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Insights into the botany, medicinal, phytochemical and pharmacological properties of *Combretum caffrum*

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Background: *Combretum caffrum* (Eckl. & Zeyh.) Kuntze is a small-to-medium-sized deciduous tree widely used in traditional medicines.

Aim: The current study reviews the botany, ethnopharmacology, phytochemistry and pharmacological properties of *C. caffrum*.

Setting: The current study provides an overview of the botany and ethnopharmacological properties of *C. caffrum*.

Method: A search for available information on the botany, chemical constituents and pharmacological properties of *C. caffrum* was conducted by systematically searching the scientific databases which included ScienceDirect®, PubMed®, Web of Science, SpringerLink®, Google Scholar, SciELO and Scopus®, as well as pre-electronic literature sources such as book chapters, books and other scientific publications obtained from the university library.

Results: The findings highlight the use of *C. caffrum* as a multipurpose species, providing a wide range of goods and ecosystem services. The bark, leaves, leaf juice, roots, root bark and stem bark of *C. caffrum* are used as charm for harming an enemy and tonic, as ethnoveterinary medicine and also as traditional medicine for body and leg pains, cancer and eye problems. Chemical compounds identified from *C. caffrum* include flavonoids, phenanthrene, phytosterols, stilbenoids, polyphenolics, iridoids, lignans, ketones, glycosides, fatty acids, xanthones, coumarins, tannins and triterpenoids. The crude extracts of *C. caffrum* and phytochemical compounds isolated from the species exhibited anticancer, antibacterial, antifungal, antiviral, antioxidant and cytotoxicity activities.

Contribution: This study adds to existing literature information about the botany, ethnopharmacology, phytochemistry and pharmacological properties of C. caffrum. To realise the full potential of *C. caffrum* as a valuable component of traditional pharmacopoeia, future studies should explore the active ingredients of the species using various *in vitro* and *in vivo* assays.

Keywords: bush willow family; Combretaceae; *Combretum caffrum*; materia medica; traditional medicine.

Introduction

Combretum caffrum (Eckl. & Zeyh.) Kuntze (Figure 1) is a member of the Combretaceae family commonly known as the white mangrove, Indian almond or bush willow. The Combretaceae family comprises approximately 10 genera and 530 species, which are mainly trees, shrubs, shrublets or lianas with subherbaceous forms being rare (Christenhusz & Byng 2016; Jordaan, Van Wyk & Maurin 2011; Raj, Solomon & Thangaraj 2022). Members of this family exhibit a pantropical distribution, with a few species extending into warm temperate regions. They are found in diverse habitats, including coastal scrub, savanna, grassland, rainforest, woodland, littoral and mangrove vegetation (Gere et al. 2015; Turner 2020).

Over the past five decades, there has been a notable increase in the evaluation of the ethnopharmacological properties of *Combretum* species, as highlighted in a review by Rogers and Verotta (1996). Several *Combretum* species that have been used for generations as sources of traditional remedies are known to have therapeutic healing properties and valued as materia medica in tropical Africa, including *C. caffrum*, *C. adenogonium* Steud. ex A.Rich., *C. albopunctatum* Suess., *C. apiculatum* Sond., *C. celastroides* Welw. ex M.A.Lawson, *C. coccineum* (Sonn.) Lam., *C. collinum* Fresen, *C. comosum* G.Don, *C. erythrophyllum* (Burch.) Sond., *C. hereroense* Schinz, *C. imberbe* Wawra, *C. indicum* (L.) DeFilipps, *C. kraussii* Hochst., *C. micranthum* G.Don, *C. molle* R.Br.



Source: Stefan Dressler, 2009, *Combretum caffrum (Eckl. & Zeyh.) Kuntze*, Senckenberg, Kirstenbosch Botanical Garden, Cape Town, viewed n.d., from https://www.gbif.org/occurrence/1288063203

FIGURE 1: *C. caffrum* (Eckl. & Zeyh.) Kuntze: The branches show leaves and fruits.

ex G.Don, *C. mossambicense* (Klotzsch) Engl., *C. mucronatum* Schumach. & Thonn., *C. padoides* Engl. & Diels, *C. paniculatum* Vent., *C. platypterum* (Welw.) Hutch. & Dalziel and *C. zeyheri* Sond. (Burkill 1994; Hutchings et al. 1996; Neuwinger 2000; Schmelzer & Gurib-Fakim 2013).

Combretum caffrum has notable commercial potential as medicinal plant because a patent for use of combretastatins and the combretastatin derivatives isolated from the species against cancer was filed at the United States Patent and Trademark Office (Pettit & Singh 1991). A subsequent patent by Liu (2012), outlining protocols required for producing high yields of combretastatin from *C. caffrum*, gained attention from the media over the past 10 years. Similarly, combretastatin A-4 analogues, AVE8062 and CA-4P, have been approved by the European Medicines Agency and US Food and Drug Administration (FDA) for treating gliomas, anaplastic thyroid cancer (ATC), neuroendocrine tumours, ovarian cancer and gastro-enteropancreatic neuroendocrine tumours (Patel et al. 2024). Therefore, this article provides a comprehensive review of the importance of *C. caffrum* in traditional medicine with a holistic approach that covers its botany, chemical constituents and pharmacological properties.

Methods

A search for available information on the botany, chemical constituents and pharmacological properties of *C. caffrum* was conducted by systematically searching the scientific databases, including ScienceDirect®, PubMed®, Web of Science, SpringerLink®, Google Scholar, SciELO and Scopus®, as well as pre-electronic literature sources, such as book chapters, books and other scientific publications obtained from the university library. The search was conducted from September to December 2024, using the following keywords: '*Combretum caffrum*'; its synonyms including '*C. dregeanum* C.Presl', '*C. salicifolium* E.Mey. ex Hook.' and '*Dodonaea caffra* Eckl. & Zeyh.', '*D. conglomerata* Eckl. & Zeyh.' and English common names such as 'African bush willow', 'African willow tree', 'bush willow', 'bush willow tree', 'bushveld willow' and 'Cape bush willow'. An additional search was conducted using the keywords 'biological activities of *C. caffrum*', 'pharmacological properties of *C. caffrum*', 'ethnobotany of *C. caffrum*', 'medicinal uses of *C. caffrum*', 'phytochemistry of *C. caffrum*' and 'traditional uses of *C. caffrum*'. The search covered publications from 1962 to 2024, a long period to capture literature on the botany, chemical constituents and the pharmacological properties of *C. caffrum*.

Ethical considerations

The ethical waiver to conduct this study was obtained from the University of Fort Hare Department of Biotechnology and Biological Sciences dated 15 February 2025.

Review findings

Taxonomy and morphological description of *C. caffrum*

The genus *Combretum* consists of approximately 276 species with a pantropical distribution, mainly in tropical Asia and Africa, but absent in the Pacific Islands and most of Australia (Boon, Jordaan & Van Wyk 2020; Stace 2007). About 140 species have been recorded in tropical Africa and approximately 20 species are endemic to Madagascar (Schmelzer & Gurib-Fakim 2013). Therefore, the highest number of *Combretum* species occur in tropical Africa, with the centre of diversity of the genus on the African continent (Boon et al. 2020; Stace 2007). The genus *Combretum* comprises trees, shrubs and lianas characterised by leaves that are opposite, whorled or rarely alternate, with entire margins, lacking stipules or having very small stipules, and with persistent petioles that often form hooked spines (Boon et al. 2020). The flowers are bisexual, actinomorphic, with an inferior ovary and winged fruits, or rarely an unwinged nut (Boon et al. 2020). The genus name '*Combretum*' is of classical origin, as the name was first used by the Roman naturalist, natural philosopher, naval and military commander Gaius Plinius Secundus, known in English as Pliny (23 – 79 AD), used in reference to an unknown plant (Palmer & Pitman 1972; Schmidt et al. 2017; Venter & Venter 2015). The name was later reused by the Swedish botanist Pehr Löfling (31 January 1729 – 22 February 1756) for the *Combretum* genus (Palmer & Pitman 1972; Schmidt et al. 2017; Venter & Venter 2015). The specific species name '*caffrum*' was derived from the Arabic or Hebrew word '*kafir*', '*kaffir*', '*kafri*' or '*kaffraria*', meaning 'person living on the land'. This name is often applied to plant species that naturally occur in the eastern region or the Eastern Cape province of South Africa (Glen 2004; Palmer & Pitman 1972). 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 (Palmer & Pitman 1972). Other common names of the species included 'African bush willow', 'African willow tree', 'bush willow tree', 'bushveld willow' and 'Cape bush willow'. Synonyms for the species are '*C. dregeanum* C.Presl',

'*C. salicifolium* E.Mey. ex Hook.', '*Dodonaea caffra* Eckl. & Zeyh.' and '*D. conglomerata* Eckl. & Zeyh.' (Germishuizen & Meyer 2003; Jordaan et al. 2011; Palmer & Pitman 1972).

Combretum caffrum is a small-to-medium-sized deciduous shrub or spreading tree reaching 10 metres in height (Germishuizen & Meyer 2003; Palgrave 2002; Palmer & Pitman 1972). The bark is pale grey to greyish-brown in colour. The leaves are usually opposite, subopposite or sometimes alternate, borne on flattish stalks. The leaves are narrowly elliptic or lanceolate, narrowing from the middle to both ends, bluntly or sharply pointed (Figure 1), with the margins untoothed, slightly in-rolled and often faintly waxy. When young, the leaves are often scaly and hairy, and when matured, they are grey or shiny green and smooth above, and paler, hairless and scaly below. The flowers are bisexual, regular, whitish or yellowish and borne singly in the axils of the leaves. The fruits are winged nuts, lime-green when young, and shiny, tinged pink and reddish upon ripening (Figure 1). *Combretum caffrum* is endemic to the Eastern Cape province in South Africa, occurring at an altitude ranging from 15 m to 762 m above the sea level (Germishuizen & Meyer 2003). *Combretum caffrum* has been recorded along river and stream banks, in watercourses or near water and in moist areas in the grasslands, thickets and forests (Palgrave 2002; Palmer & Pitman 1972). *Combretum caffrum* is seldom found far from water and is a common sight with its crooked, light-coloured stem and thick, drooping, willow-like foliage, overhanging streams or in damp spots (Palmer & Pitman 1972). Morphologically, *Combretum caffrum* is similar to *C. erythrophyllum* (Burch.) Sond., a species recorded in Botswana, Eswatini, Mozambique, Namibia, South Africa and Zimbabwe (Exell 1978; Germishuizen & Meyer 2003). In the Eastern Cape province of South Africa, where both species may grow in the same habitat, they can be distinguished by leaf shape and fruit colouration. *C. caffrum* is characterised by narrowly elliptic to lanceolate leaves that are hairless and by fruits that are usually tinged pink or reddish upon ripening (Jordaan et al. 2011; Van Wyk & Van Wyk 2013).

Traditional uses of *C. caffrum*

Combretum caffrum is categorised as a multipurpose species in the Eastern Cape province of South Africa. The species is widely collected from the wild for firewood, charms and/or ritual purposes, fencing poles, medicinal uses and as a source of timber (Cocks & Wiersum 2003). The wood of *C. caffrum* is bright yellow, hard, heavy, strong and compact, but not so durable as it is prone to rotting and also is susceptible to borer attacks (Maroyi 2013). Honeybees often collect nectar and pollens from the flowers of *C. caffrum*, and the honey obtained from the species is bitter but produces no harmful effects (Hutchings et al. 1996; Watt & Breyer-Brandwijk 1962). *Combretum caffrum* is an attractive shrub or tree, popular in private gardens, as it tolerates frost and moderate drought and is widely cultivated outside its natural distribution range (Palmer & Pitman 1972). It is valued for providing shade (Palmer & Pitman 1972) and the trees are often left in agricultural fields as shade trees (Maroyi 2013). *Combretum caffrum* is also traded as an ornamental tree in South Africa, the United States of America and Australia (Maroyi 2013).

Combretum caffrum is a potential forage species for ruminants, particularly livestock species such as cattle and goats, and is also used in game feeding (Tefera & Mlambo 2017). No information could be found in the literature regarding the digestibility value of the leaves, branches, twigs or fruits of *C. caffrum* for livestock or game. However, research conducted by Tefera and Mlambo (2017) and Mathipa, Mphosi and Masoko (2022) showed that *C. caffrum* is a good source of proteins, energy, and minerals such as calcium, copper, iron, magnesium, manganese, phosphorus, potassium, sodium and zinc (Table 1). The protein content of *C. caffrum* ranging from 6.0% to 13.0% suggests that its browse value is higher than that of other *Combretum* species such as *C. imberbe* that have leaves and twigs containing only 4.0% protein (McGregor 1991). Although *C. caffrum* is deciduous, the species is known to exhibit a long leaf-retention period (Palmer & Pitman 1972) and, therefore, the species could be used as a supplement, particularly in ruminant feed. Fodder trees such as *C. caffrum* are important feed sources for both livestock and game in a wide range of agricultural systems worldwide. Such species are important sources of micro- and macro-elements as well as essential nutrients such as proteins and energy (Geng et al. 2020).

Several ethnobotanical and ethnopharmacological publications cite the uses of bark, leaves, roots, root bark and stem bark of *C. caffrum* as a charm for harming an enemy and as a tonic,

TABLE 1: Proximate, mineral and trace metals composition of ashes, leaves and stems of *C. caffrum*.

Mineral	Value	Plant parts	References
Ash (%)	2.0–18.0	Leaves and stems	Mathipa et al. 2022
Moisture (%)	7.0	Leaves	Mathipa et al. 2022
Protein (%)	6.0–13.0	Ash, leaves and stems	Mathipa et al. 2022
Energy (kJ)	12.0–17.0	Ash, leaves and stems	Mathipa et al. 2022
Calcium (g/kg dry matter)	23.4	Leaves	Tefera & Mlambo 2017
Cobalt (mg/mL)	0.3–1.1	Ash, leaves and stems	Mathipa et al. 2022
Copper (ppm)	3.7	Leaves	Tefera & Mlambo 2017
Iron (ppm)	175.0	Leaves	Tefera & Mlambo 2017
Manganese (mg/mL)	0.2–3.4	Ash, leaves and stems	Mathipa et al. 2022
Magnesium (g/kg dry matter)	5.5	Leaves	Tefera & Mlambo 2017
Nickel (mg/mL)	0.4–3.1	Ash, leaves and stems	Mathipa et al. 2022
Phosphorus (g/kg dry matter)	2.4	Leaves	Tefera & Mlambo 2017
Potassium (g/kg dry matter)	7.3	Leaves	Tefera & Mlambo 2017
Sodium (mg/mL)	3.8–9.5	Ash, leaves and stems	Mathipa et al. 2022
Zinc (ppm)	12.8	Leaves	Tefera & Mlambo 2017

Note: Please see the full reference list of the article, Maroyi, A., 2025, 'Insights into the botany, medicinal, phytochemical and pharmacological properties of *Combretum caffrum*', *Journal of Medicinal Plants for Economic Development* 9(1), a282. https://doi.org/10.4102/jomped.v9i1.282, for more information.

TABLE 2: Medicinal uses of *C. caffrum*.

Medicinal uses	Plant parts used	References
Body and leg pains	Roots added to bath water	Bhat & Jacobs 1995; Maroyi 2013; Van Wyk et al. 2013
Cancer	Root bark decoction	Maroyi 2013; Pettit et al. 1982
Eye problems	Leaf juice applied topically	Maroyi 2013
Tonic	Bark decoction taken orally	Maroyi 2013
Ethnoveterinary medicine		
Conjunctivitis	Bark or leaf juice applied topically	Afolayan et al. 2002; Maposa et al. 2010; Maroyi 2013; Masika & Afolayan 2003; Masika et al. 2000; McGaw & Eloff 2008
Redwater	Stem bark or leaves	Afolayan et al. 2002; Maroyi 2013; Masika & Afolayan 2003

Note: Please see the full reference list of the article, Maroyi, A., 2025, 'Insights into the botany, medicinal, phytochemical and pharmacological properties of *Combretum caffrum*', *Journal of Medicinal Plants for Economic Development* 9(1), a282. https://doi.org/10.4102/jomped.v9i1.282, for more information.

and also as a traditional medicine for body and leg pains, cancer and eye problems (Table 2). The bark, leaf juice, leaves and stem bark are used as ethnoveterinary medicine for conjunctivitis and redwater in livestock (Afolayan et al. 2002; Maposa et al. 2010; Maroyi 2013; Masika & Afolayan 2003; Masika, Van Averbeke & Sonandi 2000; McGaw & Eloff 2008). The Zulu people in the KwaZulu-Natal province of South Africa use *C. caffrum* extract as a spear poison for hunting purposes (Hutchings et al. 1996; Watt & Breyer-Brandwijk 1962). *C. caffrum* is an important component of the South African traditional pharmacopoeia and, therefore, the species is included in medicinal monographs, such as '*Medicinal and Magical Plants of Southern Africa: An Annotated Checklist*' and '*Medicinal Plants of South Africa*', written by Arnold et al. (2002) and Van Wyk et al. (2013), respectively. Similarly, the bark, leaves and roots of *C. caffrum* are sold in informal herbal medicine markets as sources of traditional medicines in South Africa (Maroyi 2013; Williams, Balkwill & Witkowski 2001). A herbal concoction prepared from the bark decoction of *C. caffrum* is sold in informal herbal medicine markets in South Africa as an anticancer remedy (Cunningham 1990; Maroyi 2013). Van Wyk and Wink (2017) argued that *C. caffrum* is a 'commercialised medicinal plant' since the bark of the species is the major source of numerous phenanthrenes and stilbenoids, such as combretastatin A-4 and its derivatives, which are renowned for their strong anticancerous properties.

Phytochemistry and pharmacological properties of *C. caffrum*

Qualitative and quantitative phytochemical analyses of *C. caffrum* fruits, leaves, stems, stem wood and twigs have revealed the presence of various bioactive compounds, including flavonoids, phenanthrene, phytosterols, stilbenoids, polyphenolics, iridoids, lignans, ketones, glycosides, fatty acids, xanthones, coumarins, tannins and triterpenoids (Table 3) (El-Zayat et al. 1993; Kovács, Vasas & Hohmann 2008; Mariri et al. 2023; Mariri, Mongalo & Makhafola 2024; Pettit, Cragg & Singh 1987a; Pettit et al. 1982, 1987b, 1988a, 1988b, 1995; Pettit & Singh 1987). Some of the phytochemical compounds isolated from *C. caffrum* and its crude extracts exhibited anticancer, antibacterial, antifungal, antiviral, antioxidant and cytotoxic activities, supporting its traditional medicinal uses.

Antibacterial activities

Eloff (1999) evaluated the antibacterial activities of acetone extracts of *C. caffrum* leaves against *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis* and *Pseudomonas aeruginosa* using the two-fold serial dilution method, with gentamicin as a positive control. The extracts exhibited activities against the tested pathogens with minimum inhibitory concentration (MIC) values ranging from 0.04 mg/mL to 6.0 mg/mL (Eloff 1999). Masika and Afolayan (2002) evaluated the antibacterial activities of acetone, methanol and water extracts of *C. caffrum* bark against *Bacillus cereus*, *Bacillus subtilis*, *Bacillus pumilus*, *Micrococcus kristinae*, *Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae* and *Serratia marcescens* using the microdilution method. The extracts exhibited activities against the tested pathogens exhibiting MIC values ranging from 0.5 mg/mL to 5.0 mg/mL (Masika & Afolayan 2002). Anokwuru et al. (2021) evaluated the antibacterial activities of methanol extracts of *C. caffrum* leaves against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus cereus*, *Staphylococcus epidermidis*, *Klebsiella pneumoniae*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella typhimurium* and *Shigella sonnei* using the microdilution assay with ciprofloxacin as a positive control. The extracts exhibited activities against the tested pathogens, with MIC values ranging from 0.25 mg/mL to >3.0 mg/mL (Anokwuru et al. 2021).

Antifungal activities

Afolayan et al. (2002) evaluated the antifungal activities of acetone extracts of *C. caffrum* bark against *Aspergillus niger*, *Alternaria alternaria*, *Mucor hiemalis*, *Schizophyllum commune* and *Penicillium notatum* using the agar dilution assay. The extracts were fungicidal at a concentration of 10.0 mg/mL and exhibited inhibition against the tested pathogens with inhibition values ranging from 49.3% to 100.0% and the median lethal concentration (LC_{50}) values ranging from 1.8 mg/mL to >10.0 mg/mL (Afolayan et al. 2002). Masika and Afolayan (2002) evaluated the antifungal activities of acetone and methanol extracts of *C. caffrum* bark against *Aspergillus alternaria*, *Aspergillus niger*, *Mucor hiemalis*, *Penicillium notatum* and *Schizophyllum commune* using the agar dilution method. At 10.0 mg/mL, the extracts exhibited activities against the tested pathogens, exhibiting inhibition values that range from 49.3% to 100.0% (Masika & Afolayan 2002). Masoko, Picard and Eloff (2007) evaluated the antifungal activities of hexane, acetone, methanol and dichloromethane extracts of *C. caffrum* leaves against *Candida albicans*, *Aspergillus fumigatus*, *Cryptococcus neoformans*, *Sporothrix schenckii* and *Microsporum canis* using the microdilution assay, with amphotericin B as a positive control. The extracts exhibited activities against the tested pathogens, with MIC values ranging from 0.02 mg/mL to >2.5 mg/mL (Masoko et al. 2007). Dikhoba et al. (2019) evaluated the antifungal activities of acetone extracts of *C. caffrum* leaves against *Aspergillus ochraceous*, *Aspergillus flavus* and *Fusarium verticillioides* using the microplate dilution method, with amphotericin B as a

TABLE 3: Phytochemical composition of *C. caffrum*.

Phytochemical compound	Formula	Parts	References
2,7-Dihydroxy-3,4,6-trimethox-9,10 dihydrophenanthrene	$C_{17}H_{18}O_5$	Stem wood	Pettit et al. 1988a
2*α*-Hydroxymaprounic acid 2,3-bis-*p*-hydroxybenzoate	$C_{44}H_{56}O_8$	Leaves	Mariri et al. 2024
2-Decene, 7-methyl-, (*Z*)-	$C_{11}H_{22}$	Leaves	Mariri et al. 2023
2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, [*R*-[*R**, *R**-(E)]]-	$C_{20}H_{40}O$	Leaves	Mariri et al. 2023
3,3′,4′-Tri-O-methylellagic acid	$C_{17}H_{12}O_8$	Fruits, leaves, stems and twigs	Pettit et al. 1987a
3,8,9-Trimethoxy-6H-dibenzo[b,d]pyran-6-one	$C_{34}H_{41}N_7O_6$	Leaves	Mariri et al. 2023
5,7-Dihydroxy-2-(4-hydroxyphenyl)-3-[(3,4,5-trihydroxy-6-methyloxan-2-yl)oxy]-4H-chromen-4-one	$C_{21}H_{20}O_{10}$	Leaves	Mariri et al. 2024
6-O-(4-Methoxybenzoyl)-ajugol	$C_{23}H_{30}O_{11}$	Leaves	Mariri et al. 2024
6,7-Dihydroxy-2,3,4-trimethoxy-9,10-dihydrophenanthrene	$C_{17}H_{18}O_5$	Stem wood	Kovács et al. 2008; Pettit et al. 1988b
7-Hydroxy-2.3,4,6-tetramethoxyphenanthrene	$C_{18}H_{18}O_5$	Stem wood	Kovács et al. 2008; Pettit et al. 1988b
7-Hydroxy-2.3,4,6-tetramethoxy-9,10-dihydrophenanthrene	$C_{18}H_{20}O_5$	Stem wood	Pettit et al. 1988b
(7*R**,8*R**)-3-Methoxy-3′,4,7,9,9′-pentahydroxy-8,4′-oxyneolignan 4-xyloside	$C_{24}H_{32}O_{11}$	Leaves	Mariri et al. 2024
8-Octadecenoic acid, methyl ester	$C_{19}H_{36}O_2$	Leaves	Mariri et al. 2023
Acacetin	$C_{16}H_{12}O_5$	Fruits, leaves, stems and twigs	Pettit et al. 1987a
A-Friedooleanan-3-one	$C_{30}H_{50}O$	Leaves	Mariri et al. 2023
Bibenzyls 7–9	$C_{14}H_{14}$	Fruits, leaves, stems and twigs	Pettit et al. 1988a
Bilobetin	$C_{31}H_{20}O_{10}$	Leaves	Mariri et al. 2024
Butyl (*S*)-3-hydroxybutyrate [arabinosyl-(1->6)-glucoside]	$C_{19}H_{34}O_{12}$	Leaves	Mariri et al. 2024
Combretastatin A-1	$C_{18}H_{20}O_6$	Fruits, leaves, stems, stem wood and twigs	Pettit et al. 1987a, 1987b
Combretastatin A-2	$C_{17}H_{16}O_5$	Stem wood	Pettit & Singh 1987
Combretastatin A-3	$C_{17}H_{18}O_5$	Stem wood	Pettit & Singh 1987
Combretastatin A-4	$C_{18}H_{20}O_5$	Stem wood	El-Zayat et al. 1993; Pettit et al. 1982, 1988a, 1995
Combretastatin A-5	$C_{18}H_{22}O_6$	Stem wood	Pettit et al. 1995
Combretastatin A-6	$C_{18}H_{22}O_6$	Stem wood	Pettit et al. 1995
Combretastatin B-1	$C_{18}H_{22}O_6$	Fruits, leaves, stems, stem wood and twigs	Pettit et al. 1987a
Combretastatin B-2	$C_{17}H_{20}O_5$	Stem wood	Pettit & Singh 1987
Combretastatin B-3	$C_{17}H_{20}O_5$	Fruits, leaves, stems, stem wood and twigs	Pettit et al. 1988a, 1988b
Combretastatin B-4	$C_{17}H_{20}O_5$	Fruits, leaves, stems, stem wood and twigs	Pettit et al. 1988a, 1988b
Combretastatin D-1	$C_{18}H_{16}O_5$	Stem wood	Pettit et al. 1988b
Croweacin	$C_{11}H_{12}O_3$	Leaves	Mariri et al. 2023
Dimethyl 4,6-dioxo-5,6-dihydro-4H-pyrido [3,2,1-jk] carbazole-5-spirocyclohexane-1,3-dicarboxylate	$C_{24}H_{21}NO_6$	Leaves	Mariri et al. 2023
Docosanoic acid, methyl ester	$C_{23}H_{46}O$	Leaves	Mariri et al. 2023
Eicosanoic acid, methyl ester	$C_{20}H_{40}O_2$	Leaves	Mariri et al. 2023
Garcinone D	$C_{24}H_{28}O_7$	Leaves	Mariri et al. 2024
Hexadecanoic acid	$C_{16}H_{32}O_2$	Leaves	Mariri et al. 2023
Hexadecanoic acid, methyl ester	$C_{17}H_{34}O_2$	Leaves	Mariri et al. 2023
Lupenone	$C_{30}H_{48}O$	Leaves	Mariri et al. 2023
Lupeol (Fagarasterol)(beta-Viscol)	$C_{30}H_{50}O$	Leaves	Mariri et al. 2023
Methyl (*S*)-flavogallonate	$C_{22}H_{12}O_{13}$	Leaves	Mariri et al. 2024
n-Tricosane	$C_{23}H_{48}$	Leaves	Mariri et al. 2023
Octadecanoic acid, methyl ester	$C_{19}H_{34}O$	Leaves	Mariri et al. 2023
Phenol, 2,4-bis(1,1-dimethylpropyl)-	$C_{16}H_{26}0$	Leaves	Mariri et al. 2023
Phenol, 4-(1,1-dimethylpropyl)-	$C_{11}H_{16}O$	Leaves	Mariri et al. 2023
Philonotis flavone-40′′-methyl ether	$C_{31}H_{20}O_{12}$	Leaves	Mariri et al. 2024
Quercitrin	$C_{21}H_{20}O_{11}$	Leaves	Mariri et al. 2024
Sclerodione	$C_{18}H_{16}0_5$	Leaves	Mariri et al. 2023
Scopolin	$C_{16}H_{18}O_9$	Leaves	Mariri et al. 2024
Stigmast-5-en-3-ol, (3.beta.,24*S*)-	$C_{47}H_{84}O_2$	Leaves	Mariri et al. 2023
Stigmasterol	$C_{29}H_{48}O$	Leaves	Mariri et al. 2023
Valoneic acid dilactone	$C_{21}H_{10}O_{13}$	Leaves	Mariri et al. 2024
Verbasoside	$C_{20}H_{30}O_{12}$	Leaves	Mariri et al. 2024
Viminalol	$C_{30}H_{50}O$	Leaves	Mariri et al. 2023

Note: Please see the full reference list of the article, Maroyi, A., 2025, 'Insights into the botany, medicinal, phytochemical and pharmacological properties of *Combretum caffrum*', *Journal of Medicinal Plants for Economic Development* 9(1), a282. https://doi.org/10.4102/jomped.v9i1.282, for more information.

positive control. The extracts exhibited activities against the tested pathogens, with MIC values ranging from 0.16 mg/mL to 0.63 mg/mL (Dikhoba et al. 2019). Mariri et al. (2023) evaluated the antifungal activities of methanol extracts of *C. caffrum* leaves against *Aspergillus parasiticus*, *Cladosporium cladosporioides*, *Aspergillus nomius*, *Penicillium haloterans*, *Fusarium verticilloides*, *Fusarium oxysporum* and *Fusarium graminearum* using the microdilution broth assay, with amphotericin B, propiconazole and tebuconazole as positive controls. The extract exhibited activities against the tested pathogens, with MIC values ranging from 0.16 mg/mL to 1.25 mg/mL (Mariri et al. 2023).

Antiviral activities

McGaw et al. (2009) evaluated the antiviral activities of acetone extract of *C. caffrum* leaves against the sensitive feline herpesvirus type 1 using an *in vitro* antiviral assay. The extract demonstrated promising activities exhibiting viral cytopathic effects (McGaw et al. 2009).

Antioxidant activities

Masoko and Eloff (2007) evaluated the antioxidant activities of acetone and methanol extracts of *C. caffrum* leaves using 2,2-diphenyl-1-picryl hydrazyl (DPPH) free radical scavenging assay. The extract exhibited moderate antioxidant activities (Masoko & Eloff 2007). Dikhoba et al. (2019) evaluated the antioxidant activities of acetone extracts of *C. caffrum* leaves using the DPPH and 2,2′-azinobis (3-ethylbenzthiazoline-6-suphonic acid) (ABTS) free radical scavenging assays, with *levo*-ascorbic acid as a positive control. The extracts exhibited activities against ABTS and DPPH with half-maximal inhibitory concentration (IC_{50}) values of 0.01 mg/mL and 0.07 mg/mL, respectively (Dikhoba et al. 2019). Mathipa et al. (2022) evaluated the antioxidant activities of 70% acetone extracts of *C. caffrum* leaves and stems using the DPPH free radical scavenging assay, with *levo*-ascorbic acid as a positive control. The extracts exhibited dose-dependent activities with scavenging activities ranging from 60.0% to 80.0% (Mathipa et al. 2022). Mariri et al. (2023) evaluated the antioxidant activities of methanol extracts of *C. caffrum* leaves using the ABTS and DPPH free radical scavenging assays, with *levo*-ascorbic acid as a positive control. The extract exhibited antioxidant activities with IC_{50} values of 10.0 µg/mL and 70.0 µg/mL against DPPH and ABTS, respectively (Mariri et al. 2023).

Anticancer activities

Pettit et al. (1982) evaluated the anticancer activities of the phytochemical compound combretastatin A-4 isolated from *C. caffrum* branches, fruits and leaves against the murine P-388 lymphocytic leukaemia using the *in vitro* astrocytoma bioassay. The phytochemical compound inhibited murine P-388 lymphocytic leukaemia cell growth demonstrating the median effective dose (ED_{50}) value of 1.0 µg/mL (Pettit et al. 1982). Other phytochemical compounds isolated from *C. caffrum* that showed potent *in vitro* and *in vivo* activities in the P-388 lymphocytic leukaemia bioassay include combretastatin A-1, 6,7-dihydroxy-2,3,4-trimethoxy-9,10-dihydrophenanthrene, combretastatin B-3, 7-hydroxy-2.3,4,6-tetramethoxyphenanthrene, combretastatin B-4, 2,7-dihydroxy-3,4,6-trimethox-9,10 dihydrophenanthrene, bibenzyls 7, 8 and 9, and 7-hydroxy-2.3,4,6-tetramethox-9,10-dihydrophenanthrene (El-Zayat et al. 1993; Pettit et al. 1987a, 1988a, 1988b). On the other hand, combretastatin A-4 and A-1 are the most potent compounds, which exhibited *in vitro* and *in vivo* efficacy in a wide variety of tumour cell types (Kingston 2009; Singh 2024).

Cytotoxic activities

McGaw, Elgorashi and Eloff (2010) evaluated the cytotoxic activities of acetone extracts of *C. caffrum* leaves against bovine dermis cells and Vero kidney cells. The extracts demonstrated activities against both cell types exhibiting LC_{50} values which were <50.0 µg/mL (McGaw et al. 2010). Mariri et al. (2024) evaluated the cytotoxic activities of methanol extracts of *C. caffrum* leaves against the African green monkey kidney (Vero) cells and the human colorectal adenocarcinoma cell line (Caco-2) using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide colorimetric assay. The extract was cytotoxic to Vero cells at 500.0 µg/mL and demonstrated cytotoxic activities against Caco-2 cells in a dose-dependent manner (Mariri et al. 2024).

Conclusion

As outlined in the present review, *C. caffrum* is characterised by important and diverse values as a multipurpose species. While extensive evaluations of combretastatins have been undertaken, the ethnobotanical knowledge of the species has not been properly studied. To realise the full potential of *C. caffrum*, future studies should explore additional active anti-tumour phytochemical compounds using various *in vitro* and *in vivo* models. Such extensive research can make a valuable contribution to the growing knowledge about *C. caffrum* and its active ingredients, and this could potentially lead to the commercial development of anti-tumour pharmaceutical and cosmetic products.

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