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Review

Millingtonia hortensis L.f. (tree jasmine): botany, ethnopharmacology, chemical constituents, biological activities of extracts and essential oils—an updated review

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Abstract

Millingtonia hortensis is extensively grown for decorative purposes due to its beautiful flowers and fragrant characteristics. *Millingtonia hortensis* is an unexplored plant for utilization of its chemical constituents for therapeutic applications. Therefore, the present review thoroughly analyzes the botanical features, chemical composition, and biological and pharmacological effects of *M. hortensis* essential oil (MHEO) and extracts. This review employed the leading scientific databases Google Scholar, Scopus, Web of Science, and PubMed between 2013 and the end of September 2024 and combined terms, *Millingtonia hortensis,* Botany, essential oil, phytochemistry and pharmacological activity. The MHEO yield varied between 0.02 and 3.57%. The main constituents of *M. hortensis* extract and essential oil include solanesol (25.7%), trans-farnesol (19.7%), and nerolidol (8.2%). MHEO and its active chemical constituents exhibit various biological capabilities, such as antioxidant, antimicrobial, anticancer, anti-inflammatory, and larvicidal, among other activities. However, several biological and pharmacological investigations lacked appropriate experimental settings, such as proper doses and positive and negative controls. Furthermore, many pharmacological investigations were exclusively carried out utilizing cell lines and animal models. Thus, this study suggested that further research investigations should be carried out in a proper scientific experimental setting to perform MHEO on human patients. This would broaden its scope of use in the pharmaceutical industry.

Keywords Antioxidant · Antimicrobial · Antiinflammatory · Essential oil yield · Larvicidal activity · *Millingtonia hortensis*

Abbreviations

DPPH	2,2-Diphenyl-1-picrylhydrazyl
IC_{50}	Inhibitory concentration
LC_{50}	Lethal concentration
MBC	Minimum bactericide concentration
MFC	Minimum fungicidal concentration
MIC	Minimum inhibition concentration
MHEO	*M. hortensis* Essential oil
ROS	Reactive oxygen species

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1 Introduction

Millingtonia hortensis L.f. is a member of the Bignoniaceae family and is native to South and Southeast Asia, specifically nations like India, Sri Lanka, Myanmar, Thailand, and Malaysia [1, 2]. It is frequently encountered in tropical and subtropical areas and flourishes in damp, well-drained soil [3]. *Millingtonia hortensis* can be propagated by sowing its seeds or using vegetative methods such as stem cuttings. The tree is widely grown for its aesthetically pleasing blossoms and aromatic qualities [4]. Furthermore, it is extensively grown as a decorative plant in gardens, parks and roadsides because of its sizable, heart-shaped foliage and attractive characteristics [5–7]. *Millingtonia hortensis* is highly esteemed for its aesthetic appeal and therapeutic qualities [8, 9]. The different components of *M. hortensis*, such as the bark, leaves, blossoms, and roots, have been utilized in traditional medicine to treat various conditions, such as fever, inflammation, asthma, sinusitis, and discomfort [5]. Furthermore, several societies incorporate flowers in religious ceremonies and rituals [9].

The plant mainly comprised significant active chemical constituents: tannins, alkaloids, cyclohexylethanoids, flavonoids, and phenolic compounds [2, 10]. Leaves contain several chemicals, including hispidulin, dinatin, and carotene [11]. The bark contains astringent compounds, including tannins. The plant's flowers contain high levels of hispidulin, scutellarein, scutellarein-5-galactoside, hortensin, and other compounds [12–14]. Deethae et al. [15] found that the main chemical constituents in *M. hortensis* stem bark ethanolic extracts were trans-13-octadecenoic acid, oleic acid, and isopropyl palmitate. The essential oil of *M. hortensis* flowers was obtained using hydrodistillation, yielding 0.5–2% [16]. The plant flower essential oil had significant chemical constituents of β-caryophellene, α-bergamotene,1-octen-3-ol, linalyl anthranilate, 2,3-dimethyl octane, 3-methyl undecane, trans-β-caryophellene, solanesol, trans-farnesol, nerolidol, palmitic acid, vanillin, and linalool [17, 18]. The various parts of the plant have shown a diverse array of therapeutic properties, including antibacterial, antifungal, antioxidant, anticancer, antiproliferative, anti-inflammatory, anthelmintic, antimutagenic, hepatoprotective, cardiovascular, and larvicidal effects [14, 15, 19–38].

Nevertheless, the pharmacological potential of organic chemical extracts and essential oils from *M. hortensis* and their active constituents has yet to be thoroughly investigated using rigorous scientific experimental procedures such as testing on specific organisms, determining appropriate dosages, and including control groups. Hence, the primary objective of this study is to comprehensively examine the botanical characteristics, essential oil yield, chemical composition, and biological and pharmacological properties of *M. hortensis* until November 2024. Furthermore, it identifies gaps in the current body of research for further investigation. It helps the public and scientists with the diverse biological and pharmacological properties of the extracts, MHEO, and their critical components for potential applications in the future.

2 Search strategy

This review provides a concise overview of the findings from a comprehensive literature search carried out from 2013 to 2024 on *Millingtonia hortensis*, tree jasmine, botany, ethnopharmacology, phytochemistry, pharmacology, and biological activities. The material and findings of this review were acquired not only via library searches for books and journals, but also from electronic journals available on websites such as Google Scholar, PubMed, Elsevier, Springer, Tyler and Francis, ACS, Science Direct, Frontiers, Willey, and Research Gate.

3 Ethnopharmacological uses

The ethnopharmacological significance of the aqueous extract of the *M. hortensis* flower was extensively used as an herbal treatment in Southeast Asia. This aqueous extract has been highly regarded in traditional medicine for its documented calming and anxiolytic effects [39]. Various parts of *M. hortensis* are utilized in traditional medicines. Leaves are utilized for their fever-reducing, sinusitis-relieving, bile-promoting, and tonic properties. Dried flowers are utilized as a pulmonary tonic and provide advantages in coughing-related respiratory conditions [14, 15]. *Millingtonia hortensis* dried flowers have been traditionally utilized in Thai folklore medicine as a component in cigarette production. These cigarettes are designed to emit a pleasant fragrance and a calming odour [40]. Asthma is treated with the inhalation of dried flower smoke. Flowers are also used to treat sinusitis. The root is used as a lung tonic and antiasthmatic [41, 42]. In traditional medicine, Mon people from Myanmar used root decoction of *M. hortensis* to treat hypertension and cancer [36]. In

Thailand's traditional medicine, the plant is used to treat chronic respiratory and cancer diseases [43, 44]. The plant includes hispidulin, a chemical that has been shown to have a bronchodilator effect on the trachea of rats [16].

4 Botanical description

Taxonomic classification

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Lamiales

Family: Bignoniaceae

Genus: Millingtonia

Species: hortensis

Botanical name: *Millingtonia hortensis* L.f.

Vernacular names

Tamil: Maramalli

English: Tree jasmine, Indian cork tree

Hindi: Neem Chameli

Telugu: Kavuki

Kannada: Akaya mallige [45]

4.1 Geographical distribution and cultivation

M. hortensis tree exhibits drought resistance and is widespread throughout central India. These trees are predominantly distributed in tropical forests and need direct sunshine for their growth and development. However, it likes a humid climate. Propagation is done through the seeds. The tree is indigenous to Burma and Malaysia but extensively grows in most parts of India [1, 2]. This species is distributed in India, Burma, Thailand, and Southern China. The plant features sizable, lustrous green leaves, producing aromatic, white, bell-shaped flowers blossoming in groups [46, 47]. Due to its aesthetic appeal, the tree is frequently cultivated in gardens, parks, and roadsides [2, 6].

4.2 Morphological characteristics

Millingtonia hortensis L.f. belongs to the Bignoniaceae family. The tree is of moderate to large size, with a maximum height of 25 m [47, 48]. The leaves of *M. hortensis* exhibit compound, opposite, and pinnate characteristics. Typically, each long leaf has two or three widely separated pinnae, each with 5–7 smooth leaflets [4]. The leaflets are oval-shaped and pointed, have a slightly round-toothed edge, and have a length ranging from 1 to 3 inches [1, 2]. At times, the lower pinnae may experience additional division, forming a single pair of three-leaved pinnae, 1–2 pairs of leaflets, and one leaflet at the end [6]. Without ever being wholly devoid of foliage, the tree experiences leaf shedding

from January to March and then leaf renewal from April to May. Notwithstanding the shedding and rejuvenation processes, the tree retains the leaf's resemblance. The leaves do not have a noticeable smell or slight bitterness [7].

The *M. hortensis* tree bears sizable, eye-catching, funnel-shaped white flowers with a pleasant scent and is placed in clusters at the ends of its branches [49]. The plant produces large clusters of white, asymmetrical blooms that provide a delightful scent [4]. Every flower possesses an elongated tubular corolla, including five lobes and a conspicuous golden throat. The flowers flourish profusely during the blossoming season, usually in the summer. The bark is initially greyish-brown and smooth but becomes rough as it ages and develops fissures [2]. *Millingtonia hortensis* produces elongated capsules that house a multitude of tiny seeds with wings. When the capsules reach maturity, they dehisce, releasing the seeds for wind dispersal [4]. The morphological identification of the complete *M. hortensis* tree, with its stem with bark, leaves, and flowers, is shown in Fig. 1.

5 Phytochemistry

5.1 MHEO yield

The extracts and MHEO derived from *M. hortensis* have diverse phytochemical components, such as terpenoids, phenolics, and other volatile constituents [50]. The essential oil from *M. hortensis* was extracted using solid phase micro-extraction (SPME), solvent extraction (petroleum ether), solvent extraction (95% ethanol), enfleurage, and hydrodistillation extraction techniques. Of these methods, the solvent extraction (95% ethanol) technique has a greater efficiency in extracting essential oils (Table 1). The MHEO yield ranged from 0.02 to 3.57% on a dry basis, depending on the variety, origin, extraction, and plant parts used [15, 17, 51, 52]. Earlier studies also reported that the essential oil yield and chemical constituents can differ based on various factors, including the specific parts of the plant, climate conditions, soil type, geographic location, and the procedures used for extraction [53–59].

5.2 MHEO and extracts chemical composition

Limited studies have been conducted to analyze the phytochemicals in the extract and essential oils of *M. hortensis*. GC–MS analysis of methanolic extracts of *M. hortensis* flowers mainly contains coumarin, trans-isoeugenol, phytol

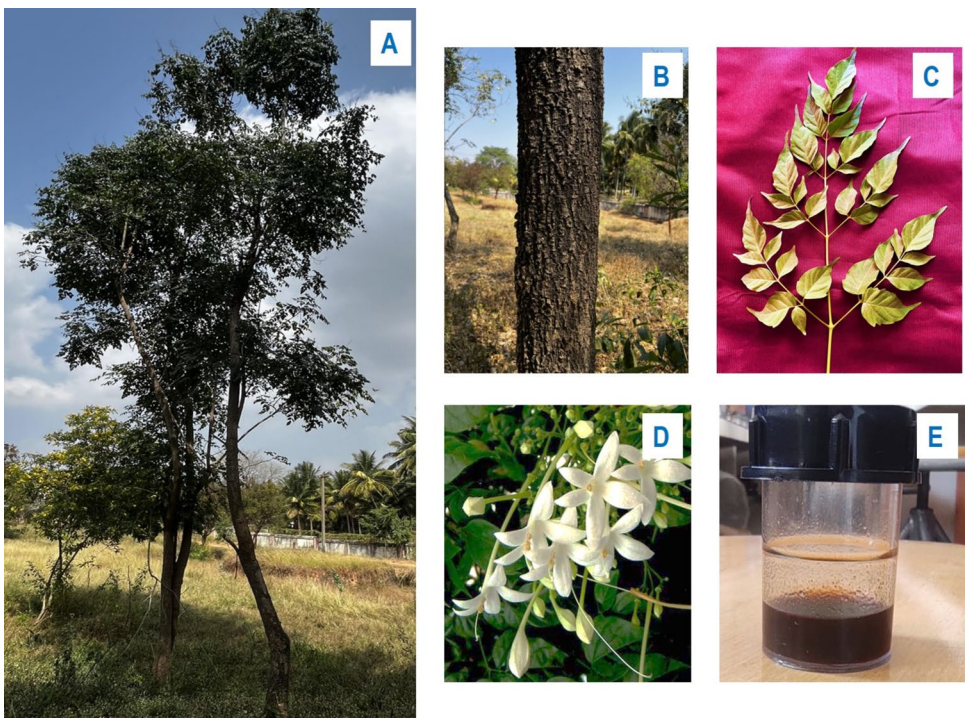


Fig. 1 Morphological identification of *Millingtonia hortensis* **A** The young tree; **B** stem bark; **C** leaves of the tree; **D** flowers; **E** extract

Table 1 Yield of essential oil from various parts of *Millingtonia hortensis*

Parts	Extraction time (hours)	Extraction method	Yield (%)	Reference
Flowers	25	Solid phase micro-extraction (SPME)	Not reported	[17]
Flowers	12	Solvent extraction (petroleum ether)	0.02	[52]
Stem bark	3	Solvent extraction (ethanol)	Not reported	[15]
Flowers	1	Solvent extraction (95% ethanol)	3.57	[51]
Flowers	5	Enfleurage	0.37	[51]
Flowers	11	Hydrodistillation	0.04	[51]

acetate, phytol, methyl palmitate, palmitic acid, methyl linoleate, linolenic acid, heneicosane, aspidoseprmidin 17-ol, 2-methyltetracosane, alfaxalone cis-13, stigmata-5, 22-dien-3-ol, ß-sitosterol, stigmata-5,24 (28)-dien-3-ol, and botulin [60, 61]. However, the South India-grown *M. hortensis* methanolic leaves extract had vital constituents, including heptadecanoic acid, oleic acid, 15-methyl-methyl ester, and estra-1,3,5(10)-trien-17a-ol. These compounds play a role in determining the overall composition and properties of the extracts [62].

The profiling of essential oils of *M. hortensis* flowers sampled from Chiang Rai Province and Phitsanulok Province, Thailand, predominantly exhibited solanesol (25.72%), trans-farnesol (19.71%), nerolidol (8.54%), palmitic acid (6.77%), vanillin (6.20%), oleic acid (4.54%), linoleic acid (3.87%), and linalool (3.37%), Paibon et al. [51] and Thongpoon and Machan [18] indicated that the flowers of *M. hortensis* collected across the growing region of Thailand chiefly contained solanesol, trans-farnesol, and nerolidol. However, Oman grown *M. hortensis* essential oil had significant constituents of linalool (29.16%), α-farnesene (11.80%), nerolidol (11.34%), pentacosane (9.69%), l-octen-3-ol (7.62%), (E)-isoeugenol (4.87%), and α-terpineol (3.82%), [63]. The Oman-grown *M. hortensis* flower essential oil chemical constituents varied from Thailand-grown MHEO. These changes in chemical constituents are due to flowers collected from differing origins, soil types, and tree ages. The major chemical constituents of MHEO across growing regions are presented in Table 2.

The yield of minor constituents of MHEO consists of hexanal (1.67%), 5-ethyldecane (1.63%), (Z)-β-farnesene (1.39%), α-curcumene (1.20%), methyl anthranilate (0.55%), indole (0.53%), and N-ethylaniline (2.86%) [17]. Recognizing the significant variations in the chemical composition of essential oils is vital, owing to numerous considerations. Further examination of the phytochemistry of MHEO may uncover more compounds and elucidate their potential pharmacological effects.

6 Pharmacological potential

The MHEO and *M. hortensis* extracts have various pharmacological and biological properties, such as antioxidant, antimicrobial, anti-inflammatory, anticancer, larvicidal, and other miscellaneous activities listed in Table 3. The potential biological effects of *M. hortensis* are diagrammatically illustrated in Fig. 2.

6.1 Antioxidant activity

Antioxidants assist in the neutralisation of potentially damaging free radicals within the body, thus lowering the risk of chronic diseases and reducing the amount of oxidative stress. An earlier study reported that methanolic leaf extract with an IC_{50} of 300 µg/ml showed maximum radical scavenging activity with 92.49% inhibition [64]. Another study found that *M. hortensis* ethanolic leaf extract with an IC_{50} value of 70 µg/ml had 80% scavenging activity [62]. Khobjai et al. [61] examined the DPPH scavenging activity of the extract from *M. hortensis* leaves and flowers, comparing it to ascorbic acid. They found that the IC_{50} values for DPPH activity in the flower extract of *M. hortensis* were 45.08 mg/ml in chloroform, 11.49 mg/ml in methanol, 24.72 mg/ml in butanol, and 23.16 mg/ml in diethyl ether. Elnaggar et al. [65] investigated the antioxidant capacity of four different extracts of *M. hortensis* by utilisation of ABTs, ORAC, and DPPH assay techniques. Resulted that dichloromethane has the most significant effect on the scavenging of free radicals. Furthermore, the n-hexane extract exhibited the most effective free radical scavenging in the FRAP assay. However, research on the antioxidant activity of *M. hortensis* extract is limited, and no studies have been conducted to test the antioxidant activity of MHEO. In previous investigations, antioxidant properties were also tested using the DPHH assay,

Table 2 Major constituents of *Millingtonia hortensis* essential oil (MHEO) and extracts

Parts	Location	Extracts/ Essential oil	Major constituents	References
Flowers	Thailand (Chiang Mai Province	Essential oil	Trans-β-caryophellene (17.47%), α-bergamotene (13.12%), 1-octen-3-ol (8.13%), linalyl anthranilate (15.13%), 2,3-dimethyl octane (4.86%), 3-methyl undecane (4.46%), and β-caryophellene (3.67%)	[17]
Flowers	Thailand (Chiang Rai Province)	Essential oil	Solanesol (25.72%), trans-farnesol (19.71%), nerolidol (8.54%), palmitic acid (6.77%), vanillin (6.20%), oleic acid (4.54%), linoleic acid (3.87%), and linalool (3.37%)	[18]
Stem bark	Thailand (Chiang Mai and Lamphun Province)	Ethanolic extract	9,12-octadecadienoic acid (12.35%), trans-13-octadecenoic acid (9.28%), oleic acid (5.95%), and isopropyl palmitate (4.81%)	[15]
Flowers	Thailand (Phitsanulok Province)	Essential oil	Isoeugenol (2.26%), linalool (2.14%), and nerolidol (1.73%)	[51]
Flowers	Sultanate of Oman	Essential oil	Linalool (29.16%), α-farnesene (11.80%), nerolidol (11.34%), pentacosane (9.69%), l-octen-3-ol (7.62%), (e)-isoeugenol (4.87%), and α-terpineol (3.82%)	[63]

Table 3 Pharmacological potential of *M. hortensis* essential oil (MHEO), and extracts

Health benefits	Plant parts	Study extract	In vitro/In vivo	Target/Model	IC_{50}/Dosage	Control	Results/ Remarks	References
Antioxidant	Leaves	Methanolic extract	In vitro	DPPH radical scavenging assay	IC_{50}: 50–300 µg/ml	Positive: Ascorbic acid	The higher $DPPH^{\cdot}$ radical scavenging activity was observed in 92.49% inhibition at 300 µg/ml concentration	[64]
Antioxidant	Leaves	Methanolic extract	In vitro	DPPH dot plot assay	IC_{50}: 2–10 µg/ml	Positive: Ascorbic acid	Substantial antioxidant activity was observed compared to ascorbic acid	[64]
Antioxidant	Leaves	Methanolic extract	In vitro	Superoxide ($O_2.^-$) radical scavenging	IC_{50}: 10–60 µg/ml	Positive: Ascorbic acid	The maximum superoxide reduction was observed at 54.30% in 60 µg/ml concentration	[64]
Antioxidant	Leaves	Methanolic extract	In vitro	Ferric (Fe^{3+}) reducing power	IC_{50}: 20–120 µg/ml	Positive: Ascorbic acid	The maximum Fe^{3+} reduction was observed at 72.76 in 120 µg/ml concentration	[64]
Antioxidant	Leaves	Ethanolic extract	In vitro	DPPH radical scavenging assay	IC_{50}: 10–100 µg/ml	Positive: Gallic acid	At a concentration of 70 µg/ml, the ethanol leaf extract exhibited approximately 80% scavenging activity	[62]
Antioxidant	Leaves	Methanolic extract	In vitro	Superoxide ($O_2.^-$) radical scavenging assay	IC_{50}: 10–100 µg/ml	Positive: Gallic acid	At a concentration of 100 µg/ml, the methanol leaf extract exhibited approximately 70% inhibition	[62]
Antibacterial	Leaves	Methanolic extract	In vitro	Gram-positive bacteria (*B. subtilis*, *S. aureus*, *M. luteus*) and Gram-negative bacteria *(E. coli, P. vulgaris, S. flexneri*)	MIC: 125–500 µg/ml	Positive: Tetracycline	The dosage of 500 µg/ml was noted as the highest zone of inhibition for all the tested bacterial strains	[64]

Table 3 (continued)

Health benefits	Plant parts	Study extract	In vitro/In vivo	Target/Model	IC_{50}/Dosage	Control	Results/ Remarks	References
Antibacterial	Stem bark	Petroleum ether extract	In vitro	*S. aureus* *B. subtilis* *E. coli* *P. aeruginosa*	MIC: 50 µg/ml MIC: 25 µg/ml MIC: 200 µg/ml MIC: 10 µg/ml	Positive: Ampicillin Negative: DMSO	The extract was effective against *P. aeruginosa, B. substilis* and *S. aureus* with respective inhibitory concentrations	[75]
Antibacterial	Stem bark	Benzene extract	In vitro	*S. aureus* *B. subtilis* *E. coli* *P. aeruginosa*	MIC:100 µg/ml MIC:100 µg/ml MIC:100 µg/ml MIC: 50 µg/ml	Positive: Ampicillin Negative: DMSO	Significant antibacterial activity was observed in all the strains	[75]
Antibacterial	Stem bark	Chloroform & Methanol extract	In vitro	*S. aureus* *B. subtilis* *E. coli* *P. aeruginosa*	MIC:100 µg/ml MIC:100 µg/ml MIC:100 µg/ml MIC: 50 µg/ml	Positive: Ampicillin Negative: DMSO	The chloroform and methanol extract are effective against all four tested microorganisms	[75]
Antibacterial	Stem bark	Ethanolic extracts	In vitro	*Enterococcus faecalis* *E. faecium* *S. aureus* *B. cereus*	MIC:500 mg/ml MBC: 500 mg/ml	Positive: Gentamycin	The findings demonstrated that the ethanol extract derived from the stem bark of M. hortensis exhibited a wide range of antibacterial effects	[15]
Antimicrobial	Flower	Essential oil	In vitro	*S. aureus,* *S. epidermis, P. subtili,* *L. plantarum, E. coli,* *P. vulgaris*	MIC: 0.5–2 ml/l MBC:1–4 ml/l	Positive: Gentamycin	MHEO showed significant inhibitory activity against all the tested organisms	[16]
Antimicrobial	Leaves	Ethanolic extract	In vitro	*E. coli,* *S. typhi,* *P. aeruginosa,* *K. pneumonia,* *Citrobactor brakii*	MBC:10-30 µg/µl	Positive: Gentamycin	The ethanolic leaf extract showed a maximum zone diameter of 13 mm when tested against *P. aeruginosa* and a minimum zone diameter of 6.1 mm when tested against S. *typhi. K. pneumoniae, C. brakii*, and *E. coli* exhibited minimal inhibitory zone concentrations, with diameters ranging from 10 to 25 µg/µl	[62]

Table 3 (continued)

Health benefits	Plant parts	Study extract	In vitro/In vivo	Target/Model	IC_{50}/Dosage	Control	Results/ Remarks	References
Anti-Arboviral activity	Leaves	Ethanolic extract	In vitro	Zika virus (ZIKV), Chikungunya virus (CHIKV), Mayaro virus (MAYV)	EC_{50}: 134.1 µg/ml EC_{50}: 97.6 µg/ml EC_{50}: 37.8 µg/ml	Positive: Ribavirin	The ethanolic extract shown reduced efficacy against ZIKV and CHIKV, with EC_{50} values of 134.1 and 97.6 mg/ml, respectively. However, it revealed enhanced efficacy against MAYV, with an EC_{50} value of 37.8 mg/ml	[9]
Anti-Arboviral activity	Stems	Ethanolic extract	In vitro	Zika virus (ZIKV), Chikungunya virus (CHIKV), Mayaro virus (MAYV)	EC_{50}: 168.4 µg/ml EC_{50}: 176.3 µg/ml EC_{50}: 99.9 µg/ml	Positive: Ribavirin	The stem extract demonstrated considerable antiviral activity against the three arboviruses, with EC_{50} values ranging from 99.9 to 176.30 mg/ml	[9]
Cytotoxicity	Leaves	Aqueous extract	In vitro	RKO cells (Human colon cancer cell lines) & MTT assay	IC_{50}: 200, 400, & 800 µg/ml for 48 h	–	Fraction 1 decreased the viable number of RKO cells in a dose-dependent manner, resulting in reductions of 26.82%, 61.05%, and 77.85% compared to the control. Nevertheless, fractions 2 and 3 of the extract did not exhibit any reduction in RKO cells	[76]
Cytotoxicity	Flower	Aqueous extract	In vitro	SK-N-SH cells	IC_{50}: 50 µg/ml	Positive: Hispidulin	The cytotoxic effects of the aqueous flower extract and hispidulin were observed at the dosage of 50 µg/ml, resulting in respective rates of 95.0% and 94.4%	[73]

Table 3 (continued)

Health benefits	Plant parts	Study extract	In vitro/In vivo	Target/Model	IC_{50}/Dosage	Control	Results/ Remarks	References
Anti-inflammatory activity	Leaves	Aqueous extract	In vitro	Albumin protein denaturation method	IC $_{50}$: 100 µg/ml	Positive: Ibuprofen Negative: Distilled water	The aqueous extract substantially lowered BSA denaturation compared to controls	[68]
Anti-inflammatory activity	Stem bark	Ethanolic	In vitro	MTT assay against Macrophage RAW264.7 cell line	IC_{50}: 0.078–10 mg/ml	Positive: Gentamicin Negative: DMSO	The dosage of 0.625 mg/ml had 104.60% cell viability	[15]
Anti-inflammatory activity	Stem bark	Ethanolic	In vitro	Nitric oxide production in lipopolysaccharides (LPS)-stimulated RAW264.7 cell	IC $_{50}$: 0.039–0.625 mg/ml	–	A notable inhibition of 104.44% was observed. at a concentration of 0.625 mg/ml. In LPS stimulation, RAW264.7 cells exhibited the capacity to generate NO production, which plays an important role in anti-inflammatory activity	[15]
Antifertility	Leaves	Methanolic extract	In vivo	Male albino rats	150, 200, 250, and 300 mg/kg for 21 days	–	Oral administration of methanolic leaf extract with 150 mg/kg for 21 days, significantly decreased sperm count and motility	[74]
Hepato-protective activity	Flower	Ethanolic extract	In vivo	Carbon tetrachloride (CCl_4) induced hepato-toxicity in adult Wistar rats	200 and 400 mg/kg for 8 days	Positive: CCl_4 Negative: 2% acacia suspension	The ethanol extract of *M. hortensis* demonstrated a notable hepatoprotective effect against acute hepatotoxicity produced by CCl_4 in rats	[11]
Antipyretic activity	Stem bark	Methanolic extract	In vivo	Yeast-induced hyperpyrexia in adult albino rats	200, 300, 400 mg/kg for 19 h	Positive: Paracetamol Negative: Tween 80	Methanolic extract of *M. hortensis* bark has a significant antipyretic effect in dose dose-dependent manner	[77]

Table 3 (continued)

Health benefits	Plant parts	Study extract	In vitro/In vivo	Target/Model	IC_{50}/Dosage	Control	Results/ Remarks	References
Anthelmintic activity	Stem	Methanolic extract	In vitro	*Pheritima posthuman (earthworm)*	IC $_{50}$: 20 mg/ml	Positive: Albendazole Negative: Distilled water	The methanolic stem extract had significant anthelmintic activity against worms compared to the negative and positive controls	[70]
Antidiabetic activity	Leaf	Ethanolic extract	In vivo	Streptozotocin-induced diabetic rats	200 mg/kg and 400 mg/kg, p.o	Positive: Metformin Negative: Saline	Substantial decrease in blood glucose levels after 8 weeks	[78]
Diuretic activity	Leaf	Ethanolic extract	In vivo	Lipschitz model and Male albino rats	200 mg/kg and 400 mg/kg, p.o. for 7 days	Positive: Furosemide Negative: Saline	Enhanced the production of urine and elevation of sodium, potassium, chloride, and urinary electrolyte levels in comparison to the control group	[78]
Sedative activity	Flower	Aqueous extract	In vitro	Male ICR mice	IC_{50}: 2.7 and 54 mg/ml	Negative: Distilled water	*M. hortensis* dried flower's aqueous extract, at a human-equivalent dose, has sedative and hypnotic effects in rats, suggesting its potential as a natural sleep and mood aid	[39]
Larvicidal activity	Leaf	Acetone extract	In vitro	II, III, & IV larval instars of *Culex quinquefasciatus*, *Aedes aegypti,* and *Anopheles stephensi*	LC_{50}: 25, 50, 100, 250, 300 and 500 ppm for 24 h	Negative: Distilled water	The acetone extract derived from the leaves of *M. hortensis* showed efficacy against all larval developmental stages of the three mosquito species tested	[20]

Table 3 (continued)

Health benefits	Plant parts	Study extract	In vitro/In vivo	Target/Model	IC_{50}/Dosage	Control	Results/ Remarks	References
Larvicidal activity	Flower	Essential oil	In vitro	Larva of *Aedes aegypti*	LC_{50}: 25, 50, 100, 250 and 500 ppm for 24 h	Negative: Distilled water	The essential oil demonstrated capable larvicidal activity against *Ae. aegypti* following a 24-h exposure, exhibiting an LC_{50} value of 208.5 ppm	[52]

–: Not reported; EC_{50}: evaluation of antiviral activity; LC_{50}: Lethal concentration; IC_{50}: Inhibitory concentration; MIC: Minimum inhibition concentration; MBC: Minimum bactericide concentration

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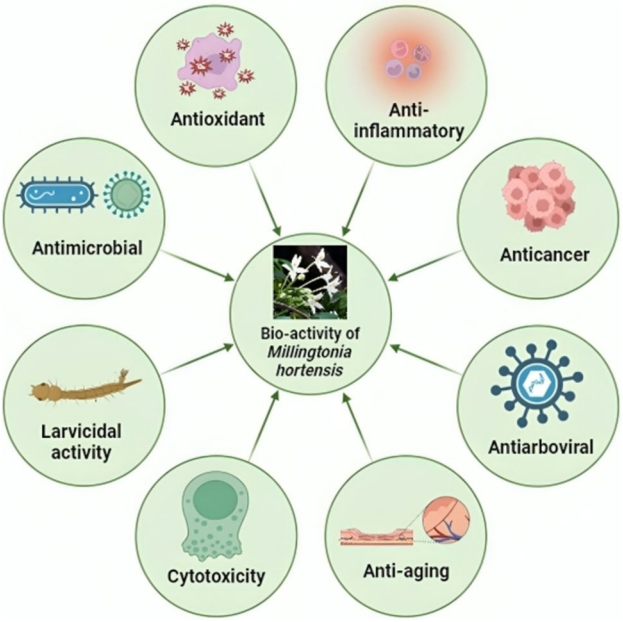


Fig. 2 Diagrammatic representation of the major pharmacological potential of *M. hortensis* extracts and essential oils

which is no longer considered to have any therapeutic importance. Because of this, it is essential to explore their potential under both in vitro and in vivo conditions [66].

6.2 Antimicrobial activity

The antibacterial activity of MHEO is due to its varied chemical composition, which consists of molecules such as monoterpenes, sesquiterpenes, and phenolic compounds. These components have the potential to disturb the integrity of microbial cell membranes, impede cellular functions, or hinder the activity of enzymes, ultimately resulting in the suppression of microbial growth and reproduction. Jetty and Iyengar [19] investigated the effectiveness of alcoholic extracts of *M. hortensis* against 20 bacterial strains susceptible to Gentamycin and Nystatin, and the extracts minimum inhibitory concentration (MIC) ranged from 6.25 to 200 µg/ml. The study revealed that a MIC of 12.5 µg/ml effectively inhibited the growth of both *B. polymixa* and *B. subtilis*. Meanwhile, *B. cereus, B. licheniformis,* and *B. pumilus* showed MIC values of 25 µg/ml. The MIC values for *E. coli, P. aeruginosa,* and Salmonella were 6.25, 12.5, and 12.5 µg/ml, respectively. Another study evaluated the efficiency of MHEO in combating six pathogenic bacteria (*S. aureus, S. epidermis, B. subtilis, L. plantarum, E. coli,* and *P. vulgaris*) with dosages of MIC: 0.5–2 ml/l and MBC: 1–4 ml/l, along with the positive control Gentamycin and results indicated that MHEO had considerable inhibitory action against all the tested species [16]. An investigation found that the methanolic extract of *M. hortensis* leaves showed antibacterial activity against several strains of both Gram-positive and Gram-negative species, and the inhibitory concentration of 500 µg/ml was identified as the maximum zone of inhibition for all the tested bacterial strains [64]. Sharma et al. [67] examine the antifungal efficacy of several extracts of *M. hortensis* against various fungal infections. The methanolic extract had much higher potency, with a MIC of 4 µg/ml, against *Candida krusei*, showing a fourfold increase in activity. This study also observed that the methanolic extract had twice the activity with a dosage value of 2 µg/ml against *Saccharomyces cerevisiae* compared to the standard fluconazole, and had a similar effectiveness against *Candida glabrata*. A recent study found that the ethanol extract of *M. hortensis* stem bark with MIC and minimum bactericidal concentration (MBC) of 500 mg/ml demonstrated significant inhibition against gram-positive bacteria, including *Enterococcus faecalis, Enterococcus faecium, Staphylococcus aureus,* and *Bacillus cereus* [15]. MHEO's antimicrobial activities make it an exciting choice for various applications, such as pharmaceutical and therapeutic drugs, to treat bacterial and fungal diseases. Research on the antifungal and antiviral effects of MHEO is scarce compared to its antibacterial characteristics. Hence, further investigation is required in this domain to understand its capacity to combat fungi and viruses comprehensively.

6.3 Anti-inflammatory activity

Inflammation is a crucial factor in the functioning of the human body. Some research has examined the anti-inflammatory properties of MHEO and extracts, suggesting they may have therapeutic advantages in treating inflammatory disorders. The anti-inflammatory activity of ethanolic extract of *M. hortensis* leaf and stem bark extracts with IC_{50} values of 0.25 and 0.41 mg/ml, respectively, were tested against macrophage cell line RAW 264.7. The study results reported that both ethanolic extracts were the most effective in inhibiting nitric oxide secretion [15]. Manubolu et al. [68] found that the aqueous extract of *M. hortensis* effectively prevented the denaturation of bovine serum albumin (BSA) in an in vitro condition. This effect was more substantial than that of the positive control, Ibuprofen. While MHEO has demonstrated anti-inflammatory effects in preclinical studies, further research is needed to exploration of MHEO's therapeutic potential in clinical trials involving human subjects to validate its efficacy and safety. Also, this study suggests investigating the synergistic effects of MHEO's constituents to understand how they might work together to enhance therapeutic outcomes.

6.4 Anthelmintic activity

A study assessed the anthelmintic properties of several extracts (aqueous, petroleum ether, benzene, chloroform, and methanol extracts) derived from the stem bark of *M. hortensis*. The study focused on their effects on adult earthworms of the species *Pheretima posthuma*, with the positive control being Piperazine. Of all the examined extracts, methanol demonstrated a dose-dependent anthelmintic effect and exhibited superior efficacy compared to the positive control. The activity of chloroform and benzene extracts at a concentration of 20 mg/ml was similar to that of piperazine citrate at a dose of 60 mg/ml [69]. Chumbhale et al. [70] found that the methanolic stem extract, at a dosage of 20 mg/ml, demonstrated significant effectiveness against earthworms (*Pheretima posthuma*). The anthelmintic activity of the methanolic extract was meaningfully more significant than the negative control (distilled water) and the positive control (Albendazole). However, as far as we know, only two studies have been carried out to examine the anthelmintic properties of *M. hortensis* stem bark extracts. None of the studies assessed the anthelmintic efficacy of MHEO. Hence, further investigations on earthworms might broaden the range of pharmacological uses for *M. hortensis* extracts and MHEO.

6.5 Anticancer and cytotoxic activity

The inhibitory effect on cell growth of the aqueous and ethanol extracts derived from the bark of *M. hortensis* was assessed by subjecting them to in vitro experiments using the MTT technique on human colon cancer cell lines, namely DLD-1, HCT15, SW48, and SW480. The result was that those aqueous extracts from *M. hortensis* effectively decreased the rate at which colon cancer cells multiplied, and this effect was directly related to the dosage of the extract. Nevertheless, this study also observed that the ethanol extract of *M. hortensis* did not exhibit any antiproliferative behaviour [71]. The antimutagenicity of hispidulin and hortensin was tested using the Salmonella/microsome liquid pre-incubation method. Both compounds were non-mutagenic and non-cytotoxic to *S. typhimurium* strains TA98 and TA100 at 100 g/plate, with or without S9 mix [72]. In a recent study, Elnaggar et al. [65] investigated the cytotoxic effect of total ethanolic, n-hexane, dichloromethane, and ethyl acetate fractions on the human colorectal cancer (LS-513) and hepatocellular carcinoma (HepG2) cell lines was evaluated using the MTT colourimetric assay. The results showed that the entire ethanolic extract had the lowest IC_{50} value of 23.8 ug/ml on both cell lines, indicating its much higher activity compared to the other fractions examined. In addition, the study proposed that further investigations should assess the anticancer effects of *M. hortensis* on human subjects.

6.6 Antiviral activity

A recent study noted that ethanolic extract of *M. hortensis* leaves with EC_{50} values of 134.1 mg/ml and 97.6 mg/ml showed low activity against Zika virus (ZIKV) and Chikungunya virus (CHIKV). On the other hand, an ethanolic leaf extract with an EC_{50} value of 37.8 mg/ml was more effective against the Mayaro virus (MAYV) [9]. One specific study has examined the antiviral properties of extracts from *M. hortensis*. Therefore, additional studies should focus on scrutinising the antiviral properties of MHEO and extracts to expand the pharmacological uses of *M. hortensis*.

6.7 Antiaging activity

A recent study investigated the potential effects of an aqueous extract derived from *Millingtonia hortensis* flowers on hydrogen peroxide (H_2O_2)-induced senescence in SK-N-SH cells in vitro. The findings revealed that the aqueous plant extract notably enhanced cell viability while reducing apoptotic cells and reactive oxygen species (ROS) production in a dose-dependent manner compared to the aging group. The treatment with *M. hortensis* extracts also led to a decrease in SA-β-gal-positive cells alongside the upregulation of the Sirt-1 protein. In addition, the extract enhanced synaptic plasticity by reducing acetylcholinesterase activity and increasing synaptophysin expression in aging neurons, as compared to the aging group [73]. This study suggests that *M. hortensis* extract could benefit neurodegenerative diseases associated with aging.

6.8 Antifertility activity

The antifertility effects of methanolic leaf extract of *M. hortensis* were evaluated in male albino rats using varying dosages of 150, 200, 250, and 300 mg/Kg. The study found that when rats were orally given a dose of 150 mg/Kg of methanolic leaf extract for 21 days, there was a noticeable decrease in both sperm count and motility. The levels of glycogen and protein in the testis and liver tissues of the rats were also reduced in the methanolic leaf extract administered to rats [74]. Nevertheless, this work needs systematic experiment methods such as positive and negative control measures and specific dosages. Hence, future research must conduct more systematic experiments to validate the antifertility properties of *M. hortensis*. In addition, Table 3 summarises the extra pharmacological potential of *M. hortensis* extracts and essential oils and their active chemical constituents.

6.9 Larvicidal activity

The MHEO-treated groups exhibited substantial, dose-dependent larval mortalities, with increasing concentrations ranging from 25 to 500 ppm. The highest mortality percentage (98%) of larval mosquitoes occurred at 500 ppm, followed by 250 ppm (46%), 100 ppm (13%), 50 ppm (4%), and 25 ppm (2%), respectively [52]. In another study, Kaushik and Saini [20] evaluated the larvicidal activity of *M. hortensis* leaves acetone extract with various concentrations (LC_{50}: 25, 50, 100, 250, 300, and 500 ppm) against various stages (II, III, and IV larval instars) of *Culex quinquefasciatus*, *Aedes aegypti*, and *Anopheles stephensi*. This study observed the highest mortality rate of 98.33% and 95% in second-instar larvae of *Cx. quinquefasciatus* and *Ae. aegypti* at a concentration of 300 ppm, respectively. In contrast, *An. stephensi* larvae exhibited relatively lower susceptibility, with a 98% mortality rate observed at a higher concentration of 500 ppm. Only two studies have been conducted on the larvicidal activity of *M. hortensis*. Therefore, additional study is needed to explore this exciting use further.

7 Conclusion

This paper provides a concise overview of ethanopharmacology, botanical descriptions, essential oil yield, chemical composition, and pharmacological and biological effects of *M. hortensis* extracts and essential oils. The plant's essential oil production and chemical compositions primarily concentrate on leaves and flowers, whereas the analysis of barks needs to be addressed or given more consideration. Gas chromatography and mass-spectrometry techniques are employed to identify chemical components present in MHEO. Currently, available data indicates that over 100 secondary metabolites have been extracted from the essential oil of *M. hortensis* flowers. Linalool is the most significant active molecule, exhibiting anticancer, antibacterial, anti-inflammatory, and analgesic properties. However, the main chemical components of MHEO and extracts were linalool, solanesol, β-caryophellene, α-bergamotene, 1-octen-3-ol, linalyl anthranilate, 2,3-dimethyl octane, 3-methyl undecane, trans-farnesol, nerolidol, palmitic acid, and vanillin. The major chemical components of MHEO are varied based on the soil types, extraction methods and

GC–MS experiment conditions. Furthermore, the chemical components found in *M. hortensis* have the potential to be a new and natural source for the food, fragrance, and pharmaceutical industries.

Millingtonia hortensis extracts and essential oils have been thoroughly investigated for their valuable components (Table 3). Nonetheless, there are weaknesses in the scientific literature regarding *M. hortensis*, and we have outlined recommendations for several topics requiring prioritized investigation.

Firstly, the currently available findings indicate that the inquiry into the structural characterisation of metabolites in *M. hortensis* flowers is restricted. Therefore, comprehensive studies on the structural identification and purification of bioactive metabolites from *M. hortensis* flowers are important.

Secondly, insufficient pharmacological studies have been conducted on *M. hortensis*. Most previous biological and pharmacological investigations did not include specific information regarding positive and negative control details. Hence, future research should conduct rigorous investigations utilizing cellular and animal models.

Thirdly, the clinical research was conducted exclusively on cell lines and animals, with no human clinical trials. Therefore, future studies should investigate the pharmacological activity of MHEO and extracts and their active components in humans. Such research will enhance future pharmacological applications of MHEO.

Fourthly, future investigations should focus on examining the bioavailability and pharmacokinetics of *M. hortensis* to identify the specific chemical constituents responsible for its effects and expand the current medical applications of *M. hortensis*.

Overall, the presence of linalool, solanesol, trans-β-caryophyllene, α-bergamotene, linalyl anthranilate, trans-farnesol, and nerolidol as predominant constituents in MHEO may represent a novel natural resource applicable in the food, fragrance, cosmetics, and pharmaceutical industries. Various previous research studies have verified that *M. hortensis* possesses antioxidant, antimicrobial, antiviral, anti-inflammatory, analgesic, anticancer, antimutagenic, antiaging, antipyretic, hepatoprotective, and larvicidal properties. However, the current pharmacological research is inadequate to evaluate the ethnobotanical applications. Additional study is necessary to enhance the medical utilization of *M. hortensis*.

Author contributions K. A. created, designed, and wrote the manuscript. M.M., P.M. and T.V. gathered literature and prepared all the figures. M.M. and K. A. revised the manuscript. All authors have reviewed and approved this version of the manuscript.

Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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