Cultural, forage, medicinal and potential applications of *Combretum collinum* Fresen. (family Combretaceae)

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Review

Abstract

Background: Ethnobotany is a relatively underdeveloped discipline in tropical Africa, and little attention has been paid to the traditional uses and the potential applications of indigenous plant species. This study was aimed at reviewing the cultural, forage, medicinal and potential applications of *Combretum collinum* Fresen., a shrub or small tree indigenous to several countries in tropical Africa.

Methods: Literature on cultural, forage and medicinal uses of *C. collinum* was obtained from multiple internet sources such as Web of Science, Scopus®, SpringerLink®, Google Scholar, SciELO, PubMed® and ScienceDirect®. Complementary information was gathered from pre-electronic sources which included book chapters, books, scientific reports and journal articles obtained from the University library.

Results: Historically, *C. collinum* was valued for forage, medicinal and cultural purposes, and as a food plant of minor importance. Literature studies showed that *C. collinum* is used as ethnoveterinary medicine, and traditional medicine against respiratory infections, gastro-intestinal problems, malaria, evil spirits, fatigue, rheumatism, epilepsy, haemorrhoids, pain, infertility in women, wounds, snake bites and skin disorders. Phytochemical research identified alkanes, alkaloids, bibenzyls, fatty acids, flavonoids, phenanthrenes, phenols, phytosterols, stilbenoids, tannins and terpenoids. Phytochemical compounds and crude extracts of *C. collinum* demonstrated anthelmintic, antibacterial, antifungal, anti-inflammatory, antioxidant, antiplasmodial, antiproliferative, antityrosinase, larvicidal and cytotoxicity activities.

Conclusion: In the last few decades, tropical Africa has seen changes in access to modern healthcare, and these changes in the socio-cultural aspects have severely affected the indigenous knowledge of useful plant species such as *C. collinum.* Therefore, results of the current study stimulate scientific documentation of indigenous knowledge, application and beneficiation of this knowledge as a strategy of supporting sustainable utilization of plant species in tropical Africa.

Keywords: Combretaceae, *Combretum collinum*, Indigenous knowledge, *Materia medica*, Traditional medicine

Background

Combretum collinum Fresen. (Fig. 1) is a very variable, aggregate of semi-deciduous shrub or small to medium-sized tree belonging to the Combretaceae family commonly known as the white mangrove, Indian almond or bush willow family. The Combretaceae family consists of about 530 species distributed in 10 genera (Leistner 2000, Christenhusz & Byng 2016, Raj *et al.* 2022). *Combretum collinum* is a multi-purpose plant species which support livelihoods of local communities in tropical Africa through several ecosystem goods and services such as timber, firebreak, traditional medicines, firewood, charcoal, fodder, mulch and cultural services (Palmer & Pitman 1972, Rodin 1985, Bekele-Tesemma *et al.* 1993, Katende *et al.* 1995, Maroyi 2013, Dharani 2019). The wood of *C. collinum* is strong, hard, durable, resistant to fungi, boring insects and termites, easy to saw and work, and widely used for construction, joinery, furniture, fence posts, animal enclosures, canoes, utensils, tool handles, carvings, bee-hives and sticks (Bekele-Tesemma *et al.* 1993, Katende *et al.* 1995, Maroyi 2013, Dharani 2019). The gum exuded from injured branches of *C. collinum* is edible and also used to cure toothache or to plug a tooth with caries (Burkill 1994, Maroyi 2013). The roots of *C. collinum* are flexible and durable, and therefore, suitable for different basketry items. In Nigeria, the species has been used as famine food while in Uganda, the wood is used for fermenting local beer (Maroyi 2013). *Combretum collinum* is an important source of firewood and charcoal throughout its distributional range as its wood burns slowly with intense heat (Constant & Tshisikhawe 2018, Magwede *et al.* 2019). *Combretum collinum* is an attractive tree that is popular in private gardens, tolerating frost and moderate drought and widely used as windbreak, shade, or ornamental plant (Palmer and Pitman 1972, Maroyi 2013, Dharani 2019). The species is an integral part of the agroforestry system in tropical Africa, as *C. collinum* is used for intercropping purposes with different agricultural crops and its flowers serve as bee foraging and important source of honey (Bekele-Tesemma *et al.* 1993, Katende *et al.* 1995, Maroyi 2013, Dharani 2019). The fruits, leaves, branches and twigs of *C. collinum* are browsed by game and livestock (Palmer & Pitman 1972, Van Wyk 2008, Chepape *et al.* 2011, Maroyi 2013, Van Wyk & Van Wyk 2013, Marius *et al.* 2017, Schmidt *et al.* 2017, Mudau *et al.* 2021, Ravhuhali *et al.* 2022). Recent research evaluated the variation of chemical composition and *in vitro* dry matter degradability of *C. collinum,* and the acid detergent fibre, neutral detergent fibre, tannin and minerals' content exhibited by the species are comparable to the fodder characteristics of other plant species which are widely used as supplementary feed for ruminants such as cattle, goats and game in semi-arid regions in tropical Africa (Mudau *et al.* 2021, Ravhuhali *et al.* 2022). Thus, *C. collinum* is a potential forage species for ruminants as the leaves and twigs have protein content ranging from 13.2% to 14.9% (McGregor 1991) and the seeds of the species are also a good source of energy, crude fats, carbohydrates, amino acids, fatty acids, minerals such as calcium, copper, iron, magnesium, manganese, phosphorus, potassium, sodium and zinc (Bougma *et al.* 2021).

Today, in informal herbal medicine markets throughout tropical Africa, the bark, roots, seeds, stems and stem bark of *C. collinum* are widely sold as medicinal ingredients for various human and animal ailments (Maroyi 2013). In South Africa, the winged fruits are locally commercialized for ornamental purposes (Maroyi 2013). In South Africa, the winged fruits can be strung together to make attractive room-dividers or spray-painted as Christmas decorations (Maroyi 2013). Woodroses, parasitic mistletoes belonging to *Erianthemum dregei* (Eckl. & Zeyh.) Tiegh. and *Pedistylis galpinii* (Schinz ex Sprague) Wiens (both species are members of Loranthaceae family) which cause odd flower-like outgrowths are often found on *C. collinum* (Dzerefos & Witkowski 1997, Dzerefos *et al.* 1999, Van Wyk & Gericke 2018). In the Limpopo and Mpumalanga provinces of South Africa, Eswatini, Mozambique and Zimbabwe, local people remove the mistletoe and harvest the woodroses which they sale as a carved ornament or curio (Dzerefos & Witkowski 1997, Dzerefos *et al.* 1999, Van Wyk & Gericke 2018). Similarly, several *Combretum* species are used as sources of traditional medicines in tropical Africa (Irvine 1961, Watt & Breyer-Brandwijk 1962, Burkill 1994, Hutchings *et al.* 1996, Neuwinger 2000, Arnold *et al.* 2002, Kokwaro 2009, Schmelzer & Gurib-Fakim 2013), and these include *C. adenogonium* Steud. ex A.Rich., *C. albopunctatum* Suess., *C. apiculatum* Sond., *C. caffrum* (Eckl. & Zeyh.) Kuntze, *C. celastroides* Welw. ex M.A.Lawson, *C. coccineum* (Sonn.) Lam., *C. comosum* G.Don, *C. erythrophyllum* (Burch.) Sond., *C. hereroense* Schinz, *C. imberbe* Wawra, *C. indicum*, *C. kraussii* Hochst., *C. micranthum* G.Don, *C. microphyllum* Klotzsch, *C. mkuzense* J.D.Carr & Retief, *C. molle* R.Br. 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. (Irvine 1961, Watt & Breyer-Brandwijk 1961, Burkill 1994, Hutchings *et al.* 1996, Neuwinger 2000, Arnold *et al.* 2002, Kokwaro 2009, Schmelzer & Gurib-Fakim 2013). It is therefore, within this context that the current study was undertaken aimed at reviewing the cultural, forage and medicinal uses of *C. collinum*.

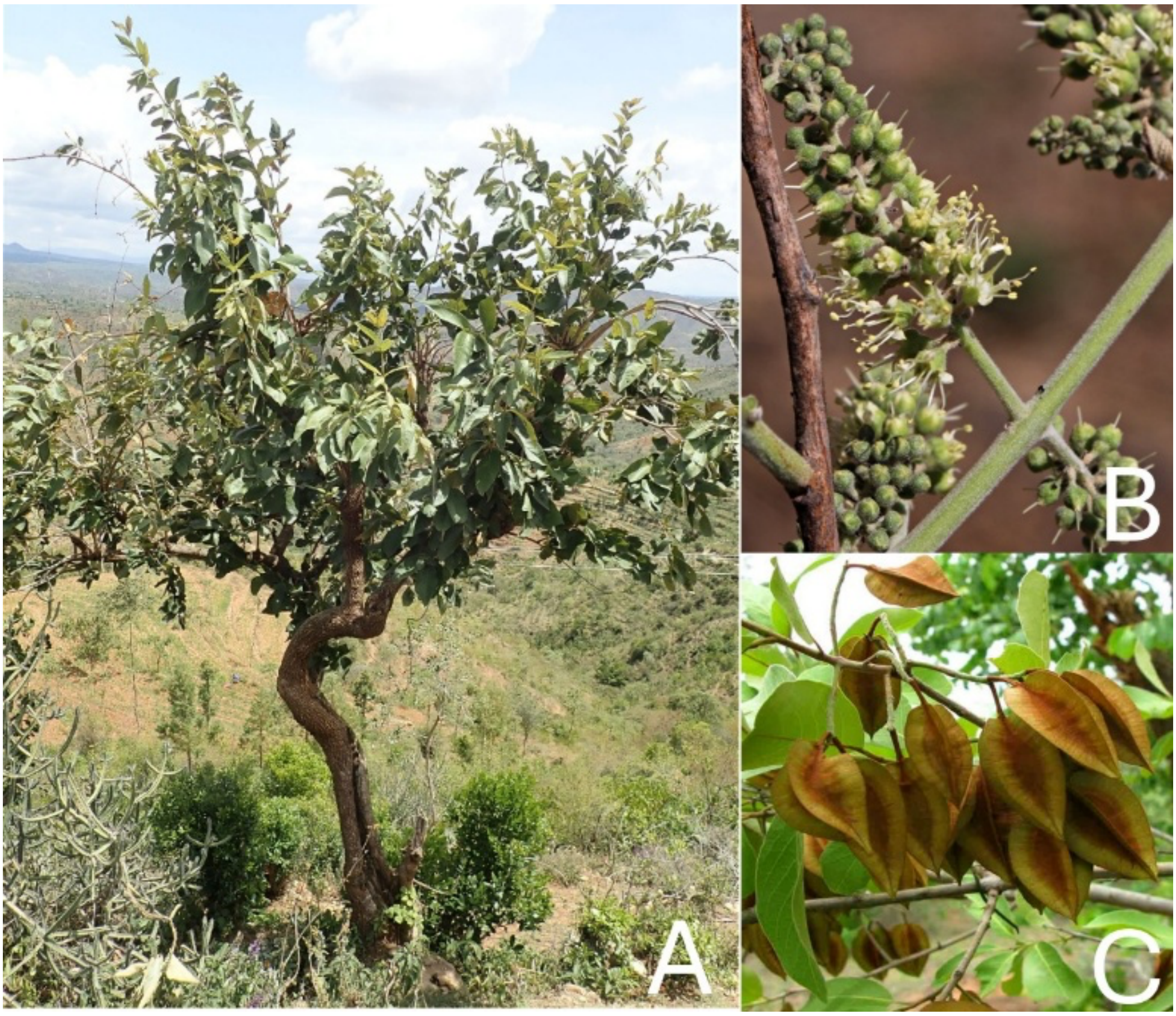

Figure 1. *Combretum collinum*: A: entire plant, B: branch showing flowers and C: branch showing leaves and fruits (photos: A (O Weber), B (M Hyde) and C (H Pickering)

Materials and Methods

Information on the cultural, forage and medicinal uses of *C. collinum* was exhaustively surveyed from different electronic databases such as Web of Science (https://www.webofknowledge.com), Scopus® (http://www.scopus.com/), SpringerLink® (https://link.springer.com/), Google Scholar (https://scholar.google.com/), SciELO (https://search.scielo.org/), PubMed® (https://pubmed.ncbi.nlm.nih.gov/) and ScienceDirect® (https://www.sciencedirect.com/search), and pre-electronic sources such as books, book chapters, journal articles, dissertations, and thesis obtained from the University library. The search covered publications from 1961 to 2025, a long period to identify and capture relevant scholarly publications and literature that were aligned with the study objectives.

Results and Discussion

Taxonomy and species description

The genus *Combretum* Loefl. consists of about 276 species with a pantropical distribution mainly in tropical Asia and Africa, but absent in the Pacific Islands and most of Australia, with the centre of diversity of the genus on the African continent (Stace 2002, 2007, Jordan *et al.* 2011, 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 army commander Gaius Plinius Secundus, known in English as Pliny (23-79 AD), used in reference for an unknown plant (Palmer & Pitman 1972, Schmidt *et al.* 2017). The name was also re-used by the Swedish botanist Pehr Löfling (31 January 1729-22 February 1756) for the *Combretum* genus (Palmer & Pitman 1972, Schmidt *et al.* 2017). *Combretum collinum* is named after Collina, the Roman goddess of the hills (Palgrave 2002) and hence the specific name "*collinum*", is derived from the Latin word "*collinus*" meaning "growing on a hill" (Palmer & Pitman 1972) in reference to the habitat of the species, that is, hilly terrain, high ground or mountainous areas. *Combretum collinum* is a variable species, divided into 11 subspecies, namely subsp. *binderianum* (Kotschy) Okafor, subsp. *collinum*, subsp. *dumetorum* (Exell) Okafor, subsp. *elgonense* (Exell) Okafor, subsp. *gazense* (Swynn. & Baker f.) Okafor, subsp. *geitonophyllum* (Diels) Okafor, subsp. *hypopilinum* (Diels) Okafor, subsp. *kwangense* (J.Duvign.) Okafor, subsp. *ondongense* (Engl. & Diels) Okafor, subsp. *suluense* (Engl. & Diels) Okafor and subsp. *taborense* (Engl.) Okafor (Wicken 1973, Exell 1978, Edwards *et al.* 1995, Jordan *et al.* 2011). The synonyms associated with the name *C. collinum* include *C. angustilanceolatum* Engl., *C. bajonense* Sim, *C. binderanum* Kotschy, *C. brosigianum* Engl. & Diels, *C. burttii* Exell, *C. cognatum* Diels, *C. coriaceum* Schinz, *C. crotonoides* Hutch. & Dalziel, *C. dumetorum* Exell, *C. elaeagnifolium* Planch., *C. elgonense* Exell, *C. englerianum* Exell, *C. eylesii* Exell, *C. fischeri* Engl., *C. flaviflorum* Exell, *C. frommii* Gilg ex Engl., *C. fulvotomentosum* Engl. & Diels, *C. gazense* Swynn. & Baker f., *C. geitonophyllum* Diels, *C. goetzenianum* Engl. ex Diels, *C. hypopilinum* Diels, *C. junodii* Dummer, *C. kabadense* Exell, *C. karaguense* Engl. & Diels, *C. kerengense* Engl. & Diels, *C. laboniense* M.B.Moss, *C. laeteviride* Engl. & Gilg, *C. lamprocarpum* Diels, *C. makindense* Gilg ex Engl., *C. mechowianum* O.Hoffm., *C. monticola* Engl. & Gilg, *C. mwanzense* Exell, *C. ondongense* Engl. & Diels, *C. pachycarpum* Engl. & Gilg, *C. populifolium* Engl. & Diels, *C. psammophilum* Engl. & Diels, *C. ritschardii* De Wild. & Exell, *C. rubiginosum* Welw. ex M.A.Lawson, *C. schinzii* Engl. ex Engl. & Diels, *C. singidense* Exell, *C. suluense* Engl. & Diels, *C. taborense* Engl., *C. tenuipes* Engl., *C. truncatum* Engl., *C. verticillatum* Engl. & Diels and *C. wildemanii* M.G.Gangop. & Chakrab. (Wicken 1973, Exell 1978, Thulin 1993, Edwards *et al.* 1995, Jordan *et al.* 2011). Therefore, several subspecies and synonyms associated with *C. collinum* implies that its taxonomy is complex, in need of detailed studies focusing on geographically isolated populations which exhibit some degree of genetic or morphological differentiation. The English common names of *C. collinum* include "bicoloured bush-willow", "Kalahari bush-willow", "silver bush-willow", "variable bush-willow", "variable combretum" and "weeping bush-willow (Palmer & Pitman 1972, Palgrave 2002, Van Wyk 2008, Maroyi 2013, Thomas & Grant 2013, Van Wyk & Van Wyk 2013, Schmidt *et al.* 2017, Dharani 2019).

Combretum collinum is a shrub or small to medium-sized tree reaching 17 metres in height (Palgrave 2002, Thomas & Grant 2013). *Combretum collinum* has a flat or rounded and spreading crown (Fig. 1A), sometimes with branches drooping almost to the ground. The main stem of *C. collinum* is usually twisted, often single-stemmed with brownish-grey to dark grey and lightly-fissured lengthwise, rough bark and mottled with white. The young stems are light to dark green in colour and usually covered in silvery hairs. The leaves of *C. collinum* are opposite, alternate or occur in whorls, ovate to broadly elliptic or obovate in shape, upper surface rather dark green and under surface paler green to silvery in colour, variously with or without dense woolly hairs or tiny scales which are grey in colour or golden dots. The leaf apex is broadly tapering to attenuate and the base is broadly tapering to rounded, with entire margins, veins conspicuous and raised below. When young, the leaves may be slightly hairy but they become smooth with age. The flowers are small, cream to yellow in colour (Fig. 1B), sweetly scented, occurring in axillary spikes, often with the old leaves and conspicuous when the tree is in full flower. The fruit is four-winged (Fig. 1C), variable in outline, round or sometimes narrowed towards the apex, rusty-red when young, becoming dark chocolate-brown or deep golden brown when mature, with a marked metallic sheen caused by scales (Palgrave 2002). *Combretum collinum* has been recorded in Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Democratic Republic of Congo, Eritrea, Eswatini, Ethiopia, Gambia, Ghana, Guinea, Guinea-Bissau, Cote d'Ivoire, Kenya, Malawi, Mali, Mozambique, Namibia, Niger, Nigeria, Rwanda, Senegal, Somalia, South Africa, South Sudan, Sudan, Tanzania, Togo, Uganda, Zambia and Zimbabwe (Wicken 1973, Drummond 1975, Exell 1978, Thulin 1993, Edwards *et al.* 1995, Germishuizen & Meyer 2003, Setshogo & Venter 2003, Mapaura & Timberlake 2004, Burrows & Willis 2005, Loffler & Loffler 2005, Setshogo 2005, Figueiredo & Smith 2008, Mannheimer & Curtis 2009, Jordan *et al.* 2011, Kalema & Beentje 2012, Darbyshire *et al.* 2015, Burrows *et al.* 2018, Govaerts *et al.* 2021) (Fig. 2). *Combretum collinum* has been recorded in arid, semi-arid and savanna, open woodland, wooded grassland, bushveld, thickets, termite mounds, from sea level to 2200 m above sea level (Germishuizen & Meyer 2003, Maroyi 2013, Dharani 2019).

Cultural and medicinal uses of *Combretum collinum*

In Ethiopia, *C. collinum* is used to smoke milking and brewing pots (Bekele-Tesemma *et al.* 1993, Mengistu *et al*. 2019). This traditional practice of smoking and cleaning milk utensils such as pots with *C. collinum* extracts is aimed at improving and keeping the organoleptic properties of raw milk (Asefa & Abrha 2021). Similarly, the smoke from *C. collinum* leaves and other parts of the species is believed to repel evil spirits (Bekele-Tesemma *et al.* 1993). Research by Jumare et al. (2022) showed that *C. collinum* is also used to get rid of evil spirits in Nigeria. *Combretum collinum* is used as a source of traditional medicines in Senegal, Guinea, Gambia, Nigeria, Ethiopia, Kenya, South Africa, Tanzania, Guinea-Bissau, Zambia, Uganda, Cote d'Ivoire, Mozambique, Namibia, Angola and Benin, that is, 45.7% of the countries where the species is indigenous (Table 1). In tropical Africa, the bark, gum, leaves, roots, seeds, stems, stem bark, twigs and twig bark of *C. collinum* are used as traditional medicines to treat or manage 58 human and animal diseases or ailments. The main ailments and diseases treated by *C. collinum* extracts (Figure 3) include its use as ethnoveterinary medicine, and traditional medicine for respiratory infections, gastro-intestinal problems, malaria, evil spirits, fatigue, rheumatism, epilepsy, haemorrhoids, pain, infertility in women, wounds, snake bites and skin disorders. In Kenya, the bark of *C. collinum* is mixed with that of *Entada abyssinica* Steud. ex A.Rich. (Fabaceae family) and *Tylosema fassoglense* (Kotschy ex Schweinf.) Torre & Hillc. (Fabaceae family) as traditional medicine for infertility in women (Kigen *et al.* 2014) while in Nigeria, the stem bark is mixed with *Waltheria indica* L. (Malvaceae family) as remedy for wounds (Nefai *et al.* 2022). In Tanzania, the roots of *C. collinum* are mixed with those of *C. molle* and *Phyllanthus reticulatus* Poir. (Phyllanthaceae family) as traditional medicine for diarrhoea (Hedberg *et al.* 1982) while the roots are mixed with those of *Searsia pyroides* (Burch.) Moffett (Anacardiaceae family) as remedy for dysentery (Moshi *et al.* 2010). Similarly, in Tanzania, the roots of *C. collinum* are mixed with the bark or roots of *Kigelia africana* (Lam.) Benth. (Bignoniaceae family) as traditional medicine for menstrual problems (Hedberg *et al.* 1982, Maroyi 2013) while the leaves are combined with those of *Erythrina abyssinica* Lam. (Fabaceae family) and *Trema orientale* (L.) Blume (Cannabaceae family) as remedy for yellow fever (Moshi *et al.* 2010).

Figure 2. Distribution of *Combretum collinum* in tropical Africa

Table 1. Medicinal uses of *Combretum collinum*

Medicinal use	Parts used	Country	Reference
Mono-therapeutic applications			
Anaemia and tonic	Leaf or root decoction or infusion taken orally	Guinea-Bissau	Watt & Breyer-Brandwijk 1962, Maroyi 2013, Catarino *et al.* 2016
Antispasmodic	Root decoction applied topically	Tanzania	Moshi *et al.* 2010
Aphrodisiac	Root decoction taken orally	Zambia	Mwambo *et al.* 2024
Arthritis	Not specified	Nigeria	Jumare *et al.* 2022
Cancer	Leaf paste applied topically	Nigeria	Okunola *et al.* 2020, Jumare *et al.* 2022

Cramps	Root infusions	South Africa	Tshikalange *et al.* 2016
Diabetes	Not specified	Nigeria	Jumare *et al.* 2022
Ear problems	Leaf sap applied topically	Kenya	Njoroge & Bussmann 2006, Maroyi 2013
Epilepsy	Root decoction taken orally	Nigeria and Uganda	Tabuti *et al.* 2003, Odda *et al.* 2008, Maroyi 2013, Jumare *et al.* 2022
Evil spirits	Not specified	Ethiopia and Nigeria	Bekele-Tesemma *et al.* 1993, Jumare *et al.* 2022
Facilitate labour	Root infusion taken orally	Uganda	Tabuti *et al.* 2003, Odda *et al.* 2008, Maroyi 2013
Fatigue	Crushed leaves used as poultices or root decoction taken orally	Côte d'Ivoire and Nigeria	Maroyi 2013, Bamba *et al.* 2020, Umar *et al.* 2020
Gastro-intestinal problems (abdominal pains, constipation, diarrhoea, dysentery and stomach ache)	Bark, gum, leaf, root or twig decoction, infusion or maceration taken orally	Gambia, Guinea, Kenya, Mozambique, Namibia, Nigeria, Tanzania, Uganda and Zambia	Hedberg *et al.* 1982, Burkill 1994, Johns *et al.* 1995, Tabuti *et al.* 2003, Kisangau *et al.* 2007, 2011, Okello & Ssegawa 2007, Odda *et al.* 2008, Kokwaro 2009, Chinsembu & Hedimbi 2010, Moshi *et al.* 2010, Cheikhyoussef *et al.* 2011a, Kamatenesi *et al.* 2011, Maroyi 2013, Conde *et al.* 2014, Chinsembu *et al.* 2015, Cock & Van Vuuren 2015, Chinsembu 2016, Dharani 2019, Hassan *et al.* 2020, Keita *et al.* 2020, Masters 2023, Mutie *et al.* 2023, Silén *et al.* 2023, Mwambo *et al.* 2024
Haemorrhoids	Bark or leaf decoction applied topically	Angola and Nigeria	Maroyi 2013, Lautenschläger *et al.* 2018, Umar *et al.* 2020, Jumare *et al.* 2022
High blood pressure	Not specified	Nigeria	Jumare *et al.* 2022
Hydrocele in children	Root infusion taken orally	Uganda	Tabuti *et al.* 2003, Odda *et al.* 2008
Infertility in women	Root decoction or maceration taken orally	Kenya and Uganda	Tabuti *et al.* 2003, Odda *et al.* 2008, Maroyi 2013, Kigen *et al.* 2014, Mutie *et al.* 2023
Malaria	Leaf, root or stem bark decoction or infusion taken orally	Côte d'Ivoire, Kenya, Nigeria and Tanzania	Hedberg *et al.* 1982, Kokwaro 2009, Maroyi 2013, Cock & Van Vuuren 2015, Bamba *et al.* 2020, Hassan *et al.* 2020, Keita *et al.* 2020, Mutie *et al.* 2023, Silén *et al.* 2023
Pain	Twig bark or root decoction taken orally	Guinea-Bissau and Mozambique	Watt & Breyer-Brandwijk 1962, Maroyi 2013, Conde *et al.* 2014, Catarino *et al.* 2016
Painful legs	Root infusions	South Africa	Tshikalange *et al.* 2016
Panaritium	Leaf decoction taken orally	Namibia	Cheikhyoussef *et al.* 2011a,b
Purgative	Leaf or root decoction or infusion taken orally	Nigeria	Maroyi 2013, Hassan *et al.* 2020
Rectal prolapse	Powdered stem bark taken orally	Tanzania	Hedberg *et al.* 1982, Maroyi 2013
Respiratory infections (bronchitis, colds, cough, influenza, lung problems, pneumonia and tuberculosis)	Bark, gum, leaf, root or twig decoction or maceration taken orally	Kenya, Namibia, Nigeria, Senegal, Tanzania, Uganda and Zambia	Hedberg *et al.* 1982, Burkill 1994, Kisangau *et al.* 2007, 2011, Kokwaro 2009, Chinsembu & Hedimbi 2010, Cheikhyoussef *et al.* 2011a,b, Kamatenesi *et al.* 2011, Maroyi 2013, Chinsembu *et al.* 2015, Cock & Van Vuuren 2015, Chinsembu 2016, Keita *et al.* 2020, Jumare *et al.* 2022, Masters 2023, Mutie *et al.* 2023, Silén *et al.* 2023, Ukwuani-Kwaja *et al.* 2024

Rheumatism	Crushed leaves or roots used as poultices	Kenya and South Africa	Maroyi 2013, Tshikalange *et al.* 2016, Mutie *et al.* 2023
Sexually transmitted infections (gonorrhoea and syphilis)	Leaf, leafy twig, root juice or root decoction, infusion or maceration taken orally	Uganda	Tabuti *et al.* 2003, Odda *et al.* 2008, Maroyi 2013
Skin disorders (pyomyositis and rash)	Root decoction or maceration applied topically	Côte d'Ivoire, Nigeria and Uganda	Tabuti *et al.* 2003, Odda *et al.* 2008, Maroyi 2013, Bamba *et al.* 2020, Jumare *et al.* 2022
Snake bite	Leaf, root, root juice or twig decoction applied topically	Kenya and Tanzania	Hedberg *et al.* 1982, Owuor *et al.* 2005, Owuor & Kisangau 2006, Kokwaro 2009, Maroyi 2013, Cock & Van Vuuren 2015, Keita *et al.* 2020, Mutie *et al.* 2023, Silén *et al.* 2023
Toothache	Gum, leaf, leafy twig or root juice applied topically	Mozambique and Nigeria	Burkill 1994, Maroyi 2013, Conde *et al.* 2014, Razão *et al.* 2024
Trypanosomiasis	Root decoction taken orally	Nigeria	Hassan *et al.* 2020, Ukwuani-Kwaja *et al.* 2024
Uterine bleeding	Not specified	Nigeria	Jumare *et al.* 2022
Wounds	Bark, leaf, root or seed maceration applied topically	Benin and Uganda	Kamatenesi *et al.* 2011, Maroyi 2013, Marquardt *et al.* 2017, Jumare *et al.* 2022, Masters 2023, Ukwuani-Kwaja *et al.* 2024
Ethnoveterinary medicine (acaricide, amoebiasis, breast ulcer, cancer, colic, constipation, diarrhoea, eye infection, intestinal worms and trypanosomiasis)	Bark, leaf, resin, root, root bark, seed, stem or stem bark	Benin, Ethiopia, Kenya, Namibia, Nigeria, South Africa, Tanzania and Uganda	Watt & Breyer-Brandwijk 1962, Hedberg *et al.* 1982, Wasswa & Olila 2006, Wanzala *et al.* 2012, Maroyi 2013, Mergesa *et al.* 2013, Chitura *et al.* 2018, Dharani 2019, Hassan *et al.* 2021, Eiki *et al.* 2022, Iwaka *et al.* 2023, Mutie *et al.* 2023, Ukwuani-Kwaja *et al.* 2024
Used in combination with other species			
Diarrhoea	Roots mixed with those of *C. molle* and *P. reticulatus*	Tanzania	Hedberg *et al.* 1982
Dysentery	Roots mixed with those of *S. pyroides*	Tanzania	Moshi *et al.* 2010
Infertility in women	Bark mixed with that of *E. abyssinica* and *T. fassoglense*	Kenya	Kigen *et al.* 2014
Menstrual problems	Roots mixed with bark or roots of *K. africana*	Tanzania	Hedberg *et al.* 1982, Maroyi 2013
Yellow fever	Leaves combined with those of *E. abyssinica* and T. *orientale*	Tanzania	Moshi *et al.* 2010
Wounds	Stem bark mixed with *W. indica*	Nigeria	Nefai *et al.* 2022

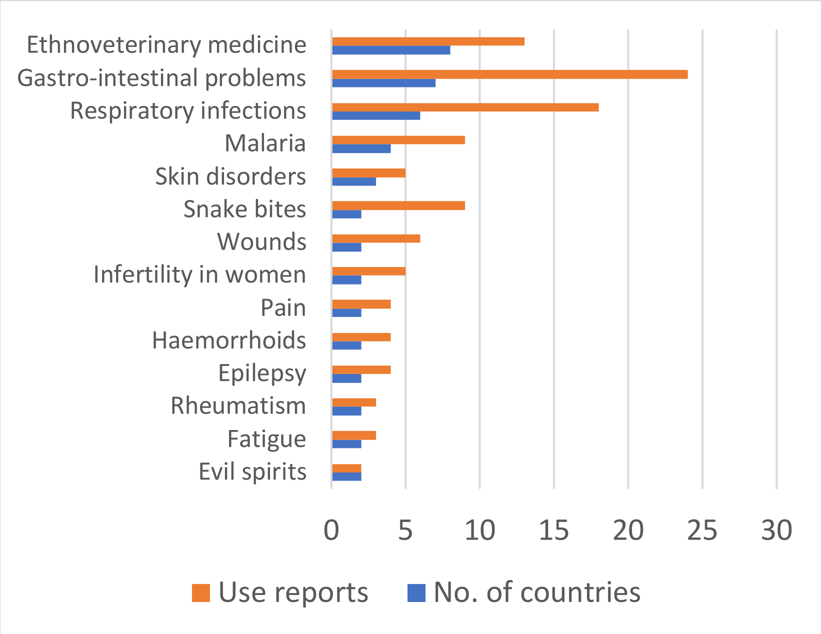

Figure 3. Major ethnomedicinal applications of *Combretum collinum* in tropical Africa

Phytochemistry and pharmacological properties of *Combretum collinum*

Qualitative and quantitative phytochemical analyses of *C. collinum* aerial parts, fruits and leaves revealed the presence of alkanes, alkaloids, bibenzyls, fatty acids, flavonoids, phenanthrenes, phenols, phytosterols, stilbenoids, tannins and terpenoids (Rogers & Coombes 1999, Katerere *et al.* 2003, 2012, Songca *et al.* 2013, Marquardt *et al.* 2017, 2019, 2020, Grimsey *et al.* 2024) (Table 2). Some of the documented phytochemical compounds and crude extracts of *C. collinum* exhibited anthelmintic, antibacterial, antifungal, anti-inflammatory, antioxidant, antiplasmodial, antiproliferative, antityrosinase, larvicidal and cytotoxicity activities.

Table 2. Phytochemical composition of *Combretum collinum*

Phytochemical compound	**Formula**	**Plant part**	**Reference**
1a,3′-dihydroxy-3,4,4′,5-tetramethoxybibenzyl	$C_{19}H_{23}NO_5$	Leaves	Katerere *et al.* 2012
5′-hydroxy-3,4,4′,5-tetramethoxybibenzyl	$C_{10}H_{14}O_5$	Leaves	Katerere *et al.* 2012
9,10-dihydro-3,6,7-trimethoxy-2,5-phenanthrenediol	$C_{17}H_{18}O_5$	Leaves	Katerere *et al.* 2012
Borneol	$C_{10}H_{18}O$	Leaves	Grimsey *et al.* 2024
Campesterol	$C_{28}H_{48}O$	Leaves	Marquardt *et al.* 2019, 2020
Camphor	$C_{10}H_{16}O$	Leaves	Grimsey *et al.* 2024
Cineole	$C_{10}H_{18}O$	Leaves	Grimsey *et al.* 2024
Combretastatins A and B	$C_{18}H_{22}O_6$	Aerial parts	Katerere *et al.* 2003
Docosanoic acid	$C_{22}H_{44}O_2$	Leaves	Marquardt *et al.* 2020
Eicosanoic acid	$C_{20}H_{40}O_2$	Leaves	Marquardt *et al.* 2020
Heptacosane	$C_{27}H_{56}$	Leaves	Marquardt *et al.* 2020
Hexacosane	$C_{26}H_{54}$	Leaves	Marquardt *et al.* 2020
Hexadecanoic acid	$C_{16}H_{32}O_2$	Leaves	Marquardt *et al.* 2020
Isomenthol	$C_{10}H_{20}O$	Leaves	Grimsey *et al.* 2024
Isomyocorene	$C_{10}H_{16}$	Leaves	Grimsey *et al.* 2024
Lignoceric acid	$C_{24}H_{48}O_2$	Leaves	Marquardt *et al.* 2019
Limonene	$C_{10}H_{16}$	Leaves	Grimsey *et al.* 2024
Malic acid	$C_4H_6O_5$	Leaves	Marquardt *et al.* 2020
Mollic acid	$C_{30}H_{48}O_4$	Leaves	Rogers & Coombes 1999
Mollic acid 3β-O-α-L-arabinopyranoside	$C_{35}H_{56}O_7$	Leaves	Rogers & Coombes 1999
Mollic acid 3β-O-β-D-glucopyranoside	$C_{36}H_{58}O_9$	Leaves	Rogers & Coombes 1999
Mollic acid 3β-O-β-D-xylopyranoside	$C_{35}H_{56}O_7$	Leaves	Rogers & Coombes 1999
Mollic acid 3β-O-β-D-4-O-acetylxylopyranoside	$C_{35}H_{56}O_9$	Fruits	Rogers & Coombes 1999

Myricetin-3-O-glucoside	$C_{21}H_{20}O_{13}$	Leaves	Marquardt *et al.* 2017, 2020
Myricetin-3-O-rhamnoside	$C_{21}H_{20}O_{12}$	Leaves	Marquardt *et al.* 2017, 2020
Myristic acid	$C_{14}H_{28}O_2$	Leaves	Marquardt *et al.* 2019
Nonacosane	$C_{29}H_{60}$	Leaves	Marquardt *et al.* 2020
Nonadecane	$C_{19}H_{40}$	Leaves	Marquardt *et al.* 2020
Octacosane	$C_{28}H_{58}$	Leaves	Marquardt *et al.* 2020
Octadecanoic acid	$C_{18}H_{36}O_2$	Leaves	Marquardt *et al.* 2020
Olean-12-ene-3-one	$C_{30}H_{48}O$	Leaves	Songca *et al.* 2013
Oleic acid	$C_{18}H_{34}O_2$	Leaves	Marquardt *et al.* 2019, 2020
Oleic acid amide	$C_{18}H_{35}NO$	Leaves	Marquardt *et al.* 2019
Palmitic acid	$C_{16}H_{32}O_2$	Leaves	Marquardt *et al.* 2019
Pentacosane	$C_{25}H_{52}$	Leaves	Marquardt *et al.* 2020
β-sitosterol	$C_{29}H_{50}O$	Leaves	Marquardt *et al.* 2019
Squalene	$C_{30}H_{50}$	Leaves	Marquardt *et al.* 2020
Stearic acid	$C_{18}H_{36}O_2$	Leaves	Marquardt *et al.* 2019
Stigmasterol	$C_{29}H_{48}O$	Leaves	Marquardt *et al.* 2019, 2020
Terpineol	$C_{10}H_{18}O$	Leaves	Grimsey *et al.* 2024
Tetradecanoic acid	$C_{14}H_{28}O_2$	Leaves	Marquardt *et al.* 2020
Tetracosanoic acid	$C_{24}H_{48}O_2$	Leaves	Marquardt *et al.* 2020
Triacontane	$C_{30}H_{62}$	Leaves	Marquardt *et al.* 2020

Anthelmintic activities

McGaw *et al.* (2001) evaluated the anthelmintic activities of acetone extracts of *C. collinum* leaves against the free-living nematode *Caenorhabditis elegans* var. *Bristol* (N2) with the standard nematocidal drug levamisole as a positive control. The extract exhibited activities against the nematode (McGaw *et al.* 2001).

Antibacterial activities

Eloff (1999) evaluated the antibacterial activities of acetone extract of *C. collinum* leaves against *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa* and *Enterococcus faecalis* using the twofold serial dilution with gentamycin as a positive control. The extract exhibited activities against the tested pathogens with minimum inhibition concentration (MIC) values ranging from 0.8 mg/ml to 3.0 mg/ml (Eloff 1999). Katerere *et al.* (2012) evaluated the antibacterial activities of the phytochemical compound 9,10-dihydro-3,6,7-trimethoxy-2,5-phenanthrenediol isolated from *C. collinum* leaves against *Proteus vulgaris, Mycobacterium fortuitum* and *Staphylococcus aureus* using the microdilution assay with streptomycin as a positive control. The phytochemical compound exhibited activities against the tested pathogen with MIC values ranging from 25.0 µg/ml to 100.0 µg/ml (Katerere *et al.* 2012). Songca *et al.* (2013) evaluated the antibacterial activities of the phytochemical compound olean-12-ene-3-one isolated from *C. collinum* leaves against *Staphylococcus aureus* using the microdilution method. The phytochemical compound demonstrated activities against the tested pathogen exhibiting MIC value of 0.6 mg/ml (Songca *et al.* 2013). Cock & Van Vuuren (2015) evaluated the antibacterial activities of methanol and water extracts of *C. collinum* leaves against *Aeromonas hydrophilia, Alicaligenes faecalis, Bacillus cereus, Citrobacter freundi, Bacillus subtilis, Escherichia coli, Proteus mirabilis, Klebsiella pneumonia, Proteus vulgaris, Pseudomonas fluorescens, Pseudomonas aeruginosa, Salmomnella typhimurin, Shigella sonnei, Serratia marcescens, Staphylococcus epidermidis* and *Stapyylococcus aureus* using the microdilution assay. The extracts demonstrated activities against the tested pathogens exhibiting MIC values ranging from 226.0 µg/ml to 2016.0 µg/ml (Cock & Van Vuuren 2015). Netshiluvhi & Eloff (2016) evaluated the antibacterial activities of acetone extracts of *C. collinum* leaves against *Pseudomonas aeruginosa, Enterococcus faecalis, Escherichia coli* and *Staphylococcus aureus* using the serial microplate dilution technique. The extract demonstrated activities against the tested pathogens exhibiting MIC values ranging from 70.0 µg/ml to 820.0 µg/ml (Netshiluvhi & Eloff 2016). Lall *et al.* (2019) evaluated the antibacterial activities of ethanol extract of *C. collinum* bark against *Cutibacterium acnes* using the microdilution assay with tetracycline as a positive control. The extract demonstrated activities against the tested pathogen exhibiting MIC value of 250.0 µg/ml (Lall *et al.* 2019). Marquardt *et al.* (2019, 2020) evaluated the antibacterial activities of ethanol extract of *C. collinum* leaves against *Staphylococcus epidermidis, Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA) using the microdilution method with gentamicin and vancomycin as positive controls. The extract demonstrated activities against the tested pathogens with MIC values ranging from 275.0 µg/ml to 385.5 µg/ml (Marquardt *et al.* 2019, 2020). Bamba *et al.* (2020) evaluated the antibacterial activities of methanol extract of *C. collinum* leaves and stem bark against methicillin-resistant *Staphylococcus aureus* strain using the microdilution method. The extracts demonstrated activities against the tested pathogens exhibiting MIC values ranging from 0.33 mg/ml to 1.25 mg/ml (Bamba *et al.* 2020). Anokwuru *et al.* (2021) evaluated the antibacterial activities of methanol extract of *C. collinum* leaves against *Staphylococcus epidermidis, Staphylococcus aureus, Bacillus cereus, Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterococcus faecalis, Escherichia coli, Shigella sonnei* and *Salmonella typhimurium* using the microdilution assay with ciprofloxacin as a positive control. The extract exhibited activities against the tested pathogens with MIC values ranging from 0.63 mg/ml to >3.0 mg/ml (Anokwuru *et al.* 2021). Grimsey *et al.* (2024) evaluated the antibacterial activities of methanol extracts of *C. collinum* leaves against *Staphylococcus aureus, Escherichia coli* and *Klebsiella pneumoniae* using the broth microdilution assay with ciprofloxacin, ampicillin, gentamycin, oxacillin and methicillin as positive controls. The extracts exhibited activities against the tested pathogens with MIC values ranging from 120.0 µg/ml to 490.0 µg/ml (Grimsey *et al.* 2024).

Antifungal activities

Fyhrquist *et al.* (2004) evaluated the antifungal activities of methanol extract of *C. collinum* leaves against *Candida krusei* using the agar diffusion method with amphotericin B and itraconazol as positive controls. The extract demonstrated activities against the tested pathogen exhibiting inhibition zone value of 18.4 mm (Fyhrquist *et al.* 2004). Katerere *et al.* (2012) evaluated the antifungal activities of the phytochemical compound 9,10-dihydro-3,6,7-trimethoxy-2,5-phenanthrenediol isolated from *C. collinum* leaves against *Candida albicans* using the microdilution assay with fluconazole as a positive control. The phytochemical compound exhibited activities against the tested pathogen with MIC value of 50.0 µg/ml (Katerere *et al.* 2012). Cock & Van Vuuren (2015) evaluated the antifungal activities of methanol and water extracts of *C. collinum* leaves against *Rhizopus stolonifera, Candida albicans* and *Aspergillus niger* using the disc diffusion assay. The extracts demonstrated activities against the tested pathogens exhibiting MIC values ranging from 141.0 µg/ml to 2873.0 µg/ml (Cock & Van Vuuren 2015). Nefai *et al.* (2022) evaluated the antifungal activities of n-butanol extracts of *C. collinum* stem bark against *Aspergillus niger* using the broth microdilution method. The extract demonstrated activities against the tested pathogen exhibiting MIC value of 15.7 mg/ml (Nefai *et al.* 2022).

Anti-inflammatory activities

Eloff *et al.* (2001) evaluated the anti-inflammatory activities of acetone extract of *C. collinum* leaves using the radiochemical cyclooxygenase bioassay against the sheep seminal vesicles. The extract demonstrated weak inhibition ranging from 42.0% to 51.0% of cyclooxygenase activity (Eloff *et al.* 2001). McGaw *et al.* (2001) evaluated the anti-inflammatory activities of acetone, water and ethyl acetate extracts of *C. collinum* leaves in an *in vitro* assay for cyclooxygenase inhibitors with indomethacin as a positive control. The extracts exhibited activities by showing cyclooxygenase inhibition ranging from 50.0% to 74.0% (McGaw *et al.* 2001). Marquardt *et al.* (2020) evaluated the *in vitro* anti-inflammatory activities of aqueous extract of *C. collinum* leaves and the phytochemical compound myricetin-3-O-rhamnoside isolated from the species in immortalized human keratinocytes (HaCaT) cells. The extract and myricetin-3-O-rhamnoside demonstrated anti-inflammatory activities (Marquardt *et al.* 2020).

Antioxidant activities

Masoko & Eloff (2007) evaluated the antioxidant activities of methanol and acetone extracts of *C. collinum* leaves using the 2,2-diphenyl-1-picryl hydrazyl (DPPH) free radical scavenging assay. The extract exhibited moderate antioxidant activities (Masoko & Eloff 2007). Marquardt *et al.* (2017) evaluated the antioxidant activities of ethanol extract of *C. collinum* leaves using the DPPH free radical scavenging assay with trolox as a positive control. The extract demonstrated activities exhibiting half maximal inhibitory concentration (IC_{50}) value of 14.0 µg/ml (Marquardt *et al.* 2017). Lall *et al.* (2019) evaluated the antioxidant activities of ethanol extract of *C. collinum* bark using the DPPH free radical scavenging assay with ascorbic acid as a positive control. The extract demonstrated activities exhibiting IC_{50} value of 1.1 µg/ml (Lall *et al.* 2019). Marquardt *et al.* (2020) evaluated the antioxidant activities of 50% ethanol extract of *C. collinum* leaves and the phytochemical compounds myricetin-3-O-rhamnoside and myricetin-3-O-glucoside isolated from the species using 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) and DPPH radical scavenging assays with trolox as a positive control. The extract and the phytochemical compounds demonstrated activities (Marquardt *et al.* 2020).

Antiplasmodial activities

Sanon *et al.* (2013) evaluated the antiplasmodial activities of dichloromethane, methanol:water extracts of *C. collinum* and alkaloids isolated from the species against chloroquine-resistant malaria strain K1 of *Plasmodium falciparum* using the *Plasmodium* lactacte dehydrogenase technique. The extract and the alkaloids demonstrated activities against the parasite exhibiting IC_{50} values ranging from 0.2 µg/ml to 2.1 µg/ml (Sanon *et al.* 2013). Ouattara *et al.* (2014) evaluated the antiplasmodial activities of chloromethylenic extract of *C. collinum* leaves and total alkaloids isolated from the species against

Plasmodium falciparum strain K1, which is resistant to chloroquine, pyrimethamine and proguanil using the fluorescence-based SYBR Green I assay. The extract and total alkaloids demonstrated activities and exhibited IC_{50} value of 4.0 µg/ml (Ouattara *et al.* 2014).

Antiproliferative activities

Fyhrquist *et al.* (2006) evaluated the antiproliferative activities of methanol extract of *C. collinum* roots against MCF 7 breast, T 24 (bladder carcinoma) and HeLa (cervical carcinoma) cancer cell lines using the Alamar Blue assay. The extract exhibited strong activities against MCF 7, T 24 and HeLa with inhibition percentage ranging from 63.3% to 77.9% (Fyhrquist *et al.* 2006). Ouattara *et al.* (2014) evaluated the antiproliferative activities of chloromethylenic extract of *C. collinum* leaves against human-derived hepatoma cell line HepG2 and Chinese hamster ovary (CHO) cells using the 3-[4,5-dimethylthyazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) assay. The extract demonstrated activities and exhibited median cytotoxic concentration (CC_{50}) values ranging from 25.0 µg/ml to 67.0 µg/ml (Ouattara *et al.* 2014).

Antityrosinase activities

Lall *et al.* (2019) evaluated the antityrosinase activities of ethanol extract of *C. collinum* bark using the mushroom tyrosinase enzyme with kojic acid as a positive control. The extract demonstrated activities exhibiting IC_{50} value of 47.9 µg/ml (Lall *et al.* 2019).

Cytotoxicity activities

Lall *et al.* (2019) evaluated the cytotoxicity activities of ethanol extract of *C. collinum* bark against the non-cancerous human keratinocyte (HaCat) cell line using the 2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxyanilide salt (XTT) method with actinomycin D as a positive control. The extract demonstrated activities exhibiting IC_{50} value of 153.0 µg/ml (Lall *et al.* 2019).

Larvicidal activities

Odda *et al.* (2008) evaluated the *in vivo* larvicidal activities of ethanol extract of *C. collinum* bark against the IV instar larvae of *Aedes aegypti* with neemazal F as a positive control. The extract demonstrated dose-dependent activities exhibiting median lethal concentration (LC_{50}) value of 0.05 mg/ml which was comparable to LC_{50} value of 0.08 mg/ml exhibited by the positive control (Odda *et al.* 2008).

Toxicity activities

Hassan *et al.* (2020) evaluated the acute and subchronic toxicity activities of methanol extract of *C. collinum* root in albino rats. The extract demonstrated median lethal dose (LD_{50}) value of 316.2 mg/kg (Hassan *et al.* 2020) and therefore, caution should be exercised when using the species extracts as traditional medicine as it is likely to be toxic at higher concentrations.

Conclusion

The current review provides a summary of the cultural, forage and medicinal uses of *C. collinum.* The ethnopharmacological interest in the species is reflected in the large numbers of recent publications focusing on its ethnomedicinal applications, phytochemical and pharmacological properties. The ethnomedicinal applications of the species are quite broad, ranging from cultural to usage against microbial infections such as sexually transmitted infections, wounds, respiratory infections and gastro-intestinal problems, and other ailments such as diabetes, malaria, epilepsy, jaundice, rheumatism, yellow fever, menstrual problems and skin diseases. *Combretum collinum* has become an important medicinal plant species in tropical Africa and the full potential of the species as a medicinal plant is yet to be explored. This wide application of *C. collinum* crude extracts require detailed pharmacological validation such as assessment of toxicity and safety, mechanisms of action *in vivo*, and clinical research of the species aimed at corroborating the ethnomedicinal applications of *C. collinum.* Future ethnopharmacological studies should also examine the combinational effects of *C. collinum* extracts with other plant species such as *C. molle, E. abyssinica, E. abyssinica, K. africana, P. reticulatus, S. pyroides, T. fassoglense, T. orientale* and *W. indica.*

Declarations

List of abbreviations: ABTS - 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid); CC_{50} - median cytotoxic concentration; CHO - Chinese hamster ovary cells; DPPH - 2,2-diphenyl-1-picryl hydrazyl; GI_{50} - median growth inhibition; HaCat - human keratinocyte; IC_{50} - half maximal inhibitory concentration; LC_{50} - median lethal concentration; LD_{50} - median lethal dose; MIC - minimum inhibition concentration; MTT - 3-[4,5-dimethylthyazol-2-yl]-2,5-diphenyltetrazolium bromide; XTT - 2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxyanilide salt

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