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A review of the ethnomedicinal uses, phytochemistry and pharmacological properties of *Melianthus comosus* Vahl

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Abstract

Melianthus comosus is a perennial shrub widely used as traditional medicine in South Africa. The present review aims to provide a comprehensive review of the botany, ethnomedicinal uses, phytochemical and pharmacological properties of *M. comosus*. 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, leaf juice and roots of *M. comosus* are widely used as traditional medicines for cancer, fractures and sprains, gastro-intestinal problems, respiratory problems, pain and painful feet, swellings, backache, snakebite, rheumatism, skin problems, septic wounds and sores. The leaves, root bark and seeds of *M. comosus* contain cardiac glycosides, flavonoids, phytosterols and triterpenoids and biological activities reported from these compounds, leaf and stem extracts of the species include antibacterial, antifungal, anti-inflammatory, antioxidant and cytotoxicity activities. There is need for clinical and toxicological evaluations of crude extracts and compounds isolated from the species since *M. comosus* contains potentially toxic compounds.

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

INTRODUCTION

Melianthus comosus Vahl is a perennial, evergreen and multi-stemmed 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, *M. comosus*, *M. dregeanus* Sond., *M. elongatus* Wijnands, *M. major* L., *M. pectinatus* Harv. and *M. villosus* Bolus.[2-7] The *Melianthus* species are characterized by large pinnate leaves with prominent stipule and erect racemes with nectar-rich flowers and these species have been recorded in South Africa, Lesotho and Namibia.[2-7] *Melianthus comosus* was promoted as an ornamental plant in Africa, America, Australia and Europe[8-10] as the species is ideal for a low-maintenance and waterwise garden.[3] *Melianthus comosus* was also introduced in other countries due to its medicinal properties. For example, *M. comosus* was grown in the Netherlands around 1700 and later in England because of its medicinal properties.[11] *Melianthus comosus* is now listed as a weed in the global collection of weeds by Randall[12] and the species has escaped from cultivation in Australia where it is now categorized as an invasive and noxious weed.[11-14] *Melianthus comosus* produces dark brown to black nectar eaten by children which resemble black coffee in appearance and taste and hence the Afrikaans common name "*koffebos*".[15,16] *Melianthus comosus* 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.[17] *Melianthus comosus* is also included in two monographs focusing on poisonous plants, "mind-altering and poisonous plants of the world" and "poisonous plants of South Africa".[9,18] In these two monographs, Wink and Van Wyk[9] and Van Wyk et al.[18] provide basic information about the poisonous ingredients, the pharmacological effects and associated symptoms of human and animal poisoning as a result of ingesting documented plant species. It is therefore, within this context that this review was undertaken aimed at reviewing the botany, ethnomedicinal uses, phytochemical and pharmacological properties of *M. somosus* so as to provide baseline data required in evaluating the therapeutic potential of the species.

Botanical profile of *Melianthus comosus*

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.[3,19] The name 'honey flower' was in use for a long time 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.[19] The species name "*comosus*", means "with a tuft of hair",[3,20] probably in reference to hairy leaves. The Afrikaans common name "*kruidjie-roer-my-nie*" which means 'touch-me-not-herb', is in reference to the unpleasant smell produced by the leaves when they are touched. The English common names include "honey flower", "melianthus" and "touch-me-not".[3] *Melianthus comosus* is a perennial, suffrutescent and multi-stemmed shrub growing up to 3 metres in height.[2,6,7,9,17] The stems of *M. comosus* are soft-wooded, often hollow and branching near the ground. The leaves are grey-green in colour, imparipinnate, lanceolate in shape with serrated leaf margins, winged rachis, apically acuminate and clustered near the apices of the stems. The leaves produce a strong, unpleasant and nutty odour when touched. The inflorescence is axillary with a nodding raceme and small, nectar-rich, bird-pollinated flowers that are borne in a short cluster. The fruits are four-winged, papery and bladdery capsule with shiny and round black seeds. *Melianthus comosus* has been recorded in permanent and seasonally dry streams in rich soils of shale origin on stony slopes, stream banks and Karoo sediments in Lesotho, Namibia and South Africa at an altitude ranging from 120 m to 2230 m above sea level.[2,5-7,19]

Medicinal uses of *Melianthus comosus*

In South Africa, the leaves, leaf juice and roots of *M. comosus* are widely used as traditional medicines for cancer, fractures and sprains, gastro-intestinal problems, respiratory problems, pain and painful feet, swellings, backache, snakebite, rheumatism, skin problems, septic wounds and sores (Table 1, Figure 1). The leaves of *M. comosus* are mixed with those of *Cyanella lutea* L.f., *Galenia africana* L., *Helichrysum litorale* Bolus, *Lobostemon fruticosus* (L.) H. Buek and *M. major* L. as traditional medicine for wounds.[21-23] The leaves of *M. comosus* are also used as ethnoveterinary medicine, usually applied on sores of livestock.[24]

Table 1: Medicinal uses of *Melianthus comosus*

Medicinal uses	Parts used	References
Backache	Leaves	Harris[3]; Van Wyk et al.[15]; Van Wyk et al.[17]; Watt and Breyer-Brandwijk[21]; Thring and Weitz[24]; De Beer and Van Wyk[25]; Lall and Kishore[26]; Sagbo and Mbeng[27]; Van Wyk and Gericke[28]; Hulley and Van Wyk[29]
Cancer	Roots	Van Wyk et al.[17]; Thring and Weitz[24]
Fractures and sprains	Leaves	Thring and Weitz[24]; Hutchings[30]
Gastro-intestinal problems (diarrhoea, dyspepsia and stomach pain)	Leaves and roots	Hutchings et al.[31]; Iwalewa et al.[32]; Stark et al.[33]; Ndhlala et al.[34]
Gout	Leaves	Hulley and Van Wyk[29]
Gum diseases	Leaves	Van Wyk[35]
Headache	Roots	Ndhlala et al.[34]
Lupus	Leaves	Hutchings et al.[31]
Pain and painful feet	Leaves and roots	Van Wyk et al.[15]; De Beer and Van Wyk[25]; Van Wyk and Gericke[28]; Hulley and Van Wyk[29]; Hutchings et al.[31]; Iwalewa et al.[32]; Stark et al.[33]; Frum[36]
Respiratory problems (sore throat and tuberculosis)	Leaves and roots	Hutchings et al.[31]; Ndhlala et al.[34]; Van Wyk[35]; Frum[36]; Scot[37]
Rheumatism	Leaves and roots	Harris[3]; Wink and Van Wyk[9]; Van Wyk et al.[15]; Van Wyk et al.[17]; Van Wyk et al.[18]; Watt and Breyer-Brandwijk[21]; Thring and Weitz[24]; De Beer and Van Wyk[25]; Lall and Kishore[26]; Sagbo and Mbeng[27]; Van Wyk and Gericke[28]; Hulley and Van Wyk[29]; Hutchings et al.[31]; Iwalewa et al.[32]; Stark et al.[33]; Frum[36]; McGaw et al.[38]; Adebayo et al.[39]; Adebayo and Amoo[40]
Septic wounds and sores	Leaves and leaf juice	Harris[3]; Wink and Van Wyk[9]; Van Wyk et al.[15]; Van Wyk et al.[17]; Van Wyk et al.[18]; Watt and Breyer-Brandwijk[21]; Mabona[22]; Mabona and Van Vuuren[23]; Thring and Weitz[24]; De Beer and Van Wyk[25]; Lall and Kishore[26]; Sagbo and Mbeng[27]; Van Wyk and Gericke[28]; Hulley and Van Wyk[29]; Hutchings[30]; Hutchings et al.[31]; Van Wyk[35]; Frum[36]; McGaw et al.[38]; Adebayo and Amoo[40]; Steyn[41]; Gerstner[42]; Wilman[43]; Githens[44]; Palmer[45]; Ambasta[46]; Kellerman et al.[47]; Roberts[48]; Shearing[49]; Hutchings[50]; Kelmanson et al.[51]; Von Koenen[52]; Kellerman et al.[53]; Mabona et al.[54]; Eloff et al.[55]; Madzinga et al.[56]; Pattanayak[57]; Okwu et al.[58]; Sagbo and Mbeng[59]
Wounds	Leaves mixed with those of C*yanella lutea* L.f., *Galenia africana* L., *Helichrysum litorale* Bolus, *Lobostemon fruticosus* (L.) H. Buek and *M. major* L.	Watt and Breyer-Brandwijk[21]; Mabona[22]; Mabona and Van Vuuren[23]
Skin problems (abscesses, boils, bruises, burns, impetigo, inflammation, ringworm and shingles)	Leaves and leaf juices	Harris[3]; Wink and Van Wyk[9]; Van Wyk et al.[15]; Van Wyk et al.[17]; Van Wyk et al.[18]; Watt and Breyer-Brandwijk[21]; Mabona and Van Vuuren[23]; Thring and Weitz[24]; Lall and Kishore[26]; Sagbo and Mbeng[27]; Van Wyk and Gericke[28]; Hulley and Van Wyk[29]; Hutchings et al.[31]; Frum[36]; Scot[37]; Gerstner[42]; Ambasta[46]; Hutchings[50]; Kelmanson et al.[51]; Madzinga et al.[56]; Pattanayak[57]; Okwu et al.[58]
Snakebite	Leaves	Harris[3]; Van Wyk et al.[17]; Watt and Breyer-Brandwijk[21]; Thring and Weitz[24]; Lall and Kishore[26]; Sagbo and Mbeng[27]; Hutchings[30]; Hutchings et al.[31]; Van Wyk[35]; Scot[37]; McGaw et al.[38]; Kelmanson et al.[51]; Madzinga et al.[56]; Okwu et al.[58]
Stroke	Leaves	Hulley and Van Wyk, 2019
Swellings	Leaves	Van Wyk et al.[15]; Mabona[22]; De Beer and Van Wyk[25]; Hulley and Van Wyk[29]; Hutchings et al.[31]; Adebayo and Amoo[40]; Mabona et al.[54]; Madzinga et al.[56]
Syphilis	Leaves	Hutchings et al.[31]
Toothache	Leaves	Hulley and Van Wyk[29]
Ulcers	Leaves	Van Wyk[35]
Ethnoveterinary medicine (sores)	Leaves	Thring and Weitz[24]

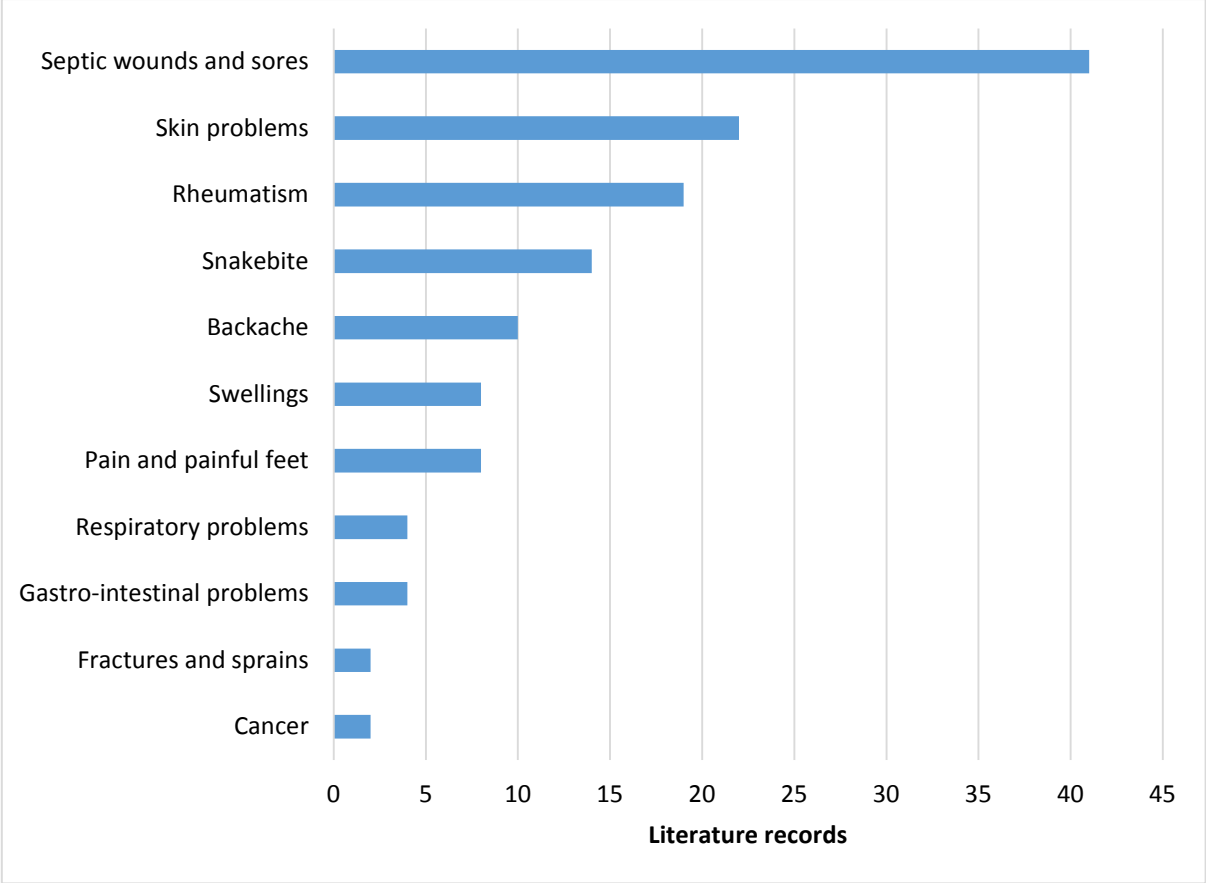

Figure 1. Medicinal applications of *Melianthus comosus* derived from literature records

Phytochemistry and biological activities of *Melianthus comosus*

The leaves, root bark and seeds of *M. comosus* contain cardiac glycosides, flavonoids, phytosterols and triterpenoids (Table 2). Wink and Van Wyk,[9] Van Wyk et al.[17] and Van Wyk et al.[18] argued that *M. comosus* contain 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. comosus* and compounds isolated from the species: antibacterial antibacterial,[22,51,54,55,60,61] antifungal,[22,54,55,62,63] anti-inflammatory,[36,38,39,64] antioxidant[36] and cytotoxicity[61] activities.

Table 2: Phytochemical compounds identified from *Melianthus comosus*

Phytochemica	Value	Plant part	Reference
6β-acetoxymelianthugenin	-	Root bark	Anderson and Koekemoer[65]; Koekemoer et al.[66]
6β-acetoxy-14-deoxy-15β,16β-epoxymelianthugenin	-	Root bark	Anderson and Koekemoer[65]; Koekemoer et al.[67]
Anhydroscillarine A	-	Seeds	Anderson and Koekemoer[68]
3-anhydroscilliglaucosidine	-	Seeds	Anderson and Koekemoer[68]
Caffeic acid	-	Root bark	Koekemoer et al.[69]
Ellagic acid	-		Anderson[70]
14-deoxy-15β,16β-epoxymelianthugenin	-	Root bark	Anderson and Koekemoer[65]; Koekemoer et al.[67]
27-(3,4-dihydroxycinnamoyloxy)-oleanolic acid	-	Root bark	Koekemoer et al.[69]; Van Schalkwyk and Kruger[71]
Helibrigenin 3-acetate	-	Root bark	Anderson and Koekemoer[65]
3-hydroxy-12-oleanen-30-oic acid	-	Leaves	Eloff et al.[62]
Melianthugenin	-	Root bark	Anderson and Koekemoer[65]; Anderson and Koekemoer[68]
Melianthusigenin	-	Root bark	Anderson and Koekemoer[65]; Anderson and Koekemoer[68]
Oleanolic acid	-	Leaves and root bark	Eloff et al.[55]; Anderson and Koekemoer[68]; Anderson and Koekemoer[72]
Oleanolic acid acetate	-		Anderson[70]
Scillaridine A	-	Seeds	Anderson and Koekemoer[68]
Total flavonoid content (mg/g QE)	0.3	Leaves	Adebayo et al.[39]
Total phenolic content (mg/g GAE)	65.0	Leaves	Adebayo et al.[39]

Antibacterial activities

Kelmanson et al.[51] evaluated the antibacterial activities of aqueous, methanolic and ethyl acetate leaf and stem extracts of *M. comosus* against *Bacillus subtilis, Escherichia coli, Kleibsiella pneumoniae, Micrococcus luteus, Pseudomonas aeruginosa, Staphylococcus aureus* and *Staphylococcus epidermidis* using disc-diffusion assay and agar dilution method with neomycin 200 (µmg/ml) as a positive control. The methanol extract was the most active, exhibiting the minimum inhibitory concentration (MIC) values ranging from 2.0 mg/ml to 8.0 mg/ml against *Bacillus subtilis, Micrococcus luteus, Staphylococcus aureus* and *Staphylococcus epidermidis*.[51] McGaw and Eloff[60] evaluated the antibacterial activities of acetone leaf extracts of *M. comosus* against *Escherichia coli, Pseudomonas aeruginosa, Enterococcus faecalis* and *Staphylococcus aureus* using two-fold serial dilution microplate method with neomycin as a positive control. The extract exhibited activities with 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.[60] Heyman et al.[61] evaluated the antibacterial activities of acetone leaf extracts of *M. comosus* 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 0.4 mg/ml to 0.5 mg/ml and 1.6 mg/ml to 2.0 mg/ml, respectively in comparison to MIC and MBC values of 2.0 µg/ml and 4.0 µg/ml exhibited by the control.[61] Mabona[22] and Mabona et al.[54] evaluated antibacterial activities of aqueous and dichlomethane : methanol (1:1) leaf extracts of *M. comosus* 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.[22,54] Eloff et al.[55] evaluated the antibacterial activities of the compound oleanolic acid isolated from the leaves of *M. comosus* against *Staphyloccocus aureus, Enteroccocus faecalis, Escherichia coli* and *Pseudomonas aeruginosa* using two-fold serial dilution microplate method. Oleanolic acid exhibited activities with MIC values ranging from 31.3 µg/ml to 125.0 µg/ml against tested pathogens.[55]

Antifungal activities

Eloff et al.[62] and Eloff et al.[63] evaluated the antifungal activities of acetone leaf extracts of *M. comosus* against *Rhizoctonia solani, Fusarium oxysporum, Penicillium janthinelum, Penicillium expansum, Colletotrichum glocosponicales, Trichoderma harzianum, Pythium ultimum, Phytophthora nicotiana, Aspergillus niger* and *Aspergillus parasiticus* using two-fold serial dilution microplate method. The extract exhibited activities with MIC values ranging from 0.04 mg/ml to 0.2 mg/ml.[62,63] Mabona[22] and Mabona et al.[54] evaluated antifungal activities of aqueous and dichlomethane : methanol (1:1) leaf extracts of *M. comosus* 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.[22,54] Eloff et al.[55] evaluated the antifungal activities of hexane, carbon tetrachloride, diethyl ether, dichloromethane, chloroform, acetone, ethanol, ethyl acetate, methanol and water leaf extracts of *M. comosus* against *Fusarium oxysporum, Penicillium janthinellum, Colletotrichum gloeosporioides, Penicillium expansum, Trichoderma harzianum, Aspergillus niger, Aspergillus parasiticus, Rhizoctonia solani, Pythium ultimum* and *Phytophthora nicotiana* using a serial microdilution assay method. The extracts exhibited activities with MIC values ranging from 20 µg/ml to 310 µg/ml against the tested pathogens. Eloff et al.[55] evaluated the antifungal activities of the compound oleanolic acid isolated from the leaves of *M. comosus* against *Colletotrichum gloeosporioides, Phytophthora nicotiana, Penicillium expansum* and *Aspergillus parasiticus* using two-fold serial dilution microplate method. Oleanolic acid exhibited activities with MIC values ranging from 7.8 µg/ml to 15.6 µg/ml against tested pathogens. When the acetone leaf extract of *M. comosus* was used in a field trial on comfrey (*Symphytum officinale* L.) with a natural rust infection it was much more effective at a concentration of 0.2 mg/ml than the commercial product containing dicarboximide at a concentration of 1.5 mg/ml.[55]

Anti-inflammatory activities

McGaw et al.[38] evaluated the anti-inflammatory activities of the aqueous and ethanol leaf extracts of *M. comosus* by assessing the inhibition of prostaglandin biosynthesis using the cyclooxygenase assay with indomethacin (0.5 µg) as a positive control. The ethanol extract exhibited good activities with percentage inhibition ranging from 72.0% to 86.0% which was comparable to 75% exhibited by the positive control.[38] Frum[36] and Frum and Viljoen[64] evaluated anti-inflammatory activities of aqueous and methanol leaf extracts of *M. comosus* through the assessment of the 5-lipoxygenase inhibitory activities by using a threefold stepwise dilution method with dimethyl sulfoxide (DMSO) and Tween®20 as negative controls and nordihydroguaiaretic acid as a positive control. The aqueous and methanol extracts exhibited 5-lipoxygenase inhibitory activities with half maximal inhibitory concentration (IC_{50}) values of 13.8 ppm and 55.1 ppm, respectively.[36,64] Adebayo et al.[39] evaluated the anti-inflammatory activities of acetone leaf extracts of *M. comosus* by assessing the ability of extracts to inhibit 15-lipoxygenase (15-LOX) enzyme with quercetin as a positive control. The extract exhibited activities with IC_{50} value of 30.0 µg/mL which was higher than IC_{50} value of 8.8 µg/mL exhibited by the positive control.[39]

Antioxidant activities

Frum[36] evaluated the antioxidant activities of aqueous and methanol leaf extracts of *M. comosus* using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging

assay. The aqueous and methanol extracts exhibited activities with IC_{50} values of 5.3 ppm and 5.6 ppm, respectively.[36]

Cytotoxicity activities

Heyman et al.[61] evaluated the cytotoxicity activities of acetone leaf extracts of *M. comosus* on Vero cells using the the 2,3-Bis-(2-methoxy-4-nitro-5-sulfophenyl]-2Htetrazolium-5-carboxyanilide salt (XTT) assay with zelaralenone as a positive control. The extract exhibited activities with IC_{50} value of 51.4 µg/ml which was higher that IC_{50} value of 2.3 µg/ml exhibited by the positive control.[61]

CONCLUSION

Melianthus comosus is a known poisonous plant[9,17,18] and there is need for detailed clinical and toxicological evaluations of crude extracts and compounds isolated from the species. At the present moment there is very little ethnobotanical information on the poisonous properties of *M. comosus*. Therefore, the widespread use of *M. comosus* in South Africa as traditional medicine suggest that the species is not taken at toxic dosages. But use of *M. comosus* for the treatment of human diseases and ailments should be treated with caution and rigorous toxicological and clinical studies of the bark, leaves, roots, stems and compounds isolated from the species are necessary.

Conflict of interest

The author declares that he has no conflict of interest.

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