

A SYNTHESIS AND REVIEW OF MEDICINAL USES, PHYTOCHEMISTRY AND BIOLOGICAL ACTIVITIES OF *HELICHRYSUM ODORATISSIMUM* (L.) SWEET

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ABSTRACT

Helichrysum odoratissimum is an important medicinal plant species in tropical Africa. The current study critically reviewed the medicinal uses, phytochemistry and biological activities of *H. odoratissimum*. Information on medicinal uses, phytochemistry and biological activities of *H. odoratissimum* were collected from multiple internet sources which included Scopus, Google Scholar, Elsevier, Science Direct, Web of Science, PubMed, SciFinder, and BMC. Additional information was gathered from pre-electronic sources such as journal articles, scientific reports, theses, books, and book chapters obtained from the university library. This study showed that *H. odoratissimum* is mainly used as an herbal medicine for insomnia, menstrual pain and sterility, and wounds and respiratory problems. Pharmacological research revealed that *H. odoratissimum* extracts and compounds isolated from the species have antibacterial, antimycobacterial, antifungal, anti-inflammatory, antioxidant, hepatoprotection, and hypoglycemic and cytotoxicity activities. There is a need to validate the documented ethnomedicinal uses of *H. odoratissimum* through phytochemical and pharmacological studies. Therefore, future studies should address these knowledge gaps through experimental animal studies, randomized clinical trials, and target-organ toxicity studies involving *H. odoratissimum* crude extracts and compounds isolated from the species.

Keywords: Asteraceae, *Helichrysum odoratissimum*, Ethnopharmacology, Herbal medicine, Southern Africa.

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INTRODUCTION

Helichrysum odoratissimum (L.) Sweet is a perennial shrub which belongs to the tribe Gnaphalieae in the Asteraceae (Compositae) or daisy family. The species has been recorded in Angola, Burundi, Cameroon, Democratic Republic of Congo, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Nigeria, Rwanda, South Africa, South Sudan, Sudan, Swaziland, Tanzania, Uganda, Zambia, Zimbabwe, and Yemen [1-6]. The genus name "Helichrysum" is derived from the Greek words "Helios" which means "sun" and "Chrysos" which means "gold," in reference to the "golden flowers" which are characteristic of the genus [7]. The specific name "odoratissimum" is in reference to the strong fragrance produced by the species [7]. Synonyms that have been associated with *H. odoratissimum* include *Achyrocline hochstetteri* A. Rich., *A. stenoptera* (DC.) Hilliard and B.L. Burt, *Gnaphalium aureofulvum* Berg., *G. hochstetteri* (A. Rich.) Sch. Bip., *Graphidium odoratissimum* L., *Graphidium pedunculare* L., *Graphidium stenopterus* (DC.) Sch. Bip., *Graphidium strigosum* Thumb., *Helichrysum hochstetteri* (A. Rich.) Hook.f., *H. odoratissimum* (L.) Sweet var. *lanatum* Sond., *H. pedunculare* (L.) DC., and *Helichrysum sarveri* S. Moore [1,2,4,5]. *H. odoratissimum* is a heavily branched, bushy, erect, aromatic perennial shrub or occasionally scrambling 20–200 cm high into surrounding vegetation [2,4]. Leaves are variable in shape, usually linear to oblanceolate, narrow at the base or broad and clasping, markedly decurrent, covered in gray to white velvet hairs on both leaf surfaces. The small bright yellow flower heads are crowded in a compound inflorescence at the end of the branches [7]. *H. odoratissimum* forms large clumps on grassy or rocky slopes in grassland, wooded grassland, thicket, forest edges, disturbed areas and on roadsides at an altitude ranging from 5 m to 3050 m above sea level [2,4,5].

The aerial parts, flowers, leaves, roots, stems, twigs and whole plant parts of *H. odoratissimum* are primary sources of herbal medicines in tropical Africa. A patented extract of *H. odoratissimum* is used in the prevention of and treatment of skin cancer in South Africa [8]. Moreover, the leaves, stems, and twigs of *H. odoratissimum* are sold as

herbal medicines in the informal herbal medicine markets in Gauteng and the Western Cape provinces in South Africa [9-13]. Research by Van Wyk [14-16] showed that the leaves of *H. odoratissimum* have commercial potential as ritual incense and sedative, while essential oils isolated from the species have commercial potential as an inhalant and aromatherapy in South Africa. Research carried out so far on *H. odoratissimum* and other plant species showed that these resources are an integral part of traditional pharmacopeia in tropical Africa with a potential contribution to primary health care of local communities in the region [11-18]. Therefore, the current study is aimed at providing a critical appraisal of the existing ethnomedicinal value, phytochemistry and biological activities of *H. odoratissimum* as well as exploring the potential of the species as herbal medicine in tropical Africa.

MEDICINAL USES OF *H. ODORATISSIMUM*

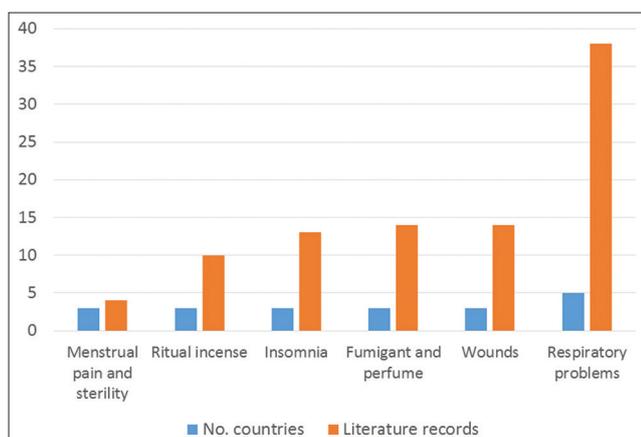
The aerial parts, flowers, leaves, roots, stems, twigs, and whole plant parts of *H. odoratissimum* are used for various traditional and medicinal applications in tropical Africa (Table 1). Following medical categorization of human diseases and ailments proposed by Cook [19], Macía *et al.* [20], Gruca *et al.* [21], and Staub *et al.* [22], *H. odoratissimum* is mainly used for ritual incense, fumigant and perfume and as herbal medicine for insomnia, menstrual pain and sterility, wounds and respiratory problems (Table 1 and Fig. 1). Other medicinal applications recorded in two countries and supported by at least two literature records include the following: Headache, heart problems, insect and parasite repellent, intestinal worms, pain, skin infections, stomach problems, and toothache (Table 1). In Lesotho, the whole plant parts of *H. odoratissimum* are mixed with *Olea europaea* L. and *Zantedeschia albomaculata* (Hook.) Baill. as an herbal medicine for backache [23].

PHYTOCHEMISTRY

H. odoratissimum flowers contain the chalcone, helichrysetin, and flavonoids 3,5-dihydroxy-6,7,8-trimethoxy flavone and 3-O-methylquercetin and 3',4',3,5-tetrahydroxy-7-methoxyflavone [24,80]. The composition of essential oils appears

Table 1: Medicinal uses of *Helichrysum odoratissimum*

Disease	Parts used	Country	References
Pain (abdominal pains and backache)	Leaves and whole plant	Lesotho and South Africa	[8,11,24-27]
Backache	Whole plant mixed with <i>Olea europaea</i> L. and <i>Zantedeschia albomaculata</i> (Hook.) Baill	Lesotho	[23]
Colic	Leaves	South Africa	[8,25]
Conjunctivitis	Leaves	South Africa	[8,25]
Convulsions	Leaves and twigs	South Africa	[11,25]
Cramps	Aerial parts and whole plant	South Africa	[11,27,28]
Diabetes	Whole plant	South Africa	[29-32]
Fever	Leaves and stems	South Africa	[8,11,25,33]
Fumigant and perfume	Leaves, stems, and whole plant	Lesotho, South Africa, and Swaziland	[7,11,23,34-44]
Headache	Leaves, stems, and whole plant	Lesotho and South Africa	[11,25,26,31,33,45]
Heart problems	Aerial parts, leaves, roots, and whole plant	Lesotho and South Africa	[24-28,46-48]
High blood pressure	Aerial parts, leaves, and roots	South Africa	[27,28,47]
Induce vomiting	Leaves	South Africa	[25]
Inflammation	Whole plant	South Africa	[27]
Insanity	Leaves and twigs	South Africa	[11,27]
Insect and parasite repellent	Leaves and whole plant	Lesotho and South Africa	[7,11,27,39,42,43,49]
Insomnia	Leaves, roots, stems, and whole plant	Lesotho, South Africa, and Swaziland	[7,8,11,25,33,37,39,43,49-53]
Intestinal worms	Roots and whole plant	Kenya and South Africa	[54,55]
Kidney problems	Aerial parts	South Africa	[27,28]
Laxative	Leaves	South Africa	[25]
Magic	Whole plant	South Africa	[27]
Menstrual pain and sterility	Leaves and whole plant	Lesotho, Rwanda, and South Africa	[8,24-27]
Nervous disorders	Leaves	South Africa	[46,48]
Postpartum bleeding	Leaves	South Africa and Tanzania	[27,56]
Prostrate problems	Whole plant	South Africa	[27]
Respiratory problems (chest pains, colds, cough, flu, and tuberculosis)	Leaves, roots, stems, and whole plant	Lesotho, South Africa, Tanzania, Uganda, and Swaziland	[7,8,11,23-28,31,33-38,41,43,46-53,55-66]
Ritual incense	Leaves, stems, and twigs	Lesotho, South Africa, and Swaziland	[7,11,36-39,44,58,67,68]
Skin infections (acne, eczema, pimples, scabies, and skin ulcers)	Flowers, leaves, stems, and whole plant	Rwanda and South Africa	[7,8,24,36,38,50-52,58,69-72]
Stomach problems and excessive bile	Aerial parts, leaves, stems, and whole plant	Lesotho and South Africa	[26,28,33]
Stroke	Leaves and roots	South Africa	[47]
Tension	Leaves and twigs	South Africa	[11]
Toothache	Leaves and stems	South Africa and Uganda	[33,73-76]
Urinary problems	Whole plant	South Africa	[27]
Wounds (including burns and infections)	Leaves, roots, twigs, and whole plant	Cameroon, South Africa, and Tanzania	[11,24,25,31,43,49,55-59,72,77-79]

Fig. 1: Traditional and medicinal applications of *Helichrysum odoratissimum* in tropical Africa

to vary with geographical origin of the specimens as shown in Table 2. The major compounds that have been identified from the species include(Z)- β -ocimene (<0.01–10.8%), docosanoic acid methyl ester (11.4%), bifloratriene (7.4–11.6%), germacrene A (1.1–11.8%), δ -cadinene (0.3–13.2%), humulene (14.1%), α -humulene (<0.01–14.6%), 1,22-docosanediol (15.1%), (E,E)-farnesol (16.8%), 1,8-cineole (2.7–17.1%), 1-isopropyl-3-methylbenzene (18.3%), α -curcumene (4.0–20.3%), caryophyllene oxide (0.1–20.6%), β -caryophyllene (1.3–25.2%), palmitic acid (27.1%), limonene (<0.01–31.6%), pelugone (34.2%), p-menthone (35.4%), α -pinene (1.1–47.1%), and β -pinene (0.1–51.6%) [38,42,43,51,65,75,78,79,81-84]. Future research should focus on evaluating the biological activities of the isolated compounds.

BIOLOGICAL ACTIVITIES

The following biological activities have been reported from *H. odoratissimum* crude extracts and compounds isolated from the species: Antibacterial [24,38,42,61,74,75,85-87],

Table 2: Phytochemical composition of *Helichrysum odoratissimum*

Phytochemical composition	Values	Plant parts	References
Acridine-9-carbaldehyde (%)	3.3	Leaves and stems	[65]
Alloaromadendrene (%)	0.1–3.6	Aerial parts, flowers, and leaves	[38,43,51,79]
(–)-Alloaromadendrene (%)	1.4	Leaves and stems	[65]
α-Amorphene (%)	0.2–1.2	Aerial parts, flowers, and leaves	[43,51]
Aromadendrene(%)	0.1–0.8	Aerial parts	[38,51,79]
α-trans-Bergamotene (%)	0.3	Flowers	[43]
trans-β-Bergamotene (%)	0.6–0.8	Aerial parts	[38,79]
Bicyclogermacrene(%)	0.1	Aerial parts	[51]
Bifloratriene (%)	7.4–11.6	Flowers and leaves	[43]
β-Bisabolol (%)	0.1–0.3	Aerial parts, flowers and leaves	[38,43,79]
β-Bisabolene (%)	0.4–2.0	Aerial parts and leaves	[38,78,79]
cis-α-Bisabolene (%)	0.4–1.3	Aerial parts	[38,79]
γ-Bisabolene (%)	0.2–0.6	Aerial parts	[38,79]
Bornyl acetate(%)	<0.01–0.2	Aerial parts, flowers, and leaves	[38,43,51,79]
Bornyl formate(%)	0.2–0.3	Flowers and leaves	[43]
β-Bourbonene (%)	0.1	Aerial parts	[51]
Borneol (%)	1.4	Aerial parts	[51]
Bulnesol (%)	0.6–2.2	Flowers and leaves	[43]
α-Bulnesene (%)	2.8	Aerial parts	[75]
Cadalene (%)	0.1–0.8	Aerial parts, flowers, and leaves	[38,43,79]
Cadina-1,4-diene (%)	<0.1–0.6	Leaves	[78]
Camphor (%)	<0.01–0.4	Aerial parts, flowers, and leaves	[43,51]
trans-Cadina-1,4-diene (%)	1.3	Flowers and leaves	[43]
α-Cadinene (%)	0.4–0.9	Flowers and leaves	[43,78]
ε-Cadinene (%)	<0.01	Leaves	[78]
δ-Cadinene (%)	0.3–13.2	Aerial parts, flowers and leaves	[38,42,43,51,75,78,79]
γ-Cadinene(%)	0.2–3.9	Aerial parts and leaves	[38,78,79]
trans-γ-Cadinene(%)	<0.01–0.1	Flowers and leaves	[43]
α-Cadinol (%)	0.4–1.0	Flowers and leaves	[43,78]
epi-α-Cadinol (%)	0.2	Flowers and leaves	[43]
δ-Cadinol (%)	<0.1	Leaves	[78]
T-Cadinol (%)	0.1–1.8	Aerial parts and leaves	[38,78,79]
α-Calacorene (%)	<0.01–0.1	Flowers and leaves	[43,79]
Calamenene (%)	0.2–0.5	Aerial parts	[38,79]
Camphene (%)	<0.01–0.3	Aerial parts, flowers, and leaves	[38,43,79]
α-Campholenal (%)	<0.01	Flowers and leaves	[43]
δ-4-Carene (%)	0.5	Aerial parts	[51]
Carvacrol(%)	<0.01–0.4	Aerial parts and flowers	[38,43,79]
Carvone (%)	0.4	Aerial parts	[38,79]
cis-Carveol (%)	0.1	Aerial parts	[38,79]
trans-Carveol (%)	0.2–0.3	Aerial parts	[38,51,79]
cis-Carvyl acetate (%)	0.1–0.2	Aerial parts	[38,79]
trans-Carvyl acetate(%)	0.3–0.6	Flowers and leaves	[43]
Caryophyllene (%)	2.2	Leaves and stems	[65]
α-Caryophyllene (%)	1.5–4.7	Leaves and stems	[42,65]
β-Caryophyllene (%)	1.3–25.2	Aerial parts, flowers, and leaves	[38,43,51,75,78-80,82]
Caryophylla-4(14),8(15)-dien-5-ol (%)	0.2	Flowers and leaves	[43]
Caryophyllene oxide (%)	0.1–20.6	Aerial parts, flowers, leaves, and stems	[38,42,43,51,65,78,79]
Caryophyllenol-I (%)	0.4	Aerial parts	[38,79]
Cedren-13-ol (%)	1.6	Leaves and stems	[65]
β-Chamigrene (%)	0.1–1.1	Aerial parts, flowers, and leaves	[38,43,79]
1,8-Cineole (%)	2.7–17.1	Aerial parts, flowers, and leaves	[38,43,51,79]
Clovenol (%)	0.1	Aerial parts	[38,79]
α-Copaene (%)	0.9–7.3	Aerial parts, flowers, and leaves	[38,43,51,75,78,79]
β-Copaene (%)	<0.1	Flowers	[43]
α-Copaene (%)	0.6	Leaves	[42]
Cubebol(%)	0.3	Flowers and leaves	[43]
1-epi-Cubenol (%)	0.08–2.3	Aerial parts, flowers, and leaves	[38,43,79]
ar-Curcumene (%)	3.9	Aerial parts	[38,79]
α-Curcumene (%)	4.0–20.3	Leaves	[78]
γ-Curcumene (%)	1.6–5.4	Aerial parts	[38,51,79]
Cyclooctanone (%)	1.7	Leaves and stems	[65]
Cyclosativene (%)	<0.01–0.4	Flowers and leaves	[43]
p-Cymen-8-ol (%)	0.2	Aerial parts	[38,79]
o-Cymene (%)	0.1–0.8	Flowers and leaves	[43]
p-Cymene(%)	1.0–3.7	Aerial parts	[38,79]
p-Cymenene=α,p-Dimethylstyrene (%)	<0.01–0.03	Aerial parts	[38,79]
Decanal(%)	<0.01	Flowers	[43]
5,7-Di-epi-a-eudesmol (%)	<0.01–0.3	Flowers and leaves	[43]
2,7-dimethyl-2,6-Octadiene (%)	1.4	Leaves and stems	[65]

(Contd...)

Table 2: (Continued)

Phytochemical composition	Values	Plant parts	References
3,5-Dimethylcyclohex-1-ene-4-carboxaldehyde (%)	4.9	Leaves and stems	[65]
3 α ,7 α -dimethyl-hexahydro-2(3H)-Benzofuranone (%)	3.2	Leaves and stems	[65]
19,19-Dimethyl-eicosa-8,11-dienoic acid (%)	3.8	Aerial parts	[75]
Docosanoic acid methyl ester (%)	11.4	Leaves and stems	[65]
1,22-Docosanediol (%)	15.1	Leaves and stems	[65]
Dodecanal dimethyl acetal (%)	3.2	Leaves and stems	[65]
Drimenol (%)	0.7	Leaves	[42]
β -Elemene (%)	0.1–0.4	Aerial parts and leaves	[42,51]
δ -Elemene(%)	0.2–0.6	Flowers and leaves	[43]
2-ethyl-1,4-dimethyl-benzene (%)	2.2	Leaves and stems	[65]
5-ethyl-m-xylene (%)	1.2	Leaves and stems	[65]
10-epi- γ -Eudesmol (%)	0.1–0.4	Flowers and leaves	[43]
(E,E)-Farnesol (%)	16.8	Leaves	[81]
Farnesene (%)	1.1	Leaves	[78]
(E)- β -Farnesene(%)	0.4–2.1	Leaves	[82,78]
(E,E)- α -Farnesene (%)	0.7	Leaves	[42]
Fenchyl acetate (%)	0.1	Aerial parts	[38,79]
(E)-Geranyl acetate (%)	<0.01–0.04	Aerial parts	[38,79]
9-Geranyl-p-cymene (%)	0.7–1.1	Aerial parts	[38,79]
Germacrene A (%)	1.1–11.8	Aerial parts, flowers, and leaves	[43,51]
Germacrene D(%)	1.3–5.1	Aerial parts, flowers, and leaves	[42,43,51,78]
Gleenol (%)	<0.01	Flowers and leaves	[43]
δ -Guaiene (%)	0.4	Aerial parts	[38,79]
α -Guaiene (%)	0.1–4.8	Aerial parts, flowers, and leaves	[38,43,51]
α -Gurjunene (%)	0.07–0.4	Aerial parts and flowers	[43,51,79]
γ -Gurjunene (%)	0.3–0.4	Aerial parts	[51]
Heneicosane (%)	2.8	Leaves and stems	[65]
Heptenyl acetate (%)	0.1	Aerial parts	[38]
Heptadecyloxirane (%)	1.9	Leaves and stems	[65]
Hexadecanoic acid methyl ester (%)	1.8	Leaves and stems	[65]
(Z)-3-Hexen-1-ol (%)	0.05–0.1	Aerial parts	[38,79]
α -Himachalene (%)	5.3–7.3	Flowers and leaves	[43]
β -Himachalene (%)	<0.01–0.3	Flowers and leaves	[43]
γ -Himachalene (%)	1.4	Flowers and leaves	[43]
Himachalol (%)	0.2–0.3	Flowers and leaves	[43]
Humulene (%)	14.1	Aerial parts	[75]
α -Humulene (%)	<0.01–14.6	Aerial parts, flowers, and leaves	[38,42,43,51,78,79,81-83]
Humulene epoxide (%)	<0.01–0.7	Leaves	[78]
Humulene epoxide I (%)	0.2–0.5	Aerial parts	[38,79]
Humulene epoxide II (%)	0.4–1.7	Aerial parts and leaves	[38,42,79]
Humulene epoxide III (%)	0.06–0.1	Aerial parts	[38,79]
10-Hydroxy calamenene (%)	0.4	Aerial parts	[38]
neo-Intermedeol (%)	0.5	Flowers and leaves	[43]
Intermedeol (%)	0.2	Flowers and leaves	[43]
Isoborneol (%)	0.3	Flowers	[43]
1-isopropyl-3-methylbenzene (%)	18.3	Leaves and stems	[65]
Isoaromadendrene epoxide (%)	2.8	Leaves and stems	[65]
Isobornyl acetate(%)	2.9	Flowers	[43]
Isocaryophyllene oxide (%)	0.1–1.3	Aerial parts	[38,79]
1-(2-Isopropyl-5-methylcyclopentyl)ethanone (%)	2.1	Leaves and stems	[65]
Cis-Isopulegone (%)	1.6	Aerial parts	[51]
Italicene (%)	0.05–1.5	Aerial parts	[38,79]
Cis-Jasmone (%)	0.1	Aerial parts	[51]
Juniper camphor (%)	0.2–0.4	Flowers and leaves	[43]
Levomenol (%)	7.3	Aerial parts	[75]
Limonene (%)	<0.01–31.6	Aerial parts, flowers, and leaves	[38,42,43,51,78,79]
trans-1,2-Limonene epoxide (%)	0.08–0.1	Aerial parts	[38,79]
Linalool (%)	<0.01–3.9	Leaves	[42,78]
Longifolene (%)	<0.01	Flowers and leaves	[43]
Ethyl linolenate (%)	3.9	Aerial parts	[75]
cis-p-Mentha-3-en-1,2-diol (%)	0.1	Aerial parts	[38,79]
cis-p-Mentha-2,8-diene-1-ol (%)	0.1	Aerial parts	[38,79]
(+)-p-Mentha-2,8-diene (%)	1.3	Leaves and stems	[65]
neo-Menthol(%)	<0.01	Flowers	[43]
p-Menthone (%)	35.4	Aerial parts	[51]
4 methylene-2,8,8 trimethyl-2-vinyl-bicyclo nonane (%)	1.2	Leaves and stems	[65]
para-Methylanisole (%)	1.3	Flowers	[43]
6-Methyl-5-hepten-2-one (%)	<0.01–0.04	Aerial parts	[38,79]
1-Methyl-4-acetyl-cyclohex-1-ene (%)	<0.01–0.04	Aerial parts	[38,79]
3-Methyl-N-naphthalen-1-yl-benzamide (%)	2.2	Leaves and stems	[65]
α -Muurolool (%)	0.3	Flowers and leaves	[43]

(Contd...)

Table 2: (Continued)

Phytochemical composition	Values	Plant parts	References
γ -Murolene (%)	0.6	Aerial parts	[38,79]
Myrcene (%)	<0.01–1.4	Aerial parts, flowers, and leaves	[38,43,78,79]
Myristic acid (%)	1.4	Aerial parts	[75]
trans-Myrtenol acetate (%)	0.4	Flowers and leaves	[43]
Myrtenal (%)	<0.01–0.03	Aerial parts	[38,79]
Myrtenyl acetate(%)	<0.1–0.2	Flowers and leaves	[43]
Nonanal (%)	<0.1	Flowers and leaves	[43]
2-Nerolidol (%)	3.4	Leaves and stems	[65]
(E)-Nerolidol (%)	1.1	Leaves	[42]
Nonadecanoic acid, ethyl ester (%)	1.2	Leaves and stems	[65]
(Z)- β -Ocimene (%)	<0.01–10.8	Aerial parts, flowers, and leaves	[38,43,78,79,82]
(E)- β -Ocimene (%)	<0.01–0.3	Flowers and leaves	[43,78]
Trans- β -ocimene (%)	0.2	Aerial parts	[51]
Methyl octadec-9-en-12-ynoate (%)	2.2	Aerial parts	[75]
9,15-Octadecadienoic acid methyl ester (%)	2.5	Leaves and stems	[65]
12-Octadecenoic acid methyl ester (%)	2.4	Leaves and stems	[65]
3-Octanol (%)	<0.01–0.02	Aerial parts	[38,79]
1-Octen-3-ol (%)	0.1–0.4	Aerial parts	[38,75]
1-Octen-3-yl acetate (%)	0.3–0.4	Flowers and leaves	[43]
1-Octenyl acetate (%)	1.1–1.7	Aerial parts	[38,79]
2-(2-octenyl)-cyclopentanone (%)	1.2	Leaves and stems	[65]
9,12,15-Octadecatrienoic acid ethyl ester (%)	1.4	Leaves and stems	[65]
Z,E-3,13-Octadecadien-1-ol (%)	6.3	Leaves and stems	[65]
1-Octen-3-yl acetate(%)	0.2	Flowers	[43]
Palmitic acid (%)	27.1	Aerial parts	[75]
β -Patcholene (%)	0.5–0.8	Aerial parts	[51]
Pelugone (%)	34.2	Aerial parts	[51]
Perillen (%)	<0.01–0.03	Aerial parts	[38,79]
α -Phellandrene (%)	<0.1	Flowers and leaves	[43]
2-Phenyl ethyl acetate (%)	0.09–0.1	Aerial parts	[38,79]
Phytol (%)	1.6	Aerial parts	[75]
α -Pinene (%)	1.1–47.1	Aerial parts, flowers, and leaves	[38,42,43,51,75,78,79,81-83]
β -Pinene (%)	0.1–51.6	Aerial parts, flowers, and leaves	[38,42,43,51,78]
cis-Piperitol (%)	0.05–0.1	Aerial parts	[38,79]
Piperitone (%)	0.9	Aerial parts	[51]
3-phenyl-3-methylbutanoic acid methyl ester (%)	1.3	Leaves and stems	[65]
Phthalic acid mono-2-ethylhexyl ester (%)	6.8	Leaves and stems	[65]
Phthalic acid, butyl pent-2-en-4-yn-1-yl ester (%)	7.0	Leaves and stems	[65]
trans-Pinocarvyl acetate(%)	0.1–0.2	Flowers and leaves	[43]
Piperitenone (%)	1.5	Aerial parts	[51]
Porosadienol (%)	0.2–0.3	Aerial parts	[38,79]
Rosefuran (%)	<0.01–0.03	Aerial parts	[38,79]
Sabinene (%)	<0.01–0.9	Flowers and leaves	[43,78]
cis-Sabinene hydrate(%)	<0.01–2.0	Aerial parts, flowers, and leaves	[43,51]
trans-Sabinene hydrate (%)	<0.01	Flowers and leaves	[43]
Santalene (%)	0.6–0.9	Leaves	[78]
Selina-3,7-(11)-diene (%)	0.3–3.3	Aerial parts, flowers, and leaves	[38,43,51,75,79]
Selina-5,11-diene(%)	0.8–0.9	Aerial parts	[38]
α -Selinene (%)	1.7	Aerial parts	[38]
β -Selinene (%)	0.4–3.1	Aerial parts, flowers, and leaves	[43,51,65,79]
γ -Selinene (%)	0.6–1.4	Aerial parts	[51]
Spathulenol (%)	0.1	Aerial parts	[38,79]
α -Terpinene (%)	0.2–1.8	Aerial parts, flowers, and leaves	[43,51]
δ -Terpineol (%)	<0.1	Flowers and leaves	[43]
α -Terpineol (%)	<0.01–0.7	Aerial parts, flowers, and leaves	[42,43,51,78]
4-Terpineol(%)	<0.01–0.5	Flowers and leaves	[43]
4-Terpineol acetate(%)	0.2	Flowers and leaves	[43]
γ -Terpinene(%)	0.3–1.3	Aerial parts, flowers, and leaves	[38,43,51,78,79]
Terpinolene (%)	<0.01–0.6	Aerial parts, flowers, and leaves	[43,51,78]
α -Terpinolene (%)	0.2–0.4	Aerial parts and leaves	[42,51]
Terpinen-4-ol (%)	<0.01–0.6	Aerial parts and leaves	[51,78]
α -Terpinenyl acetate (%)	0.2	Aerial parts	[51]
7-Tetradecyne (%)	1.1	Leaves and stems	[65]
3,7,11,16-tetramethyl-hexadeca-2,6,10,14-tetraen-1-ol (%)	4.3	Leaves and stems	[65]
6-(p-Tolyl)-2-methyl-2-heptenol (%)	1.2	Leaves and stems	[65]
Tricyclene (%)	0.1–0.6	Flowers and leaves	[43]
6,10,14-trimethyl-2-pentadecanone (%)	3.1	Leaves and stems	[65]
Valencene (%)	1.3–2.8	Flowers and leaves	[43,78]
Viridiflorol (%)	0.1–7.2	Aerial parts	[38,51,79]
Viridiflorene (%)	0.4–2.5	Flowers and leaves	[43]
α -Ylangene (%)	<0.01–0.4	Aerial parts, flowers, and leaves	[38,43,78,79]

antimycobacterial [61,88], antifungal [24,38,61,85,86], anti-inflammatory [89], antioxidant [8,65,88], hepatoprotection [65], hypoglycemic [90], and cytotoxicity and toxicity [8,42,65,87,90].

Antibacterial activities

Boily and Van Puyvelde [85] evaluated antibacterial activities of methanol flower, leaf, and stem extracts of *H. odoratissimum* against *Bacillus subtilis*, *Mycobacterium smegmatis*, *Pseudomonas aeruginosa*, *Salmonella gallinarum*, and *Staphylococcus aureus* using the agar dilution streak method. The flower extract exhibited activities against *B. subtilis*, *M. smegmatis*, and *S. aureus* [85]. Van Puyvelde *et al.* [24] evaluated antibacterial activities of 3,5-dihydroxy-6,7,8-trimethoxy flavone, 3-O-methylquercetin, and helichrysetin against *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *P. aeruginosa*, *Pseudomonas solanacearum*, *Salmonella typhimurium*, *Serratia marcescens*, *Shigella dysenteriae*, *B. subtilis*, *M. smegmatis*, *S. aureus*, and *Streptococcus pyogenes* using liquid dilution method with tetracycline hydrochloride as a positive control. The compound 3-O-methylquercetin exhibited activities with minimum inhibitory concentration (MIC) values ranging from 6.3 µg/ml to 100.0 µg/ml which was comparable to MIC values of 0.8 µg/ml–100.0 µg/ml exhibited by the positive control [24]. Mathekgga [86] evaluated the antibacterial activities of acetone extracts of aerial parts of *H. odoratissimum* against *Bacillus cereus*, *Bacillus pumilus*, *B. subtilis*, *Micrococcus kristinae*, *S. aureus*, *Enterobacter cloacae*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *S. marcescens* using agar dilution method. The extract exhibited activities against *B. cereus*, *B. pumilus*, *B. subtilis*, *M. kristinae*, *S. aureus*, and *E. cloacae* with MIC values ranging from 0.01 mg/ml to 1.0 mg/ml [86]. Seaman [61] evaluated the antibacterial activities of acetone and methanol leaf extracts of *H. odoratissimum* against *S. aureus*, *Enterococcus faecalis*, *B. cereus*, *P. aeruginosa*, *K. pneumoniae*, *Serratia odorifera*, and *Moraxella catarrhalis* using disc diffusion and broth microdilution methods with neomycin and ciprofloxacin as positive controls. The extracts showed activities against *S. aureus*, *E. faecalis*, and *B. cereus* with a zone of inhibition ranging from 4.1 mm to 9.4 mm and MIC values ranging from 0.5 mg/ml to >16.0 mg/ml [61]. Reddy [38] evaluated antibacterial activities of acetone and methanol extracts of aerial parts of *H. odoratissimum* as well as essential oils isolated from the species against *E. coli*, *Yersinia enterocolitica*, *Klebsiella pneumoniae*, *S. aureus*, and *B. cereus* using disc diffusion assay with ciprofloxacin (0.01 mg/ml) as a positive control. The extract exhibited activities against *S. aureus* and *B. cereus* with MIC values of <0.25 mg/ml [38]. Lourens *et al.* [87] evaluated antibacterial activities of chloroform:methanol (1:1) leaf and stem extracts of *H. odoratissimum* against *S. aureus*, *Staphylococcus epidermidis*, *B. cereus*, *K. pneumoniae*, and *P. aeruginosa* using the 96-well microplate method with ciprofloxacin as a positive control. The extracts exhibited activities against *S. aureus* and *B. cereus* with MIC values ranging of 4.0 mg/ml and 2.0 mg/ml, respectively [87]. Ocheng *et al.* [74] evaluated antibacterial activities of hexane and methanol aerial parts extracts of *H. odoratissimum* against bacterial pathogens associated with periodontal diseases and dental caries which included *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Tannerella forsythia*, *Streptococcus mutans*, *Streptococcus sobrinus*, and *Lactobacillus acidophilus* using agar well-diffusion and agar-dilution assays with doxycycline (30 µg) as a positive control. The extracts were active against all the tested pathogens with the exception of *A. actinomycetemcomitans* with MIC values ranging from 0.1 mg/ml to 1.0 mg/ml [74]. Similarly, Ocheng *et al.* [75] evaluated the inhibitory effects of the essential oils isolated from the aerial parts of *H. odoratissimum* on *P. gingivalis*, *A. actinomycetemcomitans*, *S. mutans*, *Bacillus megaterium*, and *L. acidophilus* using broth dilution methods at concentrations of 1%, 0.1%, and 0.01% with chlorhexidine as the positive control. The most sensitive pathogen was *A. actinomycetemcomitans*, followed by *P. gingivalis*, *B. megaterium*, and *S. mutans*, with the oil exhibiting limited effects on *L. acidophilus* [75]. Lawal *et al.* [42] evaluated antibacterial activities of essential oil isolated from *H. odoratissimum* against *B. cereus*, *B. pumilus*, *S. aureus*, *S. aureus*, *Streptococcus faecalis*, *E. cloacae*, *E. coli*, *K. pneumoniae*, *P. vulgaris*, *P. vulgaris*, *P. aeruginosa*, and *Serratia marcescens* using the

disc diffusion and broth microdilution methods with chloramphenicol (25 µg) and tetracycline (25 µg) as positive controls. The volatile oil showed potential antibacterial activities against tested microorganisms with mean zones of inhibition and MIC values ranging from 6.7 mm to 17.0 mm and 1.3 mg/mL to 10.0 mg/mL, respectively. These antibacterial activities were comparable to the zone of inhibition of 6.0 mm to 23.7 mm and MIC values of 1.3 mg/mL to 10.0 mg/mL exhibited by the controls [42].

Antimycobacterial activities

Lall and Meyer [88] evaluated antimycobacterial activities of acetone and waterleaf extracts of *H. odoratissimum* against the drug-sensitive strain of *Mycobacterium tuberculosis* using the agar plate method and screened the activities of drug-resistant and drug-sensitive strains of *M. tuberculosis* using rapid radiometric method to confirm the inhibitory activities. The MIC values of acetone extracts against all the strains by both methods were 0.5 mg/ml [88]. Seaman [61] evaluated the antimycobacterial activities of acetone and waterleaf extracts of *H. odoratissimum* against *M. smegmatis* and *Mycobacterium aurum* using broth microdilution technique and *M. tuberculosis* using BACTEC susceptibility testing with rifampicin and ciprofloxacin as positive controls. The extracts exhibited activities with MIC values ranging from 0.3 mg/ml to 2.0 mg/ml [61].

Antifungal activities

Boily and Van Puyvelde [85] evaluated antifungal activities of methanol flower, leaf, and stem extracts of *H. odoratissimum* against *Candida albicans* using the agar dilution streak method. The flower extract exhibited activities against the tested pathogen [85]. Van Puyvelde *et al.* [24] evaluated antifungal activities of 3,5-dihydroxy-6,7,8-trimethoxy flavone, 3-O-methylquercetin and helichrysetin against *Aspergillus flavus*, *C. albicans*, *Epidermophyton floccosum*, *Microsporium canis*, and *Paecilomyces* using liquid dilution method with nystatin as a positive control. The compound 3-O-methylquercetin exhibited activities with MIC values ranging from 12.5 µg/ml to 100.0 µg/ml which was comparable to MIC values of 0.8 µg/ml–100.0 µg/ml exhibited by the positive control [24]. Mathekgga [86] evaluated the antifungal activities of acetone extracts of aerial parts of *H. odoratissimum* against *A. flavus*, *Aspergillus niger*, *Cladosporium cladosporioides*, *Cladosporium cucumerinum*, *Cladosporium sphaerospermum*, and *Phytophthora capsici* using agar dilution method. The extract exhibited activities against all tested pathogens with MIC values ranging from 0.01 mg/ml to 0.1 mg/ml [86]. Seaman [61] evaluated the antibacterial activities of acetone and methanol leaf extracts of *H. odoratissimum* against *C. albicans* using disc diffusion and broth microdilution methods with neomycin and ciprofloxacin as positive controls. The extract showed activities with MIC values ranging from 2.0 mg/ml to 8.0 mg/ml [61]. Reddy [38] evaluated antifungal activities of acetone and methanol extracts of aerial parts of *H. odoratissimum* as well as essential oils isolated from the species against *Cryptococcus neoformans*, *C. albicans*, and *Alternaria alternata* using disc diffusion assay with nystatin (30 µg) as a positive control. The acetone extract exhibited activities with a zone of inhibition of 2 mm and 3 mm against *Cryptococcus neoformans* and *C. albicans*, respectively [38].

Anti-inflammatory activities

Frum and Viljoen [89] evaluated anti-inflammatory activities of aqueous and methanol leaf extracts of *H. odoratissimum* as well as essential oils isolated from the species through the assessment of the 5-lipoxygenase inhibitory activities using a three-fold stepwise dilution method with dimethyl sulfoxide and Tween®20 as negative controls and nordihydroguaiaretic acid as a positive control. The essential oils displayed 5-lipoxygenase inhibitory activities with half maximal inhibitory concentration (IC₅₀) values of 22.5 ppm–35.9 ppm [89].

Antioxidant activities

Legoale *et al.* [80] evaluated the antioxidant activities of the flavonoid 3',4',3,5-tetrahydroxy-7-methoxyflavone isolated from *H. odoratissimum* using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging

assay. The flavonoid exhibited antioxidant activities of 32.3% [80]. Frum and Viljoen [89] evaluated the antioxidant activities of aqueous and methanol leaf extracts of *H. odoratissimum* as well as essential oils isolated from the species using the DPPH radical scavenging assay. The essential oils displayed weak DPPH antioxidant activities with an IC_{50} value of >100 ppm [89]. Twilley and Lall [8] evaluated the antioxidant activities of the ethanol leaf extracts of *H. odoratissimum* using the DPPH free radical scavenging assay. The extract showed good DPPH activities with an IC_{50} value of 5.1 $\mu\text{g/ml}$ [8]. Twilley *et al.* [65] evaluated the antioxidant activities of ethanol leaf and stem extracts of *H. odoratissimum* using the DPPH free-radical scavenging, nitric oxide inhibition (NO), hydrophilic oxygen radical absorbance capacity (H-ORAC), and lipophilic oxygen radical absorbance capacity (L-ORAC) assays. The extracts showed good DPPH activities with IC_{50} values of 5.1 $\mu\text{g/ml}$; however, the extract showed low NO scavenging activity with IC_{50} values of >100.0 $\mu\text{g/ml}$. The H-ORAC and L-ORAC values of the extracts were found to be 2542 μmoles and 3648 μmoles of Trolox equivalents per gram of extract, respectively [65].

Hepatoprotection activities

Twilley *et al.* [65] evaluated the *in vitro* hepatoprotection activities of the ethanol leaf and stem extracts of *H. odoratissimum* on the liver hepatocellular carcinoma (HepG2) cells before the hepatoprotective assay to determine the appropriate doses to be tested in the assay. The extract showed significant hepatoprotection at 25 $\mu\text{g/ml}$ on HepG2 cells exposed to D-galactosamine [65].

Hypoglycemic activities

Njagi *et al.* [90] evaluated hypoglycemic activities of aqueous leaf extracts of *H. odoratissimum* by administering 50 mg/kg body weight, 100 mg/kg body weight, and 150 mg/kg body weight in alloxan-induced diabetic Swiss albino mice. The extract exhibited a non-dose dependent response by lowering blood glucose levels in diabetic mice [90].

Cytotoxicity and toxicity activities

Lourens *et al.* [87] evaluated *in vitro* cytotoxicity activities of chloroform:methanol (1:1) leaf and stem extracts of *H. odoratissimum* against transformed human kidney epithelial (Graham) cells, MCF-7 breast adenocarcinoma, and SF-268 glioblastoma cells at a concentration of 0.1 mg/ml using the sulforhodamine B assay. The extract exhibited Graham cell growth ranging from 7.4% to 48.2% at the tested concentration [87], implying that the species may be toxic against Graham cells. Lawal *et al.* [42] evaluated the cytotoxicity of essential oils isolated from *H. odoratissimum* using the brine shrimp assay. The essential oil of *H. odoratissimum* showed significant cytotoxicity against the brine shrimp with median lethal concentration value of 31.62 $\mu\text{g/mL}$ [42]. Twilley and Lall [8] evaluated the cytotoxicity activities of ethanol leaf extracts of *H. odoratissimum* against human epidermoid carcinoma (A431) and non-cancerous cell lines such as Chang liver cells, human embryonic kidney cells (HEK293), and mouse melanocyte cells (B16F10) using the 2,3-Bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxyanilide salt (XTT) method. The extracts exhibited activities with IC_{50} values ranging from 15.5 $\mu\text{g/ml}$ to 55.5 $\mu\text{g/ml}$ against the tested line cell [8]. Twilley *et al.* [65] evaluated the cytotoxicity activities of the ethanol leaf and stem extracts of *H. odoratissimum* against human epidermoid carcinoma (A431), malignant melanoma (A375), cervical epithelial carcinoma (HeLa), and human embryonic kidney (HEK-293) cells using the XTT method. The extracts showed inhibitory activities with IC_{50} values ranging from 15.5 $\mu\text{g/ml}$ to 55.5 $\mu\text{g/ml}$ with a selectivity index value of 2.4 [65]. Njagi *et al.* [90] evaluated acute toxicity of the leaf aqueous extract of *H. odoratissimum* using Swiss albino mice by administering orally to mice a dose of 450 mg/kg body weight of the extract for 30 days. The animals were observed for any signs of acute toxicity such as hypoactivity, piloerection, and salivation. The animals showed mild perihepatitis and perivascular inflammation in the kidneys, while the renal cells, hepatocytes, and spleen tissue cells were intact, and the liver and heart muscle had no signs of pathology [90]. Therefore, the species showed no discernible toxicity on the major organs of the studied animals.

CONCLUSION

In this review, the medicinal uses, phytochemistry, biological activities, and toxicity of different extracts and compounds of *H. odoratissimum* have been summarized. The diverse medicinal uses of *H. odoratissimum* and the preliminary phytochemical and ethnopharmacological studies carried so far indicates that the species has potential as herbal medicine. Therefore, there is a need to validate the documented ethnomedicinal uses of *H. odoratissimum* through phytochemical and pharmacological studies. Although contemporary ethnopharmacological research involving *H. odoratissimum* is promising, it is too preliminary and sometimes too general to be used to explain and support some of the medicinal uses of the species. Therefore, future studies should address these knowledge gaps through experimental animal studies, randomized clinical trials, and target-organ toxicity studies involving *H. odoratissimum* crude extracts and compounds isolated from the species.

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AUTHOR'S CONTRIBUTIONS

The author declares that this work was done by the author named in this article.

CONFLICTS OF INTEREST

The author declares that they have no conflicts of interest.

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