-obesity, antibacterial, anti-cancer, antioxidant, and anti-diabetes mellitus. The compound Murranganonesenecionate has very strong anti-inflammatory properties, while coumarin has antimicrobial activity.

Keywords: *Murraya paniculata*; Anti-Depressant; Anti-microbial

1. Introduction

Kemuning (*Murraya paniculata*) is a plant easily found in various gardens in Indonesia. This plant is indigenous to East Asia, especially China (Mou et al 2021), but has spread to various countries, including Indonesia. Empirically, it appears that local Indonesians have long used the *M. paniculata* as an ornamental plant due to its beautiful, fragrant flower crowns. The *M. paniculata*, also known as orange jasmine, is economically important due to its edible fruit and diverse essential oil production (Joshi & Gohil 2023) as well as its marketable flowers.

Besides being used as an ornamental plant, *M. paniculata* has long been used as a traditional medicine. The all parts of *M. paniculata* such as bark, leaves, and flowers are used as medicine. In Nepal, *M. paniculata* is used in traditional medicine to treat stomach ache, diarrhea, stomach ache, headache, edema, and thrombosis (Dosoky et al 2016). Wu et al (2016) stated that *M. paniculata* is a of the important plants in traditional Chinese medicine which is used to treat various diseases such as fever reducer, astringent, anti-dysentery, and tonic. Rehman et al (2023) reported that *M. paniculata* is used to manage cardiovascular, intestinal, and respiratory (airway) disorders.

The use of plants as traditional medicine is related to the content of secondary metabolites and their bioactivity. The *M. paniculata* has anti-anxiety, antioxidant, antidepressant, anti-diabetic (Rehman et al 2023; Joshi & Gohil 2023), anti-obesity, antibacterial, anti-implantation, cytotoxic, anti-diarrheal (Joshi & Gohil 2023), antinociceptive, antibacterial, and analgesic bioactivity (Rehman et al 2023). Administration of hydro ethanol extract of *M. paniculata* leaves up to 5000 mg/kg body weight/day in mice has very low toxicity (Menezes et al 2015), so it has great potential to be developed as a herbal medicine.

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The utilization and bioactivity of plants are related to their secondary metabolite content. The content of secondary metabolites in plants varies greatly in both concentration and type. The coumarin compounds (murrangatin, murrangatin acetate, murranganonesenecionate, micropubescin) and flavonoids (3',4',5',7-tetramethoxyflavone) isolated from *M. paniculata* showed antibacterial activity against *Porphyromonas gingivalis* (Rodanant et al 2015).

The murranganonesenecionate has very strong anti-inflammatory properties. Coumarin from *M. paniculata* leaves has great potential for the development of antimicrobial drugs to treat periodontal disease (Rodanant et al 2015). This study aims to explain the botany, utilization, and bioactivity of *M. paniculata*.

2. Methodology

This article is based on a literature review of various research results published online in Google Scholar using words such as *M. paniculata*, *M. paniculata* bioactivity, and *M. paniculata* uses. Data analysis was conducted qualitatively. The data obtained were analyzed qualitatively. The information obtained was synthesized to obtain comprehensive information regarding the botany, bioactivity, and secondary metabolites of *M. paniculata*.

3. Results and Discussion

3.1. Botany of *M. paniculata* (L.) Jack

The genus *Murraya* is endemic to mainland South and East Asia (India, the Andaman Islands, the Indochina Peninsula, South China, the Malay Peninsula, the Indonesian Archipelago, the Philippines), New Guinea, New Caledonia, and Northeastern Australia. *Murraya* has long been cultivated primarily in tropical and subtropical regions. Flowers from April to August; fruits from September to December (Mou et al 2021).

Description: shrub or tree, up to 8 m tall. The older branches are grayish-white to pale yellowish-gray. Leaves 3–7-petiolate, lower leaves smaller; petiole rather short; leaf blade elliptic-obovate or obovate, 1–6 × 0.5–3.0 cm, glossy green, margin entire, apex rounded or obtuse, base rounded; upper surface glabrous and glossy, lower surface dull and paler, glabrous or downy on petiole, undersurface and leaf margin. Inflorescences in terminal or terminal and axillary cymes, more numerous, 5 in number, fragrant (Figure 1). The petals ovate, about 1.5 mm; sepals white, oblong, 1.0–1.5 cm. Stamens 10. Berries broadly ovate, 8–12 × 6–10 mm, orange to dark red when ripe; 1–2 seeds. Seeds are villous, with greyish white hairs (Mou et al 2021).

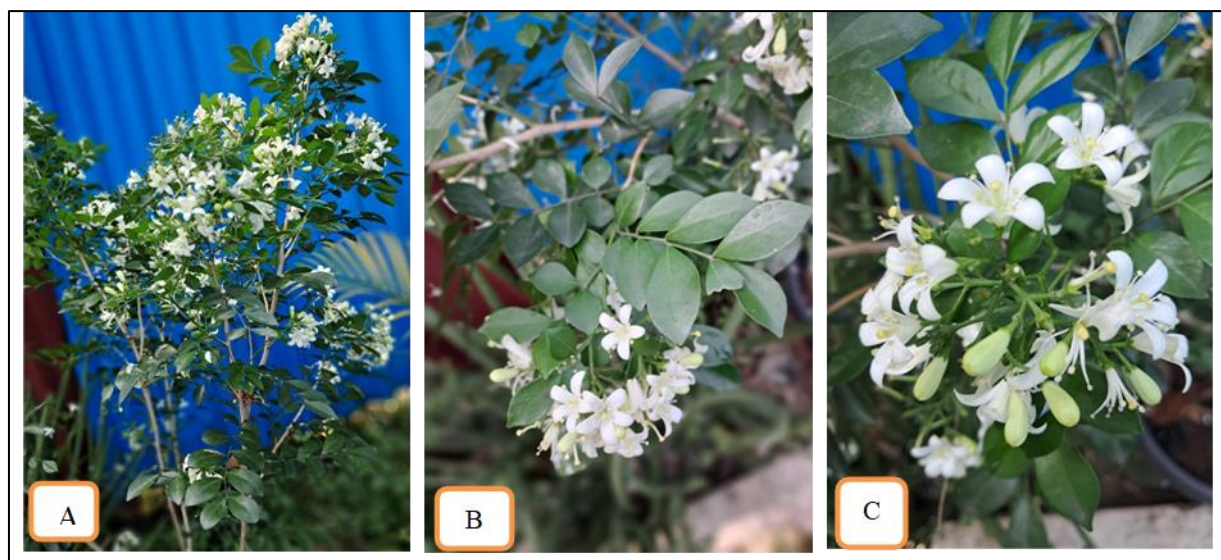


Figure 1 *Murraya paniculata*. A. The habitus; B. The branches with compound leaves; C. The flowering with open flowers and flower buds with white corolla

3.1.1. Utilization and Bioactivity

The all parts of *M. paniculata*, including the bark, leaves, and flowers, are used medicinally. The *M. paniculata* is a well-known medicinal plant, widely used to treat inflammation, stomach aches, and wounds (Zhu et al 2015). This plant also

has anti-anxiety, antioxidant, antidepressant, anti-diabetic (Rehman et al 2023; Joshi & Gohil 2023), anti-obesity, antibacterial, anti-implantation, cytotoxic, anti-diarrheal (Joshi & Gohil 2023), antinociceptive, antibacterial, and analgesic properties (Rehman et al 2023). The following will explain the benefits of *M. paniculata* as an antidepressant, cytotoxic, anti-obesity, antibacterial, anti-cancer, antioxidant, and anti-diabetes mellitus (Rehman et al 2023).

3.1.2. Anti-Microbial

Humans continually strive to protect their bodies from pathogenic microbes, while these pathogens continually replicate and mutate to infect humans (Tiwari et al 2022), which often leads to increased microbial resistance to antibiotics. Antimicrobial compounds are compounds that inhibit the growth or cause the death of microorganisms. The excessive use of antibiotics in humans has led to the emergence of antibiotic resistance, leading to ongoing exploration of new antibiotic uses (Sonter et al 2021). The *M. paniculata* can be used as a source of natural products with antibacterial resistance-modifying activity and reduced toxicity (Menezes et al 2015).

The various pathogenic microbes cause various human infectious diseases. Various pathogenic microbes in humans are *Salmonella typhimurium* (causes typhoid), *Staphylococcus aureus* (causes tooth decay and rheumatic fever) and *Escherichia coli* (causes tooth decay in infants and dysentery) (Tiwari et al 2022). The *Klebsiella pneumoniae* extended-spectrum β -lactamase is microorganisms that causes nosocomial infections that are resistant to beta-lactam antibiotics (Wiyogo et al 2021). The bioactivity of *M. paniculata* as an antibiotic has been reported by Selestino Neta et al (2017), Menezes et al (2015), Tiwari et al (2022), Wiyogo et al (2021), Rama et al (2022), and Rodanant et al (2015).

The *M. paniculata* has great potential for the development of antimicrobial drugs to treat periodontal disease (Rodanant et al 2015) and is promising and can be used in dentistry as a dental filling agent and as a nanomedicine in pharmaceuticals (Tiwari et al 2022). The extract of *M. paniculata* inhibits the growth of bacteria such as *Staphylococcus aureus* (Tiwari et al 2022; Selestino Neta et al 2017; Wiyogo et al 2021), *Escherichia coli* (Tiwari et al 2022; Wiyogo et al 2021), *Acinetobacter baumannii* (El-Shiekh et al 2024b), *Bacillus cereus* (Rama et al 2022), *P. gingivalis* (Rodanant et al 2015), *Salmonella typhimurium* (Tiwari et al 2022), *S. typhi*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Shigella flexneri*, and *Shigella sonnei* (Wiyogo et al 2021). The in vivo data from animal models support the high efficiency of *M. paniculata* stems as a promising extract for the main candidate against drug-resistant *Acinetobacter baumannii* lung infections (El-Shiekh et al 2024b). The Silver nanoparticles produced from *M. paniculata* showed the highest sensitivity against *Bacillus cereus* (Rama et al 2022). The ethyl acetate extract from *M. paniculata* leaves inhibited the growth of periodontopathic bacteria and reduced cytokines from lipopolysaccharide (LPS)-stimulated macrophages (Rodanant et al 2015).

The bioactivity of *M. paniculata* as an antimicrobial is thought to be related to its secondary metabolite content such as chlorogenic acid, caffeic acid, sinapic acid, feruloyl agmatine, and mahanimbodin (El-Shiekh et al 2024b). The ethyl acetate extract of *M. paniculata* contains coumarins (murrangatin, murrangatin acetate, murranganonesenecionate, micropubescin) and one flavonoid (3',4',5',7-tetramethoxyflavone) thought to be related to its antimicrobial properties (Rodanant et al. 2015). The *M. paniculata* is a traditional medicine believed to have antibacterial components, such as flavonoids, alkaloids, essential oils, coumarins, terpenoids, tannins, and saponins (Wiyogo et al. 2021). The total phenolic content of *M. paniculata* leaf hydroethanol extract samples varied from 66.5 to 396.8 mg equivalents of gallic acid/g extract and the flavonoid content varied from 0.3 to 31.1 mg equivalents of quercetin/g extract (Menezes et al. 2015). The essential oil β -caryophyllene showed moderate antibacterial activity and strong antifungal activity (Selestino Neta et al. 2017). The isolated coumarin compounds (murrangatin, murrangatin acetate, murranganonesenecionate, micropubescin) and one flavonoid (3',4',5',7-tetramethoxyflavone) showed antibacterial activity against *P. gingivalis* (Rodanant et al 2015).

3.1.3. Antioxidants

Antioxidants are compounds that inhibit reactive oxygen species. Free radicals are often linked to various diseases such as carcinogenesis, cardiovascular disease, and aging (Amanda et al 2019). Free radicals are directly and indirectly linked to various degenerative diseases. In traditional medicine, *M. paniculata* is widely used as an antioxidant (Menezes et al. 2017; Shanta et al. 2024), antinociceptive, anti-inflammatory, antioxidant (Menezes et al 2017), and cytotoxic (Shanta et al 2024).

Flavonoids, as active substances, can act as antioxidants by inhibiting oxidation reactions through radical scavenging mechanisms (Amanda et al 2019). The methanol extract of *M. paniculata* leaves shows flavonoid and phenolic content related to its antioxidant activity. Sonter et al (2021) reported that the acetone extract of *M. paniculata* leaves showed significant 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) inhibitory activity (IC₅₀ value: 555.18 $\pm$ 1.68 μ g/mL) and the hexane extract showed the highest H₂O₂ radical scavenging activity (IC₅₀ value: 509.84 $\pm$ 3.03 μ g/mL).

The bioactivity of *M. paniculata* as an antioxidant is influenced by various factors, including the ingredients used in the extraction. The methanol extract of *M. paniculata* showed strong antioxidant and radical scavenging activity (Zhu et al 2015). The aqueous fraction showed strong antioxidant activity compared to standard butylated hydroxytoluene, while petroleum ether, dichloromethane, chloroform and methanol extracts showed moderate antioxidant activity (Shanta et al 2024).

The bioactivity of *M. paniculata* as an antioxidant is related to its phytochemical content, including ergosterol endoperoxide, coumarin derivatives 7-methoxy-8-(3-methylbut-2-enyl)-1-benzopyran-2-one and 5,7-dimethoxy-8-(3-methylbut-2-enyl)-1-benzopyran-2-one, and a mixture of β -sitosterol and stigmasterol (Shanta et al. 2024). These compounds have shown potential to bind to the aldose reductase protein (Shanta et al 2024). Flavonoids have anti-inflammatory activity through reducing oksida nitrat (NO) production and IL-6 production (Wu et al. 2016). The roots *M. paniculata* contain various types of coumarins: murpanitin A and murpanitin B-D (Liang et al. 2020), Panitin D, trans-dehydroosthol, and exotimarin I (Wang et al 2029). The compounds Panitin D, trans-dehydroosthol, and exotimarin I showed strong inhibition of LPS-induced NO production in BV-2 microglia cells (Wang et al 2019).

3.1.4. Anti-Depressants

Depression is a mental health disorder that can affect human thoughts, feelings, and behavior. The Acetylcholinesterase (AChE) inhibitors or drugs used clinically for mental disorders, such as tacrine, donepezil, rivastigmine, and galantamine, are associated with serious side effects and a short half-life (Khalid et al 2023). Exploration of natural products to treat depression continues, including *M. paniculata* (Sharma et al. 2017; El-Shiekh et al 2024). The *M. paniculata* extract prepared with petroleum ether, chloroform, ethanol, and water has significant anxiolytic and antidepressant activity (Sharma et al. 2017). The leaf oil of *M. paniculata* exhibited potent inhibitory activity against AChE ($IC_{50}=13.2 \pm 0.9 \mu\text{g/mL}$) and butyrylcholinesterase/BChE ($IC_{50}=5.1 \pm 0.3 \mu\text{g/mL}$) (El-Shiekh et al 2024). The rats treated with *M. paniculata* fractions (50 mg/kg and 100 mg/kg) improved hypothalamic-pituitary-adrenal (HPA) axis dysfunction and increased 5-HT and Asam Gamma-Aminobutirat (GABA) levels in the hippocampus. The fraction compounds of *M. paniculata* increased A2AR expression, maintained GABAergic synaptic stability, and reduced anxiety by modulating microbiota composition, making them highly potential anxiolytic agents (Ma et al 2024).

The bioactivity of *M. paniculata* as an antidepressant is related to its various secondary metabolite contents. Natural coumarin compounds from *M. paniculata* leaves, namely 2'-O-ethylmurrangatin, murranganone, and paniculatin, have inhibitory activity against two cholinesterase (ChE) enzymes, AChE and butyrylcholinesterase (BChE) in vitro tests (Khalid et al 2023). The compound 5,7,3',4',5'-pentamethoxyflavone (PMF), a monomer extracted from *M. paniculata* leaves, has sedative and hypnotic properties (Ma et al 2024). Classical enzyme inhibition kinetics data show that murranganone and paniculatin compounds are potent inhibitors of AChE and BChE with competitive and non-competitive inhibitory mechanisms of compounds 2 and 3 against both enzymes. According to *M. paniculata* simulation studies, the stability of the ligand-AChE complex for the most active compound paniculatin was found to be comparable to that of the widely used drug, Tacrine (Khalid et al 2023).

3.1.5. Anti-Obesity

Obesity has become a global issue, impacting the emergence of various chronic diseases such as diabetes mellitus, dysplasia, heart disease, and cancer. In vitro tests to validate the potential of *M. paniculata* in treating obesity showed a significant decrease in the expression of the peroxisome proliferator-activated receptor gamma (PPARG) and histone acetyltransferase p300 (EP300) genes in mature 3T3-L1 adipocytes treated with *M. paniculata* ethanol extract starting at concentrations of 62.5 $\mu\text{g/mL}$ and 15.625 $\mu\text{g/mL}$, respectively (Fatriani et al 2024). The extract of *M. paniculata* has the potential to treat obesity by disrupting adipocyte maturation and affecting intracellular lipid metabolism (Fatriani et al 2024).

3.1.6. Anti-Cancer

Cancer is one of the leading causes of human death. Metastasis is the leading cause of death from lung carcinoma (Shi et al. 2017). In traditional Chinese medicine, *M. paniculata*, used in abortion, can function effectively for pre-metastatic chemoprevention (Jiang et al 2016). Finding safe and effective pre-metastatic preventive agents for cancer survivors is urgently needed (Shi et al 2017). *M. paniculata* contains the flavonoid glycoside, hexamethoxyl-o-[rhamnopyranosyl-(1 $\rightarrow$ 4)-rhamnopyranoside (HMFRR), which can effectively inhibit the adhesion, migration, and invasion of A549 lung adenocarcinoma cells in vitro (Shi et al 2017). Consequently, HMFRR interferes with the adhesion of A549 cells to HPMECs. HMFRR may be a good candidate for cancer metastasis chemopreventive agent by interfering with STAT3/NF- κ B/COX-2 and EGFR signaling pathways (Shi et al 2017).

The benefits of oral contraceptives in reducing cancer risk suggest molecular and cellular similarities between embryo implantation and circulating tumor cells adhesion-invasion to the endothelium (Jiang et al 2016). The extract *M. paniculata* containing flavonoids and coumarins inhibited embryo implantation to human endometrial sites and HT29 cancer cells to human endothelium in a concentration-dependent manner. This inhibition may be due to its downregulation of the expression of integrins $\beta 1$ and $\alpha 6$, and CD44 on HT29 cells, as well as E-selectin on endothelial cells. Pretreatment followed by one month of oral G administration in immunocompetent mice inoculated with mouse melanoma cells resulted in significant inhibition of lung metastasis without any apparent side effects (Jiang et al 2016).

3.1.7. Antidiabetes Mellitus

Diabetes mellitus is a metabolic disorder that results in higher than normal blood glucose levels. Various oral hypoglycemic agents and insulin have been widely used in the treatment of diabetes mellitus (DM), but exploration of natural products to reduce the effects of diabetic complications continues to increase (Menezes et al. 2017). Flavonoids are compounds thought to possess bioactivity as anti-DM agents (Zou et al 2021). The main component of *M. paniculata* leaves is flavonoids. The streptozotocin (STZ) was administered together with glycerol to rats. Diabetic rats induced with STZ and a high-fat diet showed severe histological changes and increased levels of cardiac function markers. The reactive oxygen species (ROS), inflammation, and apoptosis markers were also significantly increased, but antioxidant defenses were decreased (Zou et al 2021).

Alloxan-induced diabetic rats treated for 60 days with hydroalcoholic extract of *M. paniculata*, at doses of 100, 200, and 400 mg/kg, decreased glycemia as well as cholesterol and triglyceride levels, starting 1 week after treatment, compared with the same group before treatment. The extract of *M. paniculata* acts similarly to glibenclamide and metformin, and its glucose-lowering action is partly a consequence of inhibition of ATP-sensitive K⁺ channels (Menezes et al 2017).

3.1.8. Treating Respiratory Disorders

The *M. paniculata* is traditionally used to manage gastrointestinal, respiratory, and cardiovascular disorders (Saqib et al 2015). Application of a crude extract of *M. paniculata* relaxes spontaneous and high K⁺-induced contractions (80 mM) in rabbit jejunal preparations, shifting the calcium response curve (CRC) to the right, possibly blocking calcium channels similar to verapamil (Saqib et al 2015). In rabbit tracheas, a crude extract of *M. paniculata* produces carbachol relaxation and high K⁺-induced contractions. When the plant extract was further examined in isolated aortas for its possible vasodilator effects, it induced phenylephrine relaxation and high K⁺-induced spastic contractions at different doses. The *Murraya paniculata* exhibits antispasmodic, bronchodilator, and vasodilatory activities facilitated through a Ca⁺⁺ antagonist mechanism (Saqib et al 2015).

4. Conclusion

Murraya paniculata has a shrubby habit, scattered leaves with white flowers and a fragrant aroma.

In traditional medicine, *Murraya paniculata* is used to treat stomach ache, diarrhea, headache, edema, thrombosis, as a fever reducer, astringent, anti-dysenteric, and tonic.

The use of *Murraya paniculata* as a traditional medicine is related to its bioactivity as an antidepressant, cytotoxic, anti-obesity, antibacterial, anti-cancer, antioxidant, and anti-diabetes mellitus agent.

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