

A Systematic Review of the Phytochemical Constituents and Bioactive Properties of *Mussaenda Frondosa*

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ABSTRACT

Mussaenda frondosa (M. frondosa) is a plant with significant botanical importance and has been identified as a promising source of bioactive compounds with diverse biological activities. This review provides a comprehensive analysis of the current knowledge of the various biological roles that M. frondosa plays. The phytochemical profile of the plant is explored in great detail, revealing a rich array of alkaloids, flavonoids, terpenoids, and other compounds that contribute to its multifaceted therapeutic potential. In addition, the interplay between the chemical constituents of the plant and their potential medicinal attributes, including their anti-inflammatory, analgesic, antioxidant, hypolipidemic, diuretic, and other properties, is discussed. This review is intended to serve as a guide for researchers interested in exploring the diverse biological activities of M. frondosa and to pave the way for future studies that could harness its potential for human health and well-being.

Keywords: M. frondosa, phytochemicals, bioactivity, medicinal potential, anti-bacterial activity, anti-inflammatory

INTRODUCTION

Plant-based traditional remedies have been celebrated for centuries for their potential to offer various health benefits across various human ailments. These remedies remain an undiscovered resource within the field of medicine. Traditional Medicines encompass health practices, methods, accumulated wisdom, and beliefs employed individually or in synergy to address, diagnose, prevent illness, or promote well-being. The use of traditional herbal medicines continues to thrive in numerous regions, particularly in tribal and rural communities worldwide. Numerous traditionally significant medicinal plants have been recognized for their biological effectiveness against various diseases. Among these valuable botanical resources, *Mussaenda frondosa* (Rubeaceae), an annual shrub native to Asian countries, stands out,^{1,2}. *Mussaenda frondosa* has been documented to contain a range of phytoconstituents, including alkaloids, flavonoids, saponins, tannins, steroids, and glycosides^{3,4}. Extracts derived from *Mussaenda frondosa* have been utilized as remedies for various conditions, including skin ailments, wound healing, fever, cough, leprosy, and jaundice³. Furthermore, these extracts exhibit notable hepatoprotective⁵, anti-inflammatory⁶, anti-microbial¹, anti-oxidant⁷, and analgesic⁶ properties. This article provides a comprehensive overview of *Mussaenda frondosa* as a medicinal resource for various illnesses, consolidating the latest information available. It underscores numerous pharmacological and experimental investigations, elucidating the connections between its active constituents and multifaceted applications.

Source and Distribution:

Mussaenda frondosa is a tropical shrub that grows all over low countries such as central India, Nepal, Sri Lanka, the south and south-west of China, Bhutan, Bangladesh, Myanmar and Malaysia^{8,2}. *Mussaenda* consists of various species like *M. frondosa*, *M. macrophylla*, *M. pubescent*, *M. roxburghii*, *M. villosa* and many more^{9,8}. It has been called by different names, “Bedina” in Hindi, “Nagavalli” in Telugu, “Sriparnah” in Sanskrit, and “White queen” in the Philippines^{6,2}.

Phytography (Botany):

M. frondosa is a scrambling climber, which ranges from 1-5m in height based on the species. It consists of a root, leaf, flower, stems and petiolates bract. This plant consists of showy leaves and flowers. Leaves are bright to green, oblong, lanceolate, elliptic with an entire margin, acute to acuminate at the base, and they vary up to 5-20 cm long. The terminal flowers are orange, small, tubular corolla. Calyx has a single enlarged lobe among five lobes. It consists of creamy white modified sepals called bracts^{2,10} was shown in Figure 1.



Figure 1. *Mussaenda frondosa*

Identification of Phytocomponents in Whole Plant Ethanolic Extract of *Mussaenda Frondosa* Using GC-MS Analysis

Table 1 represent the GC-MS analysis of the ethanolic extract of *Mussaenda frondosa*'s whole plant identified 20 phytocomponents, including phytol, stigmasterol, and β -sitosterol. These components possess antioxidant, anti-inflammatory, and cholesterol-lowering properties. Other identified phytocomponents include longifolene, α -cubebene, and γ -muurolene, demonstrating anti-inflammatory, anti-tumour, and antimicrobial effects. Further research is needed to explore the therapeutic potential of these compounds in the pharmaceutical industry.

Table 1. Phytoconstituents of *Mussaenda frondosa*.¹¹

IUPAC name of the compound	Molecular Formula	Molecular Weight	Compound Nature
1,2,3-Benzenetriol	C ₆ H ₆ O ₃	126	Pyrogallol
2-Furancarboxyaldehyde, 5-(hydroxymethyl)-	C ₆ H ₆ O ₃	126	Aldehyde
4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl	C ₆ H ₈ O ₄	144	Flavonoid fraction
2-Methoxy-4-vinylphenol	C ₉ H ₁₀ O ₂	150	Phenolic
Benzaldehyde, 3-hydroxy-4-methoxy-(Isovanillin)	C ₈ H ₈ O ₃	152	Isovanillin
Butanedioic acid, diethyl ester	C ₁₀ H ₂₂ O	158	Ester
Naphthalene, decahydro-2-methoxy-	C ₁₁ H ₂₀ O	168	Naphthalene
4-((1E)-3-Hydroxy-1-propenyl)-2-methoxyphenol	C ₁₀ H ₁₂ O ₃	180	Phenolic
(1R,3R,4R,5R)-(-)-Quinic acid	C ₇ H ₁₂ O ₆	192	Quinic acid
3-O-Methyl-d-glucose	C ₇ H ₁₄ O ₆	194	Sugar moiety

9-Acetoxyanonanal	C ₁₁ H ₂₀ O 3	200	Aldehyde
Caryophyllene	C ₁₅ H ₂₄	204	Sesquiterpene
3,5-Dimethoxy-4-hydroxycinnamaldehyde	C ₁₁ H ₁₂ O 4	208	Cinnamaldehyde
8-Phenyl-6-thio-theophylline	C ₁₃ H ₁₂ N 4OS	272	Sulphur
Oleic acid	C ₁₈ H ₃₄ O 2	282	Oleic acid
Hexadecanoic acid, ethyl ester	C ₁₈ H ₃₆ O 2	284	Palmitic acid ester
Linoleic acid ethyl ester	C ₂₀ H ₃₆ O 2	308	Linoleic acid ester
Octadecanoic acid, ethyl ester	C ₂₀ H ₄₀ O ₂	312	Octadecanoic acid ester
Lactose	C ₁₂ H ₂₂ O ₁₁ 1	342	Sugar
α -D-Glucopyranoside, O- α -D-glucopyranosyl-(1 \rightarrow 3)- α -D-fructofuranosyl	C ₁₈ H ₃₂ O ₁₁ 6	504	Sugar moiety

Pharmacological activity of different parts of *Mussaenda frondosa*

Table 2 represent *Mussaenda frondosa* is a medicinal plant native to Southeast Asia. Its leaves contain compounds with anti-inflammatory, analgesic, and antipyretic properties. The stem bark has antitumor, antimicrobial, anti-inflammatory, and hepatoprotective activity. The root has bronchodilator activity and may help with asthma management. Further research is needed to understand its therapeutic potential fully.

Table 2. The pharmacological activity of different parts of *Mussaenda frondosa*

Part Used	Extraction solvent	Active constituents	Pharmacological action	Mechanism of action	Reference
Leaf	Methanol Chloroform Ethyl- acetate n-hexane	Flavonoids Tannins Triterpenes Iridoids Alkaloids Terpenoids	Anti-bacterial Anti-fungal	Act on both gram ^{+ve} and gram ^{-ve} bacteria.	1,
Leaf	Petroleum- ether Chloroform Alcohol Aqueous- solvent	N-acetyl- cysteine Flavonoids Cyanogenic- glycosides Rutin Quercetin	Hepatoprotective	Protection of liver against toxic material.	5,
Leaf	Alcohol	Steroids Saponin Mucilage Resin Flavonoids Glycoside	Wound healing	Contraction of wound occurs and there will be decrease in an epithelisation time	12,13
Bark	Chloroform	Tannins Diterpenes Steroids Flavonoids	Analgesic	Inhibits the activity of Cyclooxygenase (COX) enzyme	6,
Aerial Parts	Methanol	Flavonoids Glycoside Steroids Phenols Carbohydrates Tannins Saponin	Hypolipidemic	Inhibits the HMG-CoA enzyme that decreases the cholesterol level	14
Root	Ethanol	Flavonoids Steroids Glycosides Carbohydrates Phenols	Anti-stress	Scavenge free radicals and alleviate stress	15,16
Leaf	Methanol	Alkaloids Terpenoids Saponin Flavonoids	Anti-inflammatory	Inhibits Prostaglandin synthesis by inhibiting COX -1 and COX -2	6

		Cardiac-glycosides Steroids		and reduce inflammation	
Whole plant	Ethanol	Alkaloids Tannins Steroids Flavonoids	Diuretic	Decreases the sodium, chloride and potassium reabsorption from the renal tubule	17
Whole plant	Aqueous solvent	Alkaloids Flavonoids Tannins Polyphenols	Anti-oxidan	Inhibition of peroxidation and lipid peroxidation	7,13,15

PHARMACOLOGICAL SCREENING AND BIO POTENTIAL OF *M. FRONDOSA*:

The plant has been discovered to display diverse pharmacological effects, with numerous researchers documenting various biological activities of *Mussaenda frondosa* in both in-vitro and in-vivo test models. These findings are elaborated upon in subsequent sections.

Antioxidant activity against DPPH free radical scavenging assay

The whole *M. frondosa* plant shows antioxidant activity when extracted from ethyl alcohol and an aqueous solvent. This extract possesses increased activity at higher concentrations¹⁵. *M. frondosa* extract, along with ascorbic acid, shows increased activity⁷. The antioxidant activity, evaluated through the DPPH free radical scavenging assay, can be attributed to alkaloids and flavonoids¹⁷. The ethanolic extract of *M. frondosa* was utilized for antioxidant activity by taking BHA (butylated hydroxyanisole) as a standard antioxidant. The DPPH solution alone is considered a control. DPPH radical-scavenging activity indicates decreased absorbance of the reaction mixture and shows antioxidant activity⁷.

Anti-stress activity against DPPH superoxide and hydroxide scavenging

The anti-stress activity of *M. frondosa* is studied in albino rats using different models¹⁵. The inhibitory concentration is studied using DPPH superoxide and hydroxide scavenging activity. A root extract from *M. frondosa* that has been soaked in alcohol can normalize cold immobilization stress by lowering the amounts of norepinephrine (NE), dopamine (DA), 5-hydroxy tryptamine (5-HT), and 5-hydroxyindole acetic acid¹⁶.

Burn Wound Healing Properties

The alcoholic extract of *M. frondosa* leaves possesses burn wound healing properties. Leaves have been used for wound healing, mainly due to the presence of various secondary metabolites like steroids, saponins, mucilage, resins, flavonoids, and glycosides¹². This property is studied using the burn wound model observed in Albino rats. They are divided into three groups of six animals each. In anaesthetic conditions, the wound was made on rats semi-aseptically. One group was considered controlled, and the other two groups received quercetin and alcoholic extract. In the excision model, the quercetin group had less epithelization time than those treated with alcoholic extract. The alcoholic extract of *M. frondosa* leaves also shows significant wound-healing properties¹³.

Analgesic activity against eddy's hot plate method

The chloroform extract of *M. frondosa* bark possesses analgesic activity. This activity is observed in Swiss Albino mice using Eddy's hot plate method with acetylcholine as the standard drug. The chloroform extract shows the presence of phytochemical constituents like flavonoids, tannins, diterpenes, and steroids. *M. frondosa* shows activity that is almost similar to that of acetyl-salicylic acid⁶. In Eddy's hot plate method, rats were kept on a hot plate. Jumping from a hot plate surface or licking the forepaws were two ways to observe the response. A group of albino mice treated with a chloroform extract of *M. frondosa* bark indicated increased reaction time and showed analgesic activity¹⁸

Anti-inflammatory activity against carrageenan-induced inflammation in rats.

The methanolic extract of *M. frondosa* leaves shows anti-inflammatory activity against carrageenan-induced inflammation in rats. This activity is studied using a paw edema model. These rats are divided into two groups. One group was given diclofenac as a standard, and the other group was assigned the methanolic extract of *M. frondosa* leaf. The anti-inflammatory activity of *M. frondosa* is compared with the standard by studying paw diameter⁶.

Anti-bacterial activity against pathological bacteria

pathological bacteria such as coagulase-negative staphylococcus, staphylococcus aureus, salmonella typhi, salmonella paratyphi A, salmonella paratyphi B, pseudomonas aeruginosa, klebsiella pneumonia and E. coli due to the presence of phytoconstituents like flavonoids, tannins, triterpenes, iridoids and alkaloids¹⁹. Using *M. frondosa* leaf extract, the bacterial growth inhibition is studied through agar medium¹. *Mussaenda* leaves in dimethyl sulphoxide were extracted into previously autoclaved Muller Hinton agar. *M. frondosa* leaves are extracted by Methanol (MEFM), Chloroform (CEMF), Ethyl acetate (EEMF) and n-hexane (HEMF). These extracts show anti-bacterial activity against medium. The extract's final concentration will be 66, 67, 100, 133.33 and 166.66 µ/ml in different plates. The above plates were inoculated by bacteria and incubated at 37°C for 24 hours. Minimum inhibitory concentration was observed¹.

Anti-fungal activity against Sabouraud Dextrose Agar (SDA)

The phytoconstituents, such as alkaloids, flavonoids, terpenoids, tannins, saponins, and steroids, are obtained by leaf extract of *M. frondosa* using MEMF, HEMF, EEMF, and CEMF. These phytoconstituents show anti-fungal activity against *Trichophyton mentagrophytes*, *Trichophyton simii*, *Aspergillus niger* and *Rhizopus*, which are observed in Sabouraud Dextrose Agar slants¹. Sabouraud Dextrose Agar (SDA) was prepared and sterilized in an autoclave at 121°C, 151 lbs of pressure for 15 minutes of exposure time. *M. frondosa* leaves are extracted into four slants of SDA media of different concentrations. SDA were inoculated with different fungi and incubated at 37°C for 1-4 weeks. The results were determined by observing the presence or absence of growth on the slants¹.

Diuretic activity by Lipschitz method

The ethanolic extract of *M. frondosa* was reported to contain chemical constituents like tannins, alkaloids, steroids, phenolic compounds, and flavonoids. The diuretic activity of the extract is studied in Wistar albino rats using the Lipschitz method. Twenty-four animals are divided into four groups of 6 animals each. One is the controlled group, which receives normal saline solution (25 ml/kg); group 2 is standard, i.e., furosemide (20 mg/kg); and groups 3 and 4 receive the ethanolic extract of *M. frondosa* at 200 and 400 mg/kg, respectively. By comparing the urine volume, diuretic activity was studied. The alcoholic section of *M. frondosa* (200–400 mg/kg) shows increased concentrations of sodium, potassium, and chloride ions, along with increased urine output¹⁷.

Hepatoprotective Activity against Paracetamol induced hepatotoxicity

M. frondosa leaves are extracted using petroleum ether, chloroform, alcohol, and aqueous solvent through the soxhlet extraction method. N-acetyl cysteine is a significant chemical constituent found in alcohol. Aqueous extract of *M. frondosa* leaves show a crucial protective activity against paracetamol hepatotoxicity²⁰. The above action is studied in healthy adult male Wistar rats. The rats treated with paracetamol showed increased ALT, AST and bilirubin levels. The decreased total protein content in the rat shows hepatotoxicity. Then, the same group of animals is treated with an alcoholic extract of *M. frondosa* leaves, which contain N-acetyl cysteine, restoring the above-mentioned biochemical parameters to normal levels. A recent report shows that various anti-oxidants can also be used as hepatoprotective agents against hepatotoxicity caused by paracetamol⁵.

Anti hyperlipidaemic activity against high-fat diet-fed rat

Methanolic extract of the aerial part of *M. frondosa* gives flavonoids, steroids, glycosides, carbohydrates, phenols, tannins, and saponins¹. The hypolipidemic activity of *Mussaenda* extract (400–450 mg/kg) is studied using a high-fat diet-fed rat and taking atorvastatin as the standard dose (1-2mg). Rats subjected to a high-fat diet exhibit elevated levels of plasma cholesterol, triglycerides, free fatty acids, LDL cholesterol, and reduced levels of plasma HDL cholesterol. When the same animals are treated with a methanolic extract of *M. frondosa*, the average level of the lipids. *M. frondosa* has this effect because it stops the liver from making cholesterol. It also lowers cholesterol levels in rats that eat a high-fat diet¹⁴.

Conclusion

The extensive scientific investigation into this plant points towards its vast biological potential. *Mussaenda frondosa* plays a significant role in Chinese and Fijian traditional medicine systems³. Further clinical and pharmacological studies with standardized extracts and isolated constituents are warranted to unlock its untapped potential. This plant boasts a rich array of vital phytoconstituents, encompassing triterpenes, steroids, and flavonoids, all possessing a broad spectrum of medicinal properties. These compounds exhibit various properties, such as anti-bacterial, antioxidant, anti-inflammatory, and diuretic activities. Furthermore, *Mussaenda frondosa*'s ease of cultivation and disease resistance make it an excellent candidate for medicinal farming. This article extensively explores the plant's phytochemical and pharmacological characteristics. The potential for research on this plant is vast and could be harnessed as a valuable source of phytochemical compounds for the pharmaceutical industry.

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