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Review Article

INSIGHTS INTO THE ETHNOPHARMACOLOGICAL PROPERTIES OF *COMBRETUM APICULATUM* SOND. (FAMILY COMBRETACEAE): NARRATIVE REVIEW

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ABSTRACT

Combretum apiculatum sond. is a small to medium-sized deciduous tree which is used in traditional medicine in several countries in tropical Africa. This study was aimed at providing information on the ethnobotany, medicinal uses, phytochemistry, and pharmacological properties of *C. apiculatum*. Information about ethnobotanical applications, phytochemistry, and pharmacological properties of *C. apiculatum* was collected from the several online databases such as PubMed®, Google Scholar, ScienceDirect®, Web of Science, SpringerLink®, SciELO, and Scopus®, as well as pre-electronic literature sources which included books, book chapters and other scientific publications obtained from the university library. The findings highlight the use of the bark, fruits, leaves, roots, seeds, stems, and stem bark of *C. apiculatum* as traditional medicine for bilharzia, conjunctivitis, gastro-intestinal problems, infertility in women, leprosy, respiratory infections, sexually transmitted infections, and skin diseases. Chemical compounds identified from *C. apiculatum* include amino acids, bibenzyls (dihydrostilbenes), chalcones, flavonoids, phenanthrenes, alkaloids, lignin, phenolics, terpenoids, essential oils, resin acids, lipids, pectins, carboxylated, and hydroxylated polysaccharides. The crude extracts of *C. apiculatum* exhibited antibacterial, anthelmintic, antifungal, antioxidant, anti-inflammatory, antiproliferative, and cytotoxicity activities. Future studies should focus on detailed ethnopharmacological evaluation of *C. apiculatum*, particularly its phytochemistry, biological activities, and toxicological assessments, *in vivo* and clinical studies.

Keywords: Bush willow family, Combretaceae, *Combretum apiculatum*, *Materia medica*, Traditional medicine, Tropical Africa.

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INTRODUCTION

Combretum apiculatum sond. (Fig. 1) belongs to the *Combretaceae* family, otherwise known as the bush willow, Indian almond or white mangrove family. The Combretaceae family consists of approximately 10 genera and 530 species that are mainly trees, shrubs, shrublets or lianas and rarely subherbaceous [1-4]. Members of this family exhibit pantropical distribution with a few species extending to warm temperate regions, recorded in coastal scrub, savanna, grassland, rainforest, woodland, littoral, and mangrove vegetation [5,6]. Family Combretaceae is characterized by unicellular indumentum, compartmented hairs, multicellular glands and scales, simple leaves without stipules and bisexual or unisexual flowers [1]. Most of the Combretaceae species have distinctive fruits that are light, winged or occasionally angled with a single seed and these characteristics help in the identification of the species belonging to this family [1]. In tropical Africa, some *Combretum* Loefling species are widely used as the sources of traditional medicines and such species include *Combretum adenogonium* steud. ex A.Rich., *C. apiculatum* sond., *Combretum caffrum* (Eckl. and Zeyh.) Kuntze, *Combretum collinum* Fresen, *Combretum comosum* G.Don, *Combretum hereroense* Schinz, *Combretum erythrophyllum* (Burch.) sond., *Combretum imberbe* Wawra, *Combretum indicum*, *Combretum kraussii* Hochst., *Combretum micranthum* G.Don, *Combretum molle* R.Br. ex G.Don, *Combretum mucronatum* Schumach. and Thonn., *Combretum padoides* Engl. and Diels, *Combretum paniculatum* Vent., *Combretum platypterum* (Welw.) Hutch. and Dalziel and *Combretum zeyheri* Sond. [7-10]. *C. apiculatum* is listed in the South African [11,12] and Zimbabwean pharmacopoeia [13]. Recent research in South Africa showed that *C. apiculatum* has commercial potential as traditional medicine as the various parts of the species are sold in informal herbal medicine markets [14]. Medicinal plants are a primary source of traditional medicines in many communities in the world [15-24].

C. apiculatum is a multipurpose plant species, with its different parts used for mouth colouring [25] and bark used for tanning leather [26]. *C. apiculatum* is an excellent source of firewood and charcoal [26-30], and therefore, its wood is sold commercially as firewood [29-31]. The wood of *C. apiculatum* is yellowish-white in color, with a black heart which in old trees may be large, strong, close-grained, hard, tough, termite-, borer- and fire-resistant [26]. Therefore, its timber makes good fence posts, mine props, spokes, agricultural implements handles and also used as general construction material [26,27,30]. The leaves, shoots, or twigs of *C. apiculatum* are eaten by game and livestock [26,29,32-35]. A refreshing tea is brewed from *C. apiculatum* leaves [29] while the caterpillars of striped policeman butterfly (*Coeliades forestan*) feed on the leaves [34,36]. *C. apiculatum* is frost and drought resistant [27] easily grown from seed and widely grown as an ornamental and decorative tree in recreational parks, private gardens, and along streets in urban centres in South Africa [24]. It is, therefore, within this context that the present study was undertaken aimed at reviewing the ethnobotanical uses, medicinal applications, phytochemistry, and biological activities of *C. apiculatum*.

METHODS

The literature search for ethnobotanical uses, medicinal applications, phytochemistry, and biological activities of *C. apiculatum* was undertaken from July to November 2024 using online search databases used included Scopus®, Web of Science, SpringerLink®, SciELO, Google Scholar, ScienceDirect®, and PubMed®. The pre-electronic literature sources which included book chapters, books, journal articles, theses, and dissertations obtained from the University library were also used. The keywords used in the literature search included "*Combretum apiculatum*," the synonyms of the species "*Combretum apiculatum* Sond". and English common names "glossy *Combretum*," "hill *Combretum*," "hairy red bush willow," "kudu bush," "red bush willow," "rooibos," "russet combretum" or "variable bush willow." An additional online search was also conducted by making the use of the keywords such as "biological activities of *Combretum apiculatum*," "pharmacological properties of *Combretum apiculatum*," "medicinal uses of *Combretum*

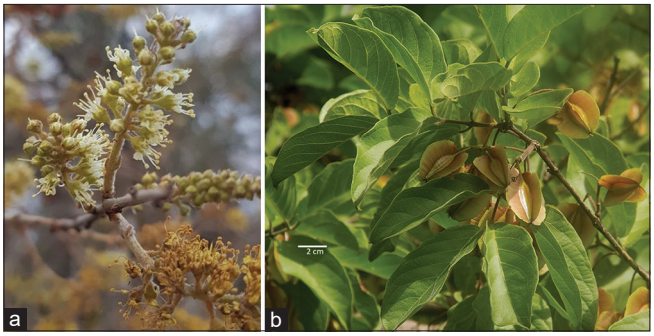

Fig. 1: *Combretum apiculatum*: (a): Branch showing flowers and, (b): Branch showing leaves and fruits (Photos: (a) (Richard Hill) and, (b) (BT Wursten)

apiculatum," "ethnobotany of *Combretum apiculatum*," "traditional uses of *Combretum apiculatum*" and "phytochemistry of *Combretum apiculatum*."

RESULTS AND DISCUSSION

Taxonomy and morphological description of *C. apiculatum*

The genus *Combretum* consists of approximately 276 species having a pantropical distribution in tropical Asia and Africa, but absent in the Pacific Islands and most of Australia, with its center of diversity on the African continent [37,38]. The genus *Combretum* comprises trees, shrubs, and lianas, characterized by the leaves which are opposite, whorled or rarely alternate, with entire margins, lacking stipules or having very small stipules, with persist petioles which often form hooked spines [38]. The flowers are bisexual, actinomorphic, inferior ovary, and winged fruits or rarely an unwinged nut [38]. The genus name "*Combretum*" is of classical origin, as the name was first used by the Roman naturalist, natural philosopher, naval and army commander Gaius Plinius Secundus, known in English as Pliny (23–79 AD), used in reference for an unknown plant [26,34,35]. The name was also re-used by the Swedish botanist Pehr Löfling (31 January 1729–22 February 1756) for the *Combretum* genus [26,34,35]. The specific name "*apiculatum*" is in reference to the characteristic features of the leaves which are short, sharp or having apiculate tips, which are curved and often somewhat twisted [26,35]. *C. apiculatum* is a variable species, divided into two subspecies, namely subsp. *apiculatum* occurring in dry deciduous woodland and bushland on better-drained soils, and characterized by hairless fruits and larger leaves which are hairless except for occasional hairs on the midrib and so far known to occur at an altitude ranging from 30 m to 1930 m above the sea level [39,40]. The other infraspecific taxa, subsp. *leutweinii* (Schinz) exell. occurs in mopane (*Colophospermum mopane* (J.Kirk ex Benth.) J. Léonard) woodland with hairy and velvety fruits, and smaller leaves which are usually sparsely to densely hairy particularly on the undersurface, and known to occur at an altitude ranging from 900 m to 1980 m above the sea level [39,40]. The subsp. *leutweinii* resembles *C. albopunctatum* Suess., but the latter has glistening white scales on the mature leaves and its fruits are hairless [39]. Researchers and ethnobotanists rarely indicate the infraspecific categories, and therefore, in this current study *C. apiculatum sensu lato*, is used rather than the two infraspecific taxa.

The synonyms associated with C. apiculatum sond. includes C. apiculatum Sond. subsp. boreale Exell, C. apiculatum Sond. var. parvifolium Baker f., C. apiculatum Sond. var. pilosiusculum Engl. and Diels, C. apiculatum Sond. var. sulphureum (Van Heurck and Müll.Arg.) Dümmer, C. apiculatum Sond. f. sulphureum Van Heurck and Müll. Arg., C. apiculatum Sond. var. viscosum (Van Heurck and Müll. Arg.) Dümmer, C. apiculatum Sond. f. viscosum Van Heurck and Müll.Arg., Cryptolepis buchananii Engl. and Diels, Cryptolepis kwebense N.E.Br., Cryptolepis leutweinii Schinz and Cryptolepis ukamense Engl. and Diels [2,40-42]. The English common names of C. apiculatum include "glossy *Combretum*," "hill *Combretum*," "hairy red bush willow," "kudu bush," "red bush willow," "rooibos," "russet *Combretum*" or "variable bush willow." The common name "bush willow" indicates a superficial resemblance to willows, that is, species belonging to the genus *Salix* L. (family Salicaceae), but "bush willows" and "willows" are not closely related to each other [26].

C. apiculatum is a medium-to-small-sized deciduous tree, reaching 10 metres in height characterized by an often twisted stems and stems growing up to an average of 30 cm in diameter [26,39]. The main stem is mostly single, occasionally multi-stemmed with grey to dark blackish or brownish-grey bark, which is smooth when young and becoming lightly fissured with age [35]. The long and slender branches sometimes arch downwards giving *C. apiculatum* a rounded crown [43]. The leaves are simple, large, opposite or occasionally alternate or in whorls, broadly oblong and narrow to slender, apex rounded with a short, pointed and diagnostically twisted tip, base rounded to slightly lobed. The leaf margins are entire and waxy, the lamina is glossy, yellow-green in colour above, paler yellow-green below, somewhat sticky while young and turning russet-brown early in the dry season, sparsely hairy or hairless on both surfaces, often with rusty hairs along the veins and a short petiole. The flowers are tiny, yellowish green in color, sweet-scented, appearing in spikes within axils of new leaves. The fruits are round to ovoid in outline, woody, yellowish green with a glossy center, turning reddish brown when ripe (Fig. 1). *C. apiculatum* is known to occur in Angola, the Democratic Republic of Congo (DRC), Botswana, Eswatini, Kenya, Mozambique, Malawi, Namibia, South Africa, Zambia, Tanzania and Zimbabwe [2,31,40-53] (Fig. 2). *C. apiculatum* has been recorded in open woodland, bushveld, grassland, thicket on stony hill slopes, on red gravelly, sandy soils, in medium-rainfall areas, often occurring in large numbers and then conspicuous when the leaves have turned [43].

Medicinal uses of *C. apiculatum*

In traditional medicine applications, the bark, leaves, fruits, roots, stem bark, seeds and stems of *C. apiculatum* are used against 30 human diseases and ailments (Table 1). These ethnomedicinal applications of *C. apiculatum* have been recorded in almost all the countries where *C. apiculatum* is indigenous with the exception of the DRC. The fact that *C. apiculatum* is widely utilized as traditional medicine and as a source of various ecosystem goods and services in tropical Africa, makes it an important plant resource in the region. The main diseases and ailments treated by *C. apiculatum* bark, leaves, fruits, roots, stem bark, seeds, and stems include its use as remedy against bilharzia, conjunctivitis, gastrointestinal problems, infertility in women, leprosy, respiratory infections, sexually transmitted infections, and skin diseases (Fig. 3). Diseases such as gastro-intestinal problems, respiratory infections, sexually transmitted infections, and skin diseases are still important public health challenges in sub-Saharan Africa [20-24].

Ethnomedicinal applications of *C. apiculatum* were identified from 40 scientific publications (Fig. 4) covering the period 1973–2025, that is, 52 years, a very long period to capture the relevant ethnomedicinal uses of the species throughout its distributional range in tropical Africa. Kenya, South Africa, Tanzania, Mozambique, and Zimbabwe (in descending order of importance) have the highest ethnomedicinal applications of *C. apiculatum* (Fig. 4). More studies need to be carried out in DRC, Angola and Malawi to document existing knowledge around indigenous knowledge systems and ethnography of the species. In Botswana, the roots of *C. apiculatum* are mixed with those of *Cucumis metuliferus* Jacques (Cucurbitaceae family) and placed where the bone is broken to heal the broken bones [36]. In Kenya, the bark of *C. apiculatum* is mixed with that of *Carissa spinarum* L. (Apocynaceae family), *Flacourtia indica* (Burm.f.) Merr. (Salicaceae family), *Prunus africana* (Hook.f.) Kalkman (Rosaceae family), *Albizia amara* (Roxb.) Boivin, *Erythrina abysynica* Lam. and *Vachellia xanthophloea* (Benth.) Banfi and Galasso (both Fabaceae family members) and taken orally as traditional medicine for hypertension [54-56]. In Kenya, the bark of *C. apiculatum* is mixed with that of *A. amara*, *Ozoroa insignis* Delile

Fig. 2: Distribution of *Combretum apiculatum* in tropical Africa

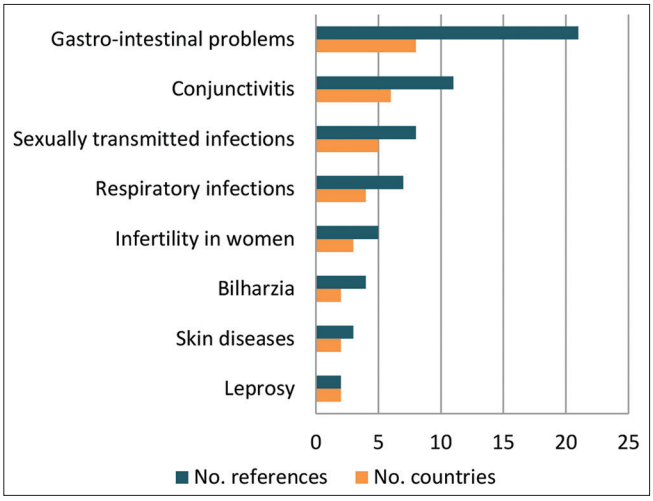

Fig. 3: Main ethnomedicinal applications of *Combretum apiculatum* in tropical Africa

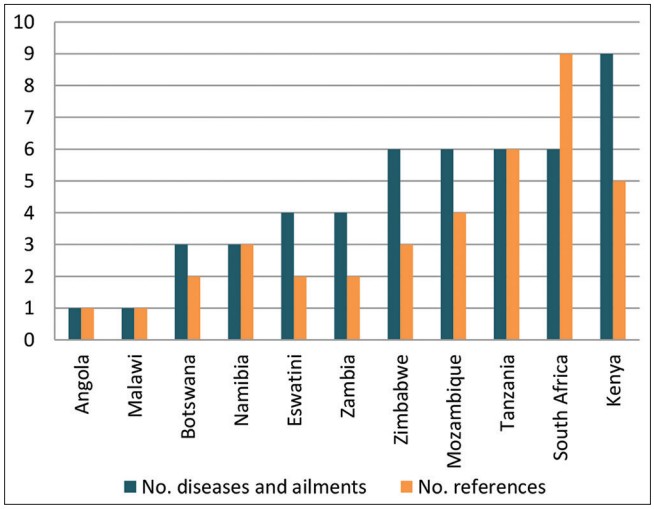

Fig. 4: Analysis of ethnomedicinal applications of *Combretum apiculatum* in tropical Africa

subsp. *reticulata* (Baker f.) J. B. Gillett (family Anacardiaceae) and *Tylosema fassoglense* (Fabaceae family) and taken orally as remedy for infertility in women [54,55]. Combining medicinal plants in African traditional medicine appear to be quite common, for example, in Ethiopia and South Africa, the leaves of *Trichilia dregeana* Sond. are mixed with those of *Albizia adianthifolia* (Schumach.) W. Wight as traditional medicine against sexually transmitted infections such as gonorrhoea and syphilis [20].

PHYTOCHEMICAL AND PHARMACOLOGICAL PROPERTIES OF *C. APICULATUM*

The gum, heartwood, and leaves of *C. apiculatum* are characterized by amino acids, bibenzyls (dihydrostilbenes), chalcones, flavonoids, and phenanthrenes [85-93] (Table 2). Histochemical analyses of the leaves and trichomes of *C. apiculatum* conducted by Parusnath *et al.* [94] detected alkaloids, lignin, phenolics, terpenoids, essential

Table 1: Medicinal uses of *Combretum apiculatum*

Medicinal use	Part used	Country	References
Mono-therapeutic applications			
Aphrodisiac	Bark decoction or infusion taken orally	Mozambique	[57]
Abdominal pains	Leaves chewed and juice swallowed	Zimbabwe	[58]
Bilharzia	Bark or root decoction taken orally	Kenya and Tanzania	[55,59-61]
Cancer	Fruit decoction taken orally	Kenya	[55,62]
Conjunctivitis	Leaf or stem decoction or infusion applied topically	Angola, Eswatini, Kenya, Mozambique, South Africa and Zambia	[8,35,39,55, 61,63-67]
Ear problems	Leaf decoction applied topically	Kenya	[55,68]
Gastro-intestinal problems (abdominal disorders, diarrhoea, dysentery and stomach problems)	Leaf decoctions used as steam baths or administered as enemas or bark, leaf, root, seed and stem decoction or infusion taken orally or leaf or stem ashes taken orally	Botswana, Eswatini, Kenya, Mozambique, Namibia, South Africa, Tanzania and Zimbabwe	[8,12,26,34-36,39,43,55, 58,61,63-67,69-73]
Hernia	Bark, leaf, root, seed and stem decoction or infusion taken orally	Mozambique	[72]
Infertility in women	Leaf decoction taken orally	Namibia and South Africa	[12,74,75]
Leprosy	Bark, leaf, root, seed or stem decoction applied topically	Mozambique and Tanzania	[61,63,69,70,72]
Malaria	Bark, leaf, root, seed and stem decoction or infusion taken orally	Mozambique	[72]
Malnutrition	Not specified	Malawi	[76]
Menstrual problems	Root infusion taken orally	Tanzania	[77]
Poison antidote	Bark, leaf, root, seed and stem decoction or infusion taken orally	Mozambique	[72]
Respiratory infections (chest pains, cough, influenza and tuberculosis)	Bark, leaf, root or stem bark decoction or infusion taken orally	Namibia, South Africa, Zambia and Zimbabwe	[12,58,74,75,78-80]
Sexually transmitted infections (gonorrhoea and venereal diseases)	Bark, leaf, root, seed or stem bark decoction taken orally	Botswana, Kenya, Mozambique, South Africa and Zambia	[12,55,60,61,72,79,81,82]
Skin diseases	Bark, leaf, root or stem ashes applied topically	Kenya and South Africa	[26,55,60]
Snake and scorpion bites	Leaf, root or stem decoction applied topically	Tanzania	[63,69,70,83,84]
Sores and wounds	Bark or root decoction applied topically	Eswatini	[12,46,64]
Weak body	Leaves inserted into vagina	Zimbabwe	[8,13,63,65]
Used in combination with other species			
Broken bones	Roots mixed with *Cucumis metuliferus* Jacques (Cucurbitaceae family) and applied topically	Botswana	[36]
Hypertension	Bark mixed with that of *Carissa spinarum* L. (Apocynaceae family), *Flacourtia indica* (Burm.f.) Merr. (Salicaceae family), *Prunus africana* (Hook.f.) Kalkman (Rosaceae family), *Albizia amara* (Roxb.) Boivin, *Erythrina abysynica* Lam. and *Vachellia xanthophloea* (Benth.) Banfi and Galasso (all Fabaceae family members) and taken orally	Kenya	[54-56]
Infertility in women	Bark mixed with that of *A. amara, Ozoroa insignis* Delile subsp. *reticulata* (Baker f.) J.B.Gillett (Anacardiaceae family) and *Tylosema fassoglense* (Fabaceae family) and taken orally	Kenya	[54,55]

oils, resin acids, lipids, pectins, carboxylated, and hydroxylated polysaccharides. Some of these chemical compounds exhibited pharmacological activities such as antifungal, antibacterial, and cytotoxicity activities. Other biological properties exhibited by the crude extracts of *C. apiculatum* leaves include antifungal, anthelmintic, anti-inflammatory, antibacterial, antioxidant, antiproliferative, and cytotoxicity activities.

Anthelmintic activities

McGaw *et al.* [95] assessed the anthelmintic properties of water, acetone, and ethyl acetate crude extracts of *C. apiculatum* leaves against the free-living nematode known as *Caenorhabditis elegans* var. Bristol (N2) with the standard nematocidal drug levamisole as positive control. The extracts demonstrated anthelmintic activities against the nematodes [95].

Antibacterial activities

Eloff [96] assessed the antibacterial properties of acetone extracts of *C. apiculatum* leaves against *Escherichia coli*, *Enterococcus faecalis*, *Staphylococcus aureus,* and *Pseudomonas aeruginosa* using the twofold serial dilution with gentamycin as the positive control. The extracts demonstrated antibacterial activities against the tested pathogens with minimum inhibitory concentration (MIC) values which ranged from 0.4 mg/mL to 3.0 mg/mL [96]. McGaw *et al.* [97] assessed the antibacterial properties of ethanolic extracts of *C. apiculatum* leaves against *Bacillus subtilis* and *S. aureus* using microdilution assay with

Table 2: Phytochemical composition of *Combretum apiculatum*

Phytochemical compound	Formula	Plant part	References
Amino acid			
Alanine	$C_3H_7NO_2$	Gum	[86]
Aspartic acid	$C_4H_7NO_4$	Gum	[86]
Glycine	$C_2H_5NO_2$	Gum	[86]
Bibenzyl			
2′-hydroxy-3,4,5-trimethoxybibenzyl	$C_{16}H_{15}O_4$	Heartwood	[87]
2,4′-dihydroxy-3,5-dimethoxybibenzyl	$C_{16}H_{18}O_4$	Heartwood	[87]
3,2′-dihydroxy-4,5-dimethoxybibenzyl	$C_{16}H_{18}O_4$	Heartwood	[87]
4′-hydroxy-3,4,5-trimethoxybibenzyl	$C_{17}H_{20}O_4$	Leaves	[91]
4,4′-dihydroxy-3,5-dimethoxy-bibenzyl	$C_{16}H_{18}O_4$	Leaves	[91]
4′,5-dihydroxy-3,4- dimethoxybibenzyl	$C_{16}H_{18}O_4$	Leaves	[91]
5-hydroxy-3,4′-dimethoxybibenzyl	$C_{16}H_{18}O_3$	Leaves	[91]
Chalcone			
Cardamomin	$C_{16}H_{14}O_4$	Leaves	[90,91]
Flawokawain A	$C_{17}H_{16}O_4$	Leaves	[91,92]
Flavonoid			
5,7-dimethoxyflavanone	$C_{17}H_{16}O_4$	Leaves	[91]
Alpinetin	$C_{16}H_{14}O_4$	Leaves	[91,92]
Chrysin	$C_{15}H_{10}O_4$	Leaves	[91]
Kaempferol	$C_{21}H_{20}O_{11}$	Leaves	[90]
Pinocembrin	$C_{15}H_{12}O_4$	Leaves	[90-93]
Rhamnocitrin	$C_{16}H_{12}O_6$	Leaves	[90]
Glycoside			
Quercetrin	$C_{15}H_{10}O_6$	Leaves	[90]
Phenanthrenes			
2′-hydroxy-3,4,6,7-tetramethoxy-9,10-dihydrophenanthrene	$C_{18}H_{20}O_4$	Heartwood	[89]
2,7-dihydroxy-3,4,6-trimethoxy-9,10-dihydrophenanthrene	$C_{17}H_{18}O_5$	Heartwood	[88,89]
3,6,7-dihydroxy-2,4-dimethoxyphenanthrene	$C_{16}H_{14}O_4$	Heartwood	[89]
4,6,7-trihydroxy-2,3-dimethoxyphenanthrene	$C_{16}H_{18}O_5$	Heartwood	[86,89]
4,7-dihydroxy-2,3,6-trimethoxyphenanthrene	$C_{17}H_{16}O_4$	Heartwood	[86,88,89]
4,7-dihydroxy-2,3,6-trimethoxy-9,10-dihydrophenanthrene	$C_{16}H_{16}O_4$	Heartwood	[89]
4,7-dihydroxy-2,6-dimethoxy-9,10-dihydrophenanthrene	$C_{16}H_{16}O_4$	Heartwood	[89]
6,7-dihydroxy-2,3,4-trimethoxy-9,10-dihydrophenanthrene	$C_{17}H_{18}O_5$	Heartwood	[89]
7-hydroxy-2,3,4,6-tetramethoxy-9,10-dihydrophenanthrene	$C_{18}H_{20}O_5$	Heartwood	[89]
9,10-dihydro-3,6,7-trimethoxy-2,5-phenanthrenediol	$C_{17}H_{18}O_5$	Heartwood	[85]

neomycin as positive control. The extracts demonstrated antibacterial activities against the tested pathogens with MIC values which ranged from 0.05 mg/mL to 0.4 mg/mL [97]. Katerere *et al.* [91] assessed the antibacterial properties of the phytochemical compounds 5-hydroxy-3,4′-dimethoxybibenzyl, cardamomin, 4′-hydroxy-3,4,5-trimethoxybibenzyl, 4′-hydroxy-2′,6′-dimethoxychalcone, pinocembrin and chrysin isolated from *C. apiculatum* leaves against *E. coli*, *Mycobacterium fortuitum*, *Proteus vulgaris* and *S. aureus* using the microtiter dilution assay with streptomycin as positive control. The phytochemical compounds demonstrate antibacterial activities against the tested pathogens with MIC values which ranged from 25.0 µg/mL to >100.0 µg/mL [91]. Katerere *et al.* [92] assessed the antibacterial properties of organic and aqueous extracts of *C. apiculatum* leaves and the phytochemical compounds alpinetin, flavokawain-A and pinocembrin isolated from the species against *S. aureus*, *P. aeruginosa*, *E. coli,* and *E. faecalis* using a serial dilution microtiter plate with gentamicin as positive control. The extracts and phytochemical compounds demonstrated antibacterial activities against the tested pathogens with MIC values which ranged from 40.0 µg/mL to 600.0 µg/mL [92]. Iikasha *et al.* [71] assessed the antibacterial properties of ethanol extracts of *C. apiculatum* leaves against *Shigella* and *Salmonella* species using the disc-diffusion assay. The extract demonstrated antibacterial activities against the tested pathogens with MIC values which ranged from 250.0 µg/mL to 1000.0 µg/mL [71]. Anokwuru *et al.* [93] evaluated the antibacterial properties of methanol extracts of *C. apiculatum* leaves against *S. aureus*, *Staphylococcus epidermidis*, *Bacillus cereus*, *S. epidermidis*, *Klebsiella pneumoniae*, *E. faecalis*, *E. coli*, *P. aeruginosa*, *Salmonella* typhimurium and *Shigella sonnei* using the microdilution assay with ciprofloxacin as a positive control. The extracts demonstrated antibacterial activities against the tested pathogens with MIC values which ranged from 0.25 mg/mL to 3.0 mg/mL [93]. Machingauta and Mukanganyama [98] evaluated the antibacterial properties of dichloromethane, hexane, methanol, and acetone extracts of *C. apiculatum* leaves against *Acinetobacter baumannii* using the broth microdilution method. The extracts exhibited properties against the tested pathogens with MIC values which ranged from 125.0 µg/mL to 500.0 µg/mL [98].

Antifungal activities

Masoko *et al.* [99] assessed the antifungal properties of hexane, acetone, methanol, and dichloromethane extracts of *C. apiculatum* leaves against *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Sporothrix schenckii,* and *Microsporum canis* using microdilution assay with amphotericin B as positive control. The extracts demonstrated antifungal activities against the tested pathogens with MIC values which ranged from 0.02 mg/mL to 2.5 mg/mL [99]. Katerere *et al.* [91] assessed the antifungal properties of the phytochemical compounds 5-hydroxy-3,4′-dimethoxybibenzyl, cardamomin, 4′-hydroxy-3,4,5-trimethoxybibenzyl, 4′-hydroxy-2′,6′-dimethoxychalcone, pinocembrin and chrysin isolated from *C. apiculatum* leaves against *C. albicans* using the microtiter dilution assay with fluconazole as positive control. The phytochemical compounds demonstrated activities against the tested pathogen with MIC values which ranged from 6.25 µg/mL to 50.0 µg/mL [91]. Mangoyi *et al.* [100] assessed the antifungal properties of ethanol extract of *C. apiculatum* leaves against *C. albicans* and *Candida krusei* using the broth dilution assay with miconazole as positive control. The extract demonstrated activities against the tested pathogens with MIC values which ranged from 0.31 mg/mL to 0.63 mg/mL [100].

Anti-inflammatory activities

Eloff *et al.* [101] evaluated the anti-inflammatory properties of acetone extract of *C. apiculatum* leaves against the radiochemical cyclooxygenase bioassay using sheep seminal vesicles. The extract showed 72.0%–85.0% inhibition of cyclooxygenase activity [101].

McGaw *et al.* [95] evaluated the anti-inflammatory properties of acetone and ethyl acetate extracts of *C. apiculatum* leaves in an *in vitro* assay for cyclooxygenase inhibitors with indomethacin as positive control. The extract demonstrated activities by showing inhibition ranging from 91.0% to 93.0% [95].

Antioxidant activities

Masoko and Eloff [102] assessed the antioxidant properties of acetone and methanol extracts of *C. apiculatum* leaves using 2,2-diphenyl-1-picryl hydrazyl (DPPH) free radical scavenging method. The extract demonstrated moderate antioxidant properties [102]. Aderogba *et al.* [90] assessed the antioxidant properties of the hexane, ethyl acetate, dichloromethane, and n-butanol extracts of *C. apiculatum* leaves and the phytochemical compounds quercetrin and kaempferol isolated from the species using the DPPH free radical scavenging method with L-ascorbic acid as a positive control. All the extracts demonstrated antioxidant activities with half maximal effective concentration (EC_{50}) values which ranged from 2.4 µg/mL to 20.3 µg/mL while the phytochemical compounds exhibited EC_{50} values ranging from 11.8 µM to 47.4 µM [90].

Antiproliferative activities

Maphutha *et al.* [103] assessed the antiproliferative activities of ethanolic extract of *C. apiculatum* leaves against human malignant melanoma (UCT-MEL1), human epidermoid carcinoma (A431), and noncancerous human keratinocytes (HaCat) cells using the PrestoBlue cell viability assay with actinomycin D as positive control. The extract demonstrated antiproliferative activities against A431, UCT-MEL1, and HaCat with half maximal inhibitory concentration (IC_{50}) values which ranged from 56.4 µg/mL to 90.5 µg/mL [103].

Cytotoxicity activities

Aderogba *et al.* [90] evaluated the cytotoxicity properties of the phytochemical compounds cardamonin and pinocembrin isolated from *C. apiculatum* leaves on Vero kidney cells using the (3-(4,5-dimethylthiazol)-2,5-diphenyl tetrazolium bromide) method with berberine as a positive control. The phytochemical compound cardamonin and pinocembrin exhibited activities with median lethal concentration (LC_{50}) values of 2.0 µg/mL and 29.5 µg/mL, respectively [90]. Loggenberg *et al.* [104] evaluated the cytotoxicity properties of ethanol extract of *C. apiculatum* leaves against MDA-MB-231 and Michigan cancer foundation-7 breast cancer cell lines and human embryo kidney cell line Hek293 using the sodium 3'-[1-(phenyl amino-carbonyl)-3,4-tetrazolium]-bis-[4-methoxy-6-nitro] benzene sulfonic acid hydrate method with doxorubicin as the positive control. The extract demonstrated cytotoxicity activities with IC_{50} values which ranged from 49.2 µg/mL to 85.9 µg/mL [104].

CONCLUSION

This study provides an overview of the ethnobotanical uses, medicinal applications, phytochemistry, and pharmacological activities of *C. apiculatum.* Such assessments are important as *C. apiculatum* is widely used as a source of traditional medicines throughout its distributional range in tropical Africa. Although systematic reviews in general provide objective and evidence-based synthesis of secondary data generated from the various sources, many researchers associate limitations such as subjective decisions about research questions, searching strategies, literature selection, analysis, and interpretation of the research findings in systematic review reports. There is therefore, need to maintain high standards when conducting systematic reviews and meta-analyses as these are the important building blocks of credible scientific research. Therefore, future research should focus on detailed phytochemical studies of *C. apiculatum*, as well as toxicological assessments, *in vivo* and clinical studies aimed at corroborating the traditional medicinal applications of *C. apiculatum*. There is also the need to assess the combinational effects of *C. apiculatum* with other plant species such as *A. amara*, *C. metuliferus*, *C. spinarum*, *E. abysynica*, *F. indica*, *O. insignis* subsp. *reticulata*, *P. africana*, *T. fassoglense* and *V. xanthophloea*.

AUTHOR CONTRIBUTION

AM conceptualized the research and wrote the manuscript.

CONFLICT OF INTEREST

No conflict of interest is associated with this research.

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