



Melianthus major L. (Francoaceae): review of its medicinal uses, phytochemistry and biological activities

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Abstract

Melianthus major is a perennial and evergreen shrub widely used to treat and manage various human ailments in South Africa. The present review aims to provide a comprehensive report on the medicinal uses, phytochemical and biological activities of *M. major*. Diverse electronic search engines and specialized reference tools such as Google, Google Scholar, Scopus, Web of Science, scientific literature, publishing sites and electronic databases (Pubmed, Springer, Wiley and Science Direct) were used for data retrieval. The leaves and roots of *M. major* are widely used as traditional medicines for fractures and sprains, pain, syphilis and venereal sores, gum diseases, ulcers, cancer, respiratory problems, backache and lumbago, rheumatism, painful feet and swellings, snakebite, skin problems, septic wounds and sores. The aerial parts and leaves of *M. major* contain esters, flavonoids, phytosterols and triterpenoids. Pharmacological research revealed that the leaf extracts of *M. major* and compounds isolated from the species exhibited antibacterial, antifungal, antioxidant, hypotensive and cytotoxicity activities. There is need for clinical and toxicological evaluations of crude extracts and compounds isolated from the species since *M. major* contains potentially toxic compounds.

Keywords: Ethnopharmacology, Francoaceae, herbal medicine, indigenous pharmacopeia, *Melianthus major*, Melianthaceae

INTRODUCTION

Melianthus major L. is a foetid-smelling, perennial and evergreen shrub belonging to the Francoaceae family. Under the Angiosperm Phylogeny Group iv classification system, the Melianthaceae family is included within the Francoaceae family.¹ The genus *Melianthus* L. consists of six species characterized by large pinnate leaves with prominent stipule and erect racemes with nectar-rich flowers.² The *Melianthus* species exhibit a broad distribution in South Africa, Lesotho and Namibia occupying a wide range of habitats.³ The genus has several unusual features, including the production of black nectar by some species and highly foetid foliage, leading to widespread ethnobotanical use and extensive phytochemical research.⁴⁻¹⁶ Several *Melianthus* species have substantial ornamental value and planted in both private gardens and public recreational parks throughout the world.^{15,17} Similarly, *M. major* is an important ornamental plant in South Africa, Zimbabwe, Australia, Europe, New Zealand, India and the United States of America as the species is grown for its lush and attractive foliage.^{15,18-21} *Melianthus major* is now listed as a weed in the global collection of weeds by Randall³² and the species has escaped from cultivation in Australia, India and New Zealand, invading natural and semi-natural habitats as well as managed afforested areas and protected areas.^{15,20,25,27,29,31-35} In South Africa, the leaves of *M. major* are sold in informal herbal medicine markets in the Eastern Cape and Western Cape provinces as sources of traditional medicines.³⁶ Moreover, *M. major* is included in the book “medicinal plants of South Africa”, a photographic guide to the most commonly used plant medicines in the country, including their botany, main traditional uses and active ingredients.¹⁶ It is therefore, within this context that this review was undertaken aimed at reviewing the medicinal uses, phytochemical and

biological activities of *M. major* so as to provide the baseline data required in evaluating the therapeutic potential of the species.

Botanical profile of *Melianthus major*

The genus name *Melianthus* is derived from two Greek words “*meli*” which means “honey” and “*anthos*” which means “flower”, translating to “honey flower” in reference to the nectar-rich flowers associated with the genus.^{2,37} The name ‘honey flower’ was in use long before its scientific name *Melianthus* was published, the species was introduced to horticulture in the Netherlands in 1673, and only named by Linnaeus in 1753.³⁷ The species name “*major*”, is derived from Latin and means ‘larger’ or ‘greater’, because this is the largest of the *Melianthus* species.³⁷ The Afrikaans common name “*kruidjie-roer-my-nie*” which means ‘touch-me-not-herb’, is in reference to the unpleasant smell of the leaves when they are touched. The English common names include “Cape honey flower”, “giant honey flower”, “greater turkeybush”, “honey flower”, “large honey flower”, “*melianthus*” and “touch-me-not”.^{2,37} *Melianthus major* is a perennial, suffrutescent and multi-stemmed shrub growing up to 2.4 metres in height.^{2,37-40} The stems of *M. major* are soft-wooded, often hollow and branching near the ground. The leaves are blue-green in colour, arranged irregularly and scattered along the stem, imparipinnate, lanceolate to narrow ovate in shape with serrated leaf margins. The leaves are smooth, deeply divided, with a winged rachis, toothed leaflets, a ruffled surface and a strong, unpleasant and nutty odour when touched. The inflorescence is subterminal with an erect, showy raceme, rising up above the leaves, with unusual dark maroon to rusty reddish colouring and growing up to 1.0 metre tall.³⁷ The fruits are four-chambered bladder-like pods, drying to pale brown and containing the shiny and round black seeds.

Melianthus major has been recorded in the Fynbos and Renosterveld biome margins of the Eastern Cape, Northern Cape and Western Cape provinces in South Africa. *Melianthus major* has been recorded on nutrient rich soils that are derived from shales or granites, common on moist habitats, seepages, bogs and gullies where there is some ground water, on sandstone and clay stone slopes, roadsides, swampy places, river banks and along edges of watercourses at an altitude ranging from 25 m to 1500 m above sea level.³⁷⁻⁴⁰

Medicinal uses of *Melianthus major*

In South Africa, the leaves and roots of *M. major* are widely used as traditional medicines for fractures and sprains, pain, syphilis and venereal sores, gum diseases, ulcers, cancer, respiratory problems, backache and lumbago, rheumatism, painful feet and swellings, snakebite, skin problems, septic wounds and sores (Table 1; Figure 1). The leaves of *M. major* are mixed with those of *Cyanella lutea* L.f., *Galenia africana* L., *Helichrysum litorale* Bolus, *Lobostemon fruticosus* (L.) H. Buek and *M. comosus* Vahl as traditional medicine for wounds.^{4,41,42}

Table 1: Medicinal uses of *Melianthus major*

Medicinal use	Part used	Reference
Backache and lumbago	Leaves	Watt and Breyer-Brandwijk ⁴ ; Van Wyk et al. ¹⁶ ; Notten ³⁷ ; Weideman ⁴³ ; Thring and Weitz ⁴⁴ ; Philander ⁴⁵ ; Wentzel and Van Ginkel ⁴⁶ ; Van Wyk and Gericke ⁴⁷
Blood purifier	Leaves	Nzue ⁴⁸
Cancer	Leaves and roots	Van Wyk et al. ¹⁶ ; Thring and Weitz ⁴⁴ ; Philander ⁴⁵ ; Srividya and Sumithra ⁴⁹ ; Lall and Kishore ⁵⁰ ; Sagbo and Mbeng ⁵¹
Fractures and sprains	Leaves	Thring and Weitz ⁴⁴ ; Hutchings ⁵²
Gum diseases	Leaves	Ambasta ⁵³ ; Van Wyk ⁵⁴ ; Pattanayak ⁵⁵
Lupus	Leaves	Wentzel and Van Ginkel ⁴⁶
Pain	Leaves	Philander ⁴⁵ ; Van Wyk and Gericke ⁴⁷
Piles	Leaves	Quattrocchi ³⁵
Respiratory problems (chest complaints and sore throat)	Leaves	Notten ³⁷ ; Nzue ⁴⁸ ; Ambasta ⁵³ ; Van Wyk ⁵⁴ ; Pattanayak ⁵⁵ ; Griffenhagen ⁵⁶
Rheumatism, painful feet and swellings	Leaves	Watt and Breyer-Brandwijk ⁴ ; Van Wyk et al. ¹³ ; Wink and Van Wyk ¹⁵ ; Van Wyk et al. ¹⁶ ; Notten ³⁷ ; Weideman ⁴³ ; Thring and Weitz ⁴⁴ ; Philander ⁴⁵ ; Van Wyk and Gericke ⁴⁷ ; Srividya and Sumithra ⁴⁹ ; Lall and Kishore ⁵⁰ ; Sagbo and Mbeng ⁵¹
Skin problems (abscesses, boils, bruises, burns, impetigo, pimples, rash and ringworm)	Leaves	Watt and Breyer-Brandwijk ⁴ ; Van Wyk et al. ¹³ ; Wink and Van Wyk ¹⁵ ; Van Wyk et al. ¹⁶ ; Quattrocchi ³⁵ ; Notten ³⁷ ; Mabona ⁴¹ ; Mabona et al. ⁴² ; Weideman ⁴³ ; Thring and Weitz ⁴⁴ ; Philander ⁴⁵ ; Wentzel and Van Ginkel ⁴⁶ ; Van Wyk and Gericke ⁴⁷ ; Srividya and Sumithra ⁴⁹ ; Lall and Kishore ⁵⁰ ; Sagbo and Mbeng ⁵¹ ; Griffenhagen ⁵⁶ ; Sagbo and Mbeng ⁵⁷
Septic wounds and sores	Leaves	Watt and Breyer-Brandwijk ⁴ ; Van Wyk et al. ¹³ ; Wink and Van Wyk ¹⁵ ; Van Wyk et al. ¹⁶ ; Quattrocchi ³⁵ ; Notten ³⁷ ; Mabona ⁴¹ ; Mabona et al. ⁴² ; Weideman ⁴³ ; Thring and Weitz ⁴⁴ ; Philander ⁴⁵ ; Wentzel and Van Ginkel ⁴⁶ ; Van Wyk and Gericke ⁴⁷ ; Nzue ⁴⁸ ; Srividya and Sumithra ⁴⁹ ; Sagbo and Mbeng ⁵¹ ; Hutchings ⁵² ; Van Wyk ⁵⁴ ; Griffenhagen ⁵⁶ ; Sagbo and Mbeng ⁵⁷ ; Hutchings et al. ⁵⁸ ; Eloff et al. ⁵⁹ ; Hulley and Van Wyk ⁶⁰ ; Okwu et al. ⁶¹ ;
Wounds	Leaves mixed with those of <i>Cyanella lutea</i> L.f., <i>Galenia africana</i> L., <i>Helichrysum litorale</i> Bolus, <i>Lobostemon fruticosus</i> (L.) H. Buek and <i>M. comosus</i> Vahl	Watt and Breyer-Brandwijk ⁴ ; Mabona ⁴¹ ; Mabona and Van Vuuren ⁴²
Snakebite	Flowers and leaves	Watt and Breyer-Brandwijk ⁴ ; Van Wyk et al. ¹⁶ ; Gomes et al. ²⁵ ; Binorkar and Jani ²⁷ ; Quattrocchi ³⁵ ; Notten ³⁷ ; Thring and Weitz ⁴⁴ ; Wentzel and Van Ginkel ⁴⁶ ; Hutchings ⁵² ; Van Wyk ⁵⁴ ; Hutchings et al. ⁵⁸
Syphilis and venereal sores	Leaves	Quattrocchi ³⁵ ; Wentzel and Van Ginkel ⁴⁶
Ulcers	Leaves	Quattrocchi ³⁵ ; Notten ³⁷ ; Ambasta ⁵³ ; Van Wyk ⁵⁴ ; Pattanayak ⁵⁵

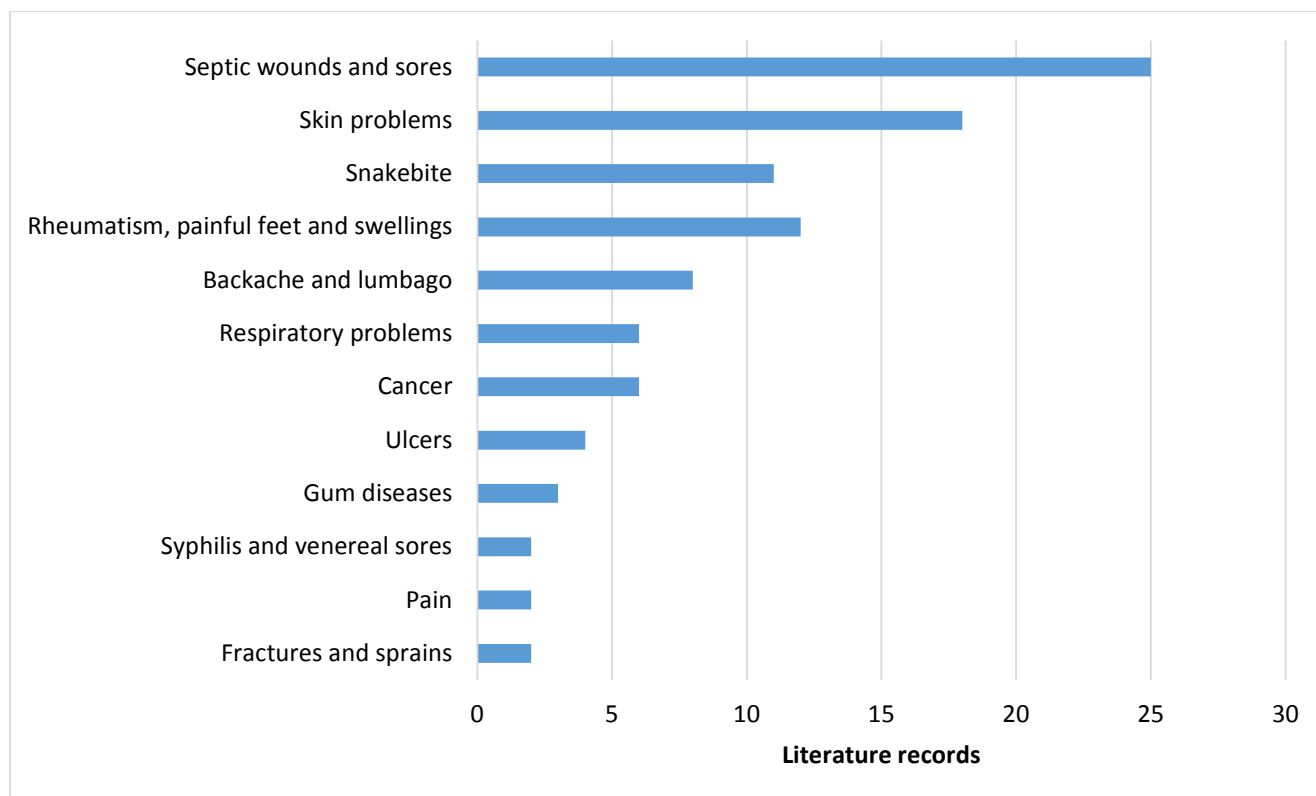


Figure 1. Medicinal applications of *Melianthus major* derived from literature records

Table 2: Phytochemical compounds identified from *Melianthus major*

Phytochemical	Plant part	Reference
Cyclolaudenol	Aerial parts	Agarwal and Rastogi ¹¹
Daucosterol	Aerial parts	Agarwal and Rastogi ¹¹
Kaempferol 3-O- α -arabinopyranoside	Leaves	Heyman et al. ⁶³
Oleanolic acid	Aerial parts	Agarwal and Rastogi ¹¹
Quercetaroic (30) caffeate	Aerial parts	Agarwal and Rastogi ¹¹
Quercetin 3-O- β -galactoside-6-gallate	Leaves	Heyman et al. ⁶³
β -Sitosterol	Aerial parts	Agarwal and Rastogi ¹¹
β -Sitosterol- β -D-glucoside	Aerial parts	Agarwal and Rastogi ¹¹
Ursolic acid	Aerial parts	Agarwal and Rastogi ¹¹

Phytochemistry and biological activities of *Melianthus major*

The aerial parts and leaves of *M. major* contain esters, flavonoids, phytosterols and triterpenoids (Table 2). Van Wyk et al.¹³, Wink and Van Wyk¹⁵ and Van Wyk et al.¹⁶ argued that *M. major* contains cardiac glycosides (bufadienolides) which usually result in toxicity in humans and animals when the plant species is ingested. The following biological activities have been reported from the leaf extracts of *M. major* and compounds isolated from the species: antibacterial,^{41,43,62-65} antifungal,^{41,49,65} antioxidant,⁴⁹ hypotensive^{11,66} and cytotoxicity^{49,62,63} activities.

Antibacterial activities

McGaw and Eloff⁶² evaluated the antibacterial activities of acetone leaf extracts of *M. major* against *Escherichia coli*, *Pseudomonas aeruginosa*, *Enterococcus faecalis* and *Staphylococcus aureus* using two-fold serial dilution

microplate method with neomycin as a positive control. The extracts exhibited activities with minimum inhibitory concentration (MIC) values ranging from 0.8 mg/ml to >6.3 mg/ml which were higher than 0.0008 mg/ml to 0.03 mg/ml exhibited by the control.⁶² Weideman⁴³ evaluated the antibacterial activities of aqueous, acetone and leaf extracts of *M. major* against *Staphylococcus aureus*, *Streptococcus pyogenes*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae* and *Proteus mirabilis* using microtitre plate and agar dilution assays. The extracts exhibited activities against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Klebsiella pneumoniae* with MIC values ranging from 0.03 mg/ml to 2.0 mg/ml.⁴³ Heyman et al.⁶³ evaluated the antibacterial activities of acetone leaf extracts of *M. major* against drug-sensitive and drug-resistant strains of *Staphylococcus aureus* using the microtitre bioassay with gentamicin as a positive control. The extract exhibited

activities with MIC and minimum bactericidal concentrations (MBC) values of 0.6 mg/ml to 0.8 mg/ml and 1.2 mg/ml to 3.1 mg/ml, respectively in comparison to MIC and MBC values of 2.0 µg/ml and 4.0 µg/ml exhibited by the control.⁶³ Mayekiso et al.⁶⁴ evaluated the antibacterial activities of acetone leaf extracts of *M. major* against *Staphylococcus aureus*, *Enterococcus coli*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Mycobacterium smegmatis* and *Mycobacterium fortuitum* using serial microdilution method. The extract exhibited activities against tested pathogens with MIC values as low as 0.02 mg/ml.⁶⁴ Mabona⁴¹ and Mabona et al.⁶⁵ evaluated antibacterial activities of aqueous and dichloromethane : methanol (1:1) leaf extracts of *M. major* using the microtitre plate dilution technique against dermatologically relevant pathogens such as *Brevibacillus agri*, *Propionibacterium acnes*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Staphylococcus epidermidis* with ciprofloxacin as the positive control. The extract showed activities with MIC values ranging from 0.1 mg/ml to 2.0 mg/ml.^{41,65}

Antifungal activities

Srividya and Sumithra⁴⁹ evaluated the antifungal activities of petroleum ether, chloroform, ethyl acetate and methanol leaf extracts of *M. major* against *Aspergillus flavus* using agar dilution method. None of the extracts showed antifungal activities even at 1000 µg/ml with the exception of chloroform extract which exhibited activities at 500 µg/ml.⁴⁹ Mabona⁴¹ and Mabona et al.⁶⁵ evaluated antifungal activities of aqueous and dichloromethane : methanol (1:1) leaf extracts of *M. major* using the microtitre plate dilution technique against dermatologically relevant pathogens such as *Candida albicans*, *Microsporum canis* and *Trichophyton mentagrophytes* with amphotericin B as the positive control. The extract showed activities with MIC values ranging from 0.05 mg/ml to 4.0 mg/ml.^{41,65}

Antioxidant activities

Srividya and Sumithra⁴⁹ evaluated the antioxidant activities of petroleum ether, chloroform, ethyl acetate and methanol leaf extracts of *M. major* using 1,1-diphenyl-2-picrylhydrazyl free radical (DPPH) free radical scavenging assay with ascorbic acid and rutin as positive controls. The petroleum ether, ethyl acetate and methanolic fractions showed activities with half maximal inhibitory concentration (IC₅₀) values of 28.1 µg/ml, 52.2 µg/ml and 4.5 µg/ml, respectively while the positive controls ascorbic acid and rutin exhibited IC₅₀ values of 54.2 and 43.6 µg/ml, respectively.⁴⁹

Hypotensive activities

The alcoholic extract of *M. major* was reported to show a transient hypotensive activity⁶⁶ at a dose of 1.0 mg/kg and hypertensive activity at 2.5 mg/kg to 10.0 mg/kg when administered intravenously to anaesthetized cats.⁶⁶ Similarly, the hexane fraction was biologically inactive, the ethyl acetate fraction showed mild hypotension at 2.5 mg/kg and the butanol fraction caused transient

hypertension at 1.0 mg/kg and hypotension at 2.5 mg/kg and both the fractions caused death at 5.0 mg/kg.¹¹ The compound queretaroic (30) caffeate caused a fall in blood pressure in cat at 1.0 mg/kg and death at 5.0 mg/kg.¹¹

Cytotoxicity activities

McGaw and Eloff⁶² evaluated the cytotoxicity activities of acetone leaf extracts of *M. major* using the brine shrimp lethality assay. At the highest concentration of 5.0 mg/ml, the extract killed 35.0% of the brine shrimps.⁶² Heyman et al.⁶³ evaluated the cytotoxicity activities of acetone leaf extracts of *M. major* and the compounds quercetin 3-O-β-galactoside-6-gallate and kaempferol 3-O-α-arabinopyranoside isolated from the species on Vero cells using the 2,3-Bis-(2-methoxy-4-nitro-5-sulphophenyl)-2Htetrazolium-5-carboxyanilide salt (XTT) assay with zelaralene as a positive control. The extract, quercetin 3-O-β-galactoside-6-gallate and kaempferol 3-O-α-arabinopyranoside exhibited activities with IC₅₀ values of 51.4 µg/ml, 64.3 µg/ml and 160.7 µg/ml, respectively which were higher than IC₅₀ value of 2.3 µg/ml exhibited by the positive control.⁶³ Srividya and Sumithra⁴⁹ evaluated the cytotoxicity activities of petroleum ether, chloroform, ethyl acetate and methanol leaf extracts of *M. major* against Human epithelial larynx carcinoma cells (Hep 2) and Dalton Lymphoma Ascites (DLA) cell lines using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) calorimetric assay. All the extracts exhibiting half maximal cytotoxicity inhibition (CTC₅₀) values ranging from 219.5 µg/ml to 579.0 µg/ml against Hep 2 cell lines and from 72.5 µg/ml to 150.0 µg/ml against DLA cell lines.⁴⁹

CONCLUSION

Melianthus major is a known poisonous plant^{13,15,16} and there is need for detailed clinical and toxicological evaluations of crude extracts and compounds isolated from the species. Much work is required on aspects of quality control to ensure safety and that potentially toxic components of *M. major* herbal products are kept below tolerance levels. Future studies should investigate any side effects and/or toxicity associated with intake of *M. major* herbal products. Therefore, the use of *M. major* for the treatment and management of human diseases and ailments should be treated with caution and rigorous toxicological and clinical studies on the different plant parts and compounds isolated from the species are necessary before they are widely prescribed for use as traditional medicine.

Conflict of interest

The author declares that he has no conflict of interest.

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