The leadwood tree (*Combretum imberbe* Wawra, family Combretaceae): Medicinal uses and ethnopharmacological properties

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Research

Abstract

Background: Combretum imberbe Wawra is a medium to large semi-deciduous tree widely used in traditional medicine in tropical Africa.

Aim: This study was aimed at reviewing the medicinal, phytochemical and pharmacological properties of *C. imberbe*.

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

Results: This study showed that the bark, leaves, roots, root bark and stems of *C. imberbe* are used as charm, anthelmintic, hair relaxant, toothpaste and as ethnoveterinary medicine. Different parts of the species are also used as traditional medicine against bilharzia, erectile dysfunction, fever, malaria, gastro-intestinal problems, infertility in women, pregnancy troubles, menstrual problems, neuralgia, respiratory infections, sexually transmitted infections, skin problems and toothache. Chemical compounds identified from *C. imberbe* include amino acids, flavonoids, polyphenolics, tannins and triterpenoids. The crude extracts of *C. imberbe* and phytochemical compounds isolated from the species exhibited antibacterial, antimycobacterial, antifungal, anti-inflammatory, antioxidant, anti-proliferative, antischistosomal and cytotoxicity activities.

Conclusion: To realize the full potential of *C. imberbe* as a valuable component of traditional pharmacopoeia in tropical Africa, future studies should focus on conducting detailed phytochemical, pharmacological and toxicological evaluations, *in vivo* and clinical research.

Keywords: bush willow family, Combretaceae, *Combretum imberbe*, *materia medica*, traditional medicine

Background

Combretaceae family consists of approximately 10 genera and 530 species which are mainly trees, shrubs, shrublets or lianas and rarely subherbaceous (Jordaan *et al.* 2011, Christenhusz & Byng 2016, Raj *et al.* 2022). Members of this family exhibit pantropical distribution with a few species extending to warm temperate regions, and recorded in coastal scrub, savanna, grassland, rainforest, woodland, littoral and mangrove vegetation (Gere *et al.* 2015, Turner 2020). The genus *Combretum* Loefl. is the type genus of the family Combretaceae, comprising approximately 140 species that have been recorded in tropical Africa with about 20 species endemic to Madagascar (Schmelzer & Gurib-Fakim 2013). The highest number of *Combretum* species occur in tropical Africa, and therefore, the centre of diversity of the genus is on the African continent (Stace 2007, 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, Venter & Venter 2015, 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, Venter & Venter 2015, Schmidt *et al.* 2017). The specific name "*imberbe*" is a Latin word meaning "beardless" in reference to the hairless leaves of the species (Palmer & Pitman 1972, Glen 2004). The common name of *C. imberbe* (Figure 1) is "leadwood", which is in reference to the heaviness of the wood (Venter & Venter 2015, Schmidt *et al.* 2017). The other common names of the species include "bastard yellow wood", "elephant trunk", "stone tree", "elephant tusk tree", "ironwood", "ivory tree" and "leadwood bush-willow" (Palmer & Pitman 1972, Palgrave 2002, Quattrocchi 2012, Van Wyk & Van Wyk 2013). The synonyms of *C. imberbe* are *Argyrodendron petersii* Klotzsch, *C. imberbe* Wawra var. *dielsii* Engl., *C. imberbe* Wawra var. *petersii* (Klotzsch) Engl. & Diels, *C. imberbe* Wawra var. *truncatum* (Welw. ex M.A.Lawson) Burtt Davy, *C. petersii* (Klotzsch) Engl. & Diels, *C. primigenum* Marloth ex Engl. and *C. truncatum* Welw. ex M.A.Lawson (Exell & Garcia 1970, Wickens 1973, Exell 1978, Germishuizen & Meyer, 2003, Figueiredo & Smith 2008, Mannheimer & Curtis 2009, Jongkind 2014, Burrows *et al.* 2018).

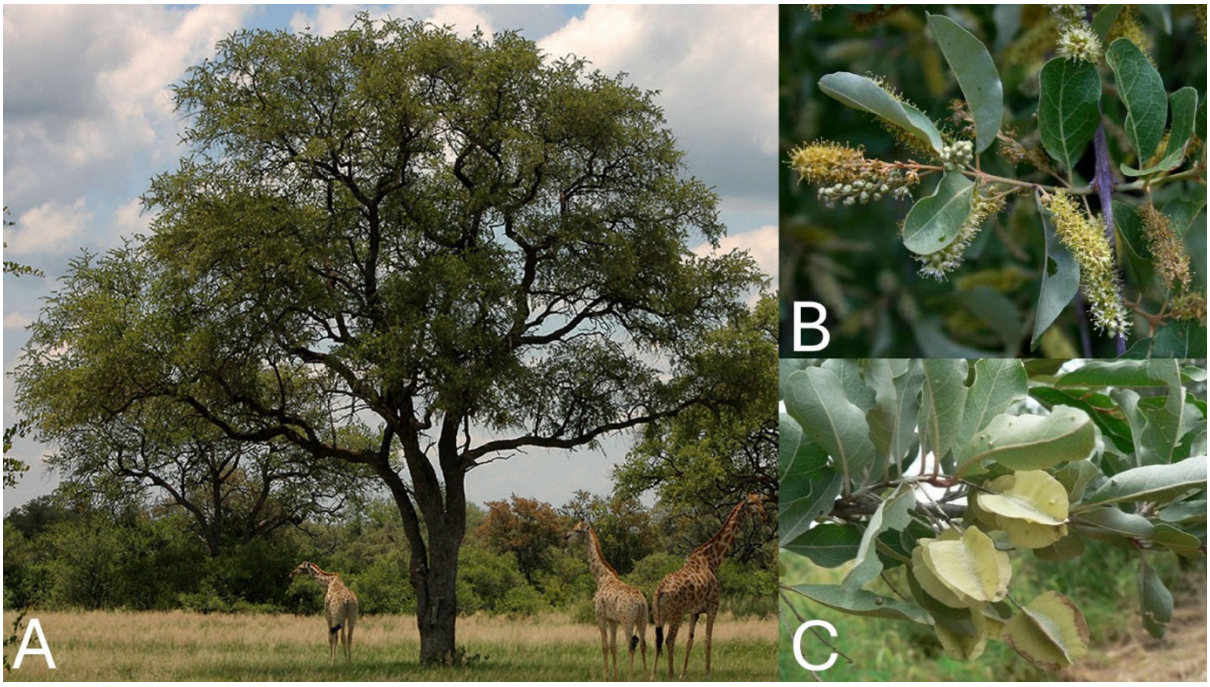

Figure 1. *Combretum imberbe*: A: entire plant showing general habit, B: branch showing leaves and flowers (photos: BT Wursten) and C: branch showing leaves and winged fruits (photo: Günter Baumann)

Combretum imberbe is a medium to large semi-deciduous tree reaching 21 metres in height (Palmer & Pitman 1972). The bole grows up to 122 cm in diameter (Palmer & Pitman 1972), usually straight, with pale grey fissured bark, which has deep furrows and transverse cracks and producing a mesh of closely packed rectangular flakes (Van Wyk & Van Wyk 2013). In terms of height and size of the bole, *C. imberbe* is the largest of all the *Combretum* species (Hermann *et al.* 2003, Mtsweni 2006), characterized by an open crown which is pyramidal in shape (Figure 1A). The young plants have opposite, stiff, horizontal, often spine-tipped shoots. The leaves are on short, opposite and often spine-tipped twigs. The leaves are simple (Figure 1B), hairless with minute silvery and occasionally brownish scales, arranged opposite to each other, obovate to oblong in shape, with round or bluntly pointed tips, the base narrowed and the margins untoothed but often waxy with hair-

like tips. The leaves are grey-green in colour above and distinctly paler beneath, giving *C. imberbe* a greyish appearance (Palgrave 2002). The petiole, inflorescence and flower buds are covered with rust-brown scales. The flowers are whitish or yellowish in colour, sweetly scented and appear with the new leaves in slender spikes, sometimes forming a terminal head or panicle. The fruit is small, winged (Figure 1C), roundish, densely covered with minute, silvery scales, characteristically green and pale yellowish when drying to pale straw-coloured when mature, giving the species a distinctive reddish appearance (Palgrave 2002). *Combretum imberbe* has been recorded in Angola, Botswana, Eswatini, Malawi, Mozambique, Namibia, South Africa, Tanzania, Zambia and Zimbabwe (Exell & Garcia 1970, Wickens 1973, Drummond 1975, Exell 1978, Germishuizen & Meyer 2003, Setshogo & Venter 2003, Mapaura & Timberlake 2004, Loffler & Loffler 2005, Setshogo 2005, Figueiredo & Smith 2008, Mannheimer & Curtis 2009, Jongkind 2014, Burrows *et al.* 2018) (Figure 2). *Combretum imberbe* has been recorded from low to medium altitudes in woodland, wooded grassland, mixed woodland, bushveld, along river channels, drainage lines, dry watercourses and in pans, damp alluvial soils and heavy clay soils at an altitude ranging from 185 m to 1650 m above sea level (Germishuizen & Meyer 2003). Although the conservation status of *C. imberbe* throughout its distributional range in tropical Africa (Figure 2) is of Least Concern based on IUCN Red List threat categories (Golding 2002, Raimondo *et al.* 2009), in South Africa, the species is one of the "protected trees" in the country in terms of the of the National Forests Act of 1998 (Act 84 of 1998) of South Africa, enacted in 2004. In terms of the National Forests Act of 1998, *C. imberbe* may not be cut, disturbed, damaged or destroyed and its products may not be possessed, collected, removed, transported, exported, donated, purchased or sold except under licence or permit granted by the Department of Water Affairs and Forestry (or a delegated authority) (Mtsweni 2006). It is against this background that the current study was undertaken aimed at reviewing the importance of *C. imberbe* in traditional medicine and its chemical and pharmacological properties.

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

Materials and Methods

A search for available information on the medicinal applications, phytochemical and pharmacological properties of *Combretum imberbe* was conducted by systematically searching the scientific databases such as SciELO, PubMed®,

ScienceDirect®, Google Scholar, Web of Science, SpringerLink® 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 July to December 2024 using the following keywords: "*Combretum imberbe*" and English common names "bastard yellow wood", "elephant trunk", "stone tree", "elephant tusk tree", "ironwood", "ivory tree" and "leadwood bush-willow". An additional search was also conducted using the keywords "biological activities of *Combretum imberbe*", "pharmacological properties of *Combretum imberbe*", "ethnobotany of *Combretum imberbe*", "medicinal uses of *Combretum imberbe*", "phytochemistry of *Combretum imberbe*" and "traditional uses of *Combretum imberbe*". The search covered publications from 1955 to 2024, a long period to capture literature on the medicinal properties, livelihood and commercial uses of *C. imberbe*.

Results and Discussion

Traditional uses of *Combretum imberbe*

The gum that exudes from damaged stems of *C. imberbe* is edible and traditionally formed the diet of the Bushmen or the San people, who are the members of the indigenous hunter-gatherer cultures of southern Africa (Mtsweni 2006, Van Wyk & Van Wyk 2013). *Combretum imberbe* is regarded as an indicator of good grazing areas and sweetveld (Venter & Venter 2015). *Combretum imberbe* is widely used throughout its distributional range as a source of building materials for houses, livestock enclosures, craft work, walking sticks, railway sleepers, sculptures, fencing posts, mine props, fuelwood, and its products sold to generate income for the household, particularly its durable heartwood which is used in the woodcarving industry (Williamson 1955, Cole & Brown 1976, Liengme 1981, 1983, Shackleton 1993, 1998, Mashabane *et al.* 2001, Venter & Venter 2015). The wood of *C. imberbe* is hard, heavy, strong and durable, the heartwood is dark brown to almost black in colour, suitable for turning, and making heavy, durable and indestructible furniture (Palgrave 2002, Van Wyk & Gericke 2018). Ornaments and sculptures are sometimes made from *C. imberbe* wood, and hoes were made from the species before metal became available (Palgrave 2002, Van Wyk & Gericke 2018). The stems of *C. imberbe* are commonly used as fencing posts, as wood borers and termites do not attack the wood (Venter & Venter 2015). *Combretum imberbe* is an important source of firewood throughout the distributional range of the species (Van Wyk & Gericke 2018). Its wood burns slowly and with intense heat, and therefore, used for brick burning (McGregor 1991). The wood of *C. imberbe* is often mixed with other firewood plant species such as *Colophospermum mopane* (J.Kirk ex Benth.) J.Léonard (family Fabaceae), *Combretum* species and *Grewia caffra* Meisn. (family Malvaceae) (Mashabane *et al.* 2001). In Malawi, *C. imberbe* is in high demand for firewood and charcoal production (Lemmens 2012). In South Africa, *C. imberbe* is usually used to supplement *C. mopane*, which is usually used as the main constituent of palisade fences (Mashabane *et al.* 2001). The wood ash from *C. imberbe* is used as toothpaste and as substitute for whitewash to decorate walls of houses (Palgrave 2002, Schmidt *et al.* 2017, Van Wyk & Gericke 2018). The trunks of *C. imberbe* are used to make traditional grain stamping mortars (Van Wyk & Gericke 2018). In Zambia, the white ash from *C. imberbe* is used as food flavouring agent and often mixed with *Tamarindus indica* L. (family Fabaceae) (Fowler 2002). *Combretum imberbe* is sometimes cultivated as an ornamental tree and making a fine shade tree (Lemmens 2012, Venter & Venter 2015) and the leaves are browsed by livestock and game (Palmer & Pitman 1972, Mtsweni 2006, Venter & Venter 2015). The root bark of *C. imberbe* is used for tanning leather (Venter & Venter 2015). *Combretum imberbe* is of considerable religious importance to the Herero and Ovambo people of Namibia as they never destroy the species believing that the trees are the ancestors of all their peoples (Palgrave 2002, Van Wyk & Van Wyk 2013). *Combretum imberbe* is long-lived, and some of the larger specimens are estimated to be well over 1000 years old (Vogel & Fuls 2005, Van Wyk & Van Wyk 2013).

Medicinal uses of *Combretum imberbe*

Several ethnobotanical and ethnopharmacological publications cite the uses of the bark, flowers, leaves, roots, root bark and stems of *C. imberbe* as charm, anthelmintic, hair relaxant, toothpaste and as ethnoveterinary medicine, and also as traditional medicine against bilharzia, erectile dysfunction, fever, malaria, gastro-intestinal problems, infertility in women, pregnancy troubles, menstrual problems, neuralgia, respiratory infections, sexually transmitted infections, skin problems and toothache (Table 1, Figure 3). In South Africa, *C. imberbe* is combined with *Sclerocarya birrea* (A.Rich.) Hochst. (Anacardiaceae family), *Diospyros lycioides* Desf. (Ebenaceae family) and *Combretum erythrophyllum* (Burch.) Sond. and used as remedy for infertility in women (Mabogo 1990, Hermann *et al.* 2003, Lemmens 2012, Silén *et al.* 2023). In South Africa, the roots of *C. imberbe* are mixed with those of *C. mopane* and *Combretum zeyheri* Sond. and used as traditional medicine for stomachache (Mashabane *et al.* 2001, Hermann *et al.* 2003). In Zimbabwe, the powdered leaves of *C. imberbe* are mixed with those of *Dysphania ambrosioides* (L.) Mosyakin & Clemants (Amaranthaceae family) and *Myrothamnus flabellifolius* Welw. (Myrothamnaceae family) and used to drive away bad spirits (Gelfand *et al.* 1985, Rogers & Verota 1996). *Combretum imberbe* 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.

Table 1. Medicinal uses of *Combretum imberbe.*

Medicinal use	Parts used	Country	Reference
Mono-therapeutic applications			
Anthelmintic	Leaf decoction taken orally	Botswana	Dude *et al.* 2022
Bilharzia	Root or root bark infusion taken orally	Mozambique, South Africa and Zimbabwe	Gelfand *et al.* 1985, Van den Eynden *et al.* 1992, Rogers & Verota 1996, Hermann *et al.* 2003, Mtsweni 2006, Cumes *et al.* 2009, Dan *et al.* 2010, Ribeiro *et al.* 2010, Dzomba *et al.* 2012, Lemmens 2012, Quattrocchi 2012, Venter & Venter 2015, Silén *et al.* 2023
Cultural and religious significance	Whole plant	Namibia	Palmer & Pitman 1972, Malan & Owen-Smith 1974, Palgrave 2002, Lemmens 2012, Quattrocchi 2012, Van Wyk & Van Wyk 2013
Erectile dysfunction	Bark, flower, leaf or root decoction taken orally	Mozambique and Namibia	Chinsembu *et al.* 2015, Nicosia et al. 2022
Fever and malaria	Root decoction taken orally	Eswatini and Namibia	Loffler & Loffler 2005, Long 2005, Dan *et al.* 2010, Dzomba *et al.* 2012, Silén *et al.* 2023
Gastro-intestinal problems (constipation, diarrhoea, dysentery and stomach problems)	Bark, flower, leaf, root or stem decoction taken orally or leaf decoction used as enema	Angola, Botswana, Mozambique, Namibia, South Africa and Zimbabwe	Gelfand *et al.* 1985, Van den Eynden *et al.* 1992, Chinemana *et al.* 1985, Rogers & Verota 1996, Hermann *et al.* 2003, Mathabe *et al.* 2006, Mtsweni 2006, Cumes *et al.* 2009, Dan *et al.* 2010, Ribeiro *et al.* 2010, Bruschi *et al.* 2011, Dzomba *et al.* 2012, Lemmens 2012, Quattrocchi 2012, Motlhanka & Nthoiwa 2013, Van Wyk *et al.* 2013, Magwenzi *et al.* 2014, Venter & Venter 2015, Urso *et al.* 2016, Nicosia et al. 2022, Richard *et al.* 2023, Silén *et al.* 2023
Hair relaxant	Boiled leaf ashes applied topically	Botswana	Heath & Heath 2009
Infertility in women and pregnancy troubles	Bark or root infusion taken orally	Angola, Mozambique, Namibia and South Africa	Cumes *et al.* 2009, Ribeiro *et al.* 2010, Lemmens 2012, Quattrocchi 2012, Van Wyk *et al.* 2013, Chinsembu *et al.* 2015, Urso *et al.* 2016, Silén *et al.* 2023
Menstrual problems	Root and stem infusion taken orally	South Africa	Tshikalange *et al.* 2016
Neuralgia	Root decoction taken orally	Zambia	Fowler 2002
Respiratory infections (chest pains, colds, cough and influenza)	Bark, flowers and leaves boiled, and fumes inhaled, leaf or powdered root decoction taken orally or leaf smoke inhaled	Botswana, Eswatini, Mozambique, Namibia and South Africa	Watt & Breyer-Brandwijk 1962, Palmer & Pitman 1972, Gelfand *et al.* 1985, Mabogo 1990, Van den Eynden *et al.* 1992, Rogers & Verota 1996, Hermann *et al.* 2003, Long 2005, Mtsweni 2006, Cumes *et al.* 2009, Heath & Heath 2009, Dan *et al.* 2010, Ribeiro *et al.* 2010, Lemmens 2012, Quattrocchi 2012, Van Wyk *et al.* 2013, Magwenzi *et al.* 2014, Venter & Venter 2015, Nicosia et al. 2022, Silén *et al.* 2023, Sitoe & Van Wyk 2024
Sexually transmitted infections	Leaf or root decoction taken orally	Botswana, Namibia, South	Chinsembu & Hedimbi 2010, Cheikhyoussef *et al.* 2011, Bhat 2013, Van Wyk *et al.* 2013;

(gonorrhoea and venereal diseases)		Africa and Zambia	Chinsembu 2016, Chinsembu *et al.* 2015, 2019, Richard *et al.* 2023, Silén *et al.* 2023
Skin diseases (injuries, leprosy, sores and wounds)	Bark, flower, leaf or root infusion applied topically	Mozambique and South Africa	Ribeiro *et al.* 2010, Lemmens 2012, Quattrocchi 2012, Van Wyk *et al.* 2013, Nicosia et al. 2022, Silén *et al.* 2023
Toothache	Root decoction applied topically	Zambia	Fowler 2002
Toothpaste	Ashes applied topically	Mozambique and South Africa	Palgrave 2002, Mtsweni 2006, Ribeiro *et al.* 2010, Lemmens 2012, Van Wyk & Van Wyk 2013, Schmidt *et al.* 2017, Van Wyk & Gericke 2018, Silén *et al.* 2023
Ethnoveterinary medicine			
Diarrhoea	Leaves and roots	Namibia	Eiki *et al.* 2022
Eye infections	Leaves and roots	Namibia	Eiki *et al.* 2022
Used in combination with other species			
Infertility	Combined with *Sclerocarya birrea* (A.Rich.) Hochst. (Anacardiaceae family), *Diospyros lycioides* Desf. (Ebenaceae family) and *Combretum erythrophyllum* (Burch.) Sond.	South Africa	Mabogo 1990, Hermann *et al.* 2003, Lemmens 2012, Silén *et al.* 2023
Stomachache	Roots are mixed with those of *C. mopane* and *Combretum zeyheri* Sond.	South Africa	Mashabane *et al.* 2001, Hermann *et al.* 2003
To drive away bad spirits	Powdered leaves mixed with those of *Dysphania ambrosioides* (L.) Mosyakin & Clemants (Amaranthaceae family) and *Myrothamnus flabellifolius* Welw. (Myrothamnaceae family)	Zimbabwe	Gelfand *et al.* 1985, Rogers & Verota 1996

Phytochemistry and pharmacological properties of *Combretum imberbe*

Qualitative and quantitative phytochemical analyses of *C. imberbe* leaves and roots revealed the presence of amino acids, flavonoids, polyphenolics, tannins and triterpenoids (Roggers 1988, Rogers & Subramony 1988, Katerere *et al.* 2003, Angeh *et al.* 2007, Anokwuru *et al.* 2022, Eiki *et al.* 2022) (Table 2). Some of the phytochemical compounds isolated from *C. imberbe* and its crude extracts exhibited antibacterial, antimycobacterial, antifungal, anti-inflammatory, antioxidant, anti-proliferative, antischistosomal and cytotoxicity activities

Antibacterial activities

Eloff (1999) evaluated the antibacterial activities of acetone extract of *C. imberbe* leaves against *Escherichia coli, Staphylococcus aureus, Enterococcus faecalis* and *Pseudomonas aeruginosa* 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.* (2003) evaluated the antibacterial activities of the phytochemical compounds 1α,3,β-hydroxyimberbic acid, 1α,3,β-hydroxyimberbic acid-23-O-α-ʟ-4-acetylrhamnopyranoside, 1α,3,β-hydroxyimberbic acid-23-O-α-ʟ-3,4-diacetyl-rhamnopyranoside and 1α,3,β-

hydroxyimberbic acid-23-α-[ʟ-3,4-diacetyl-rhamnopyranosyl]-29-O-α-rhamnopyranoside isolated from *C. imberbe* leaves against *Mycobacterium fortuitum, Staphylococcus aureus* and *Proteus vulgaris* using the microtitre dilution assay with streptomycin as a positive control. The phytochemical compounds exhibited activities against the tested pathogens with MIC values ranging from 1.56 µg/ml to >100.0 µg/ml (Katerere *et al.* 2003). Angeh *et al.* (2007) evaluated the antibacterial activities of the phytochemical compounds 1α,3β-dihydroxy-12-oleanen-29-oic, 1-hydroxy-12-olean-30-oic acid, 3,30-dihydroxyl-12-oleanen-22-one, 1,3,24-trihydroxyl-12-olean-29-oic acid and 1α,23-dihydroxy-12-oleanen-29-oic acid-3β-O-2,4-di-acetyl-l-rhamnopyranoside isolated from *C. imberbe* leaves against *Escherichia coli* and *Staphylococcus aureus* using the microplate serial dilution method with gentamycin as a positive control. The phytochemical compounds exhibited activities against the tested pathogens with MIC values ranging from 16.0 µg/ml to 62.0 µg/ml (Angeh *et al.* 2007). Anokwuru *et al.* (2021) evaluated the antibacterial activities of methanol extract of *C. imberbe* 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 extract exhibited activities against the tested pathogens with MIC values ranging from 0.09 mg/ml to 1.0 mg/ml (Anokwuru *et al.* 2021).

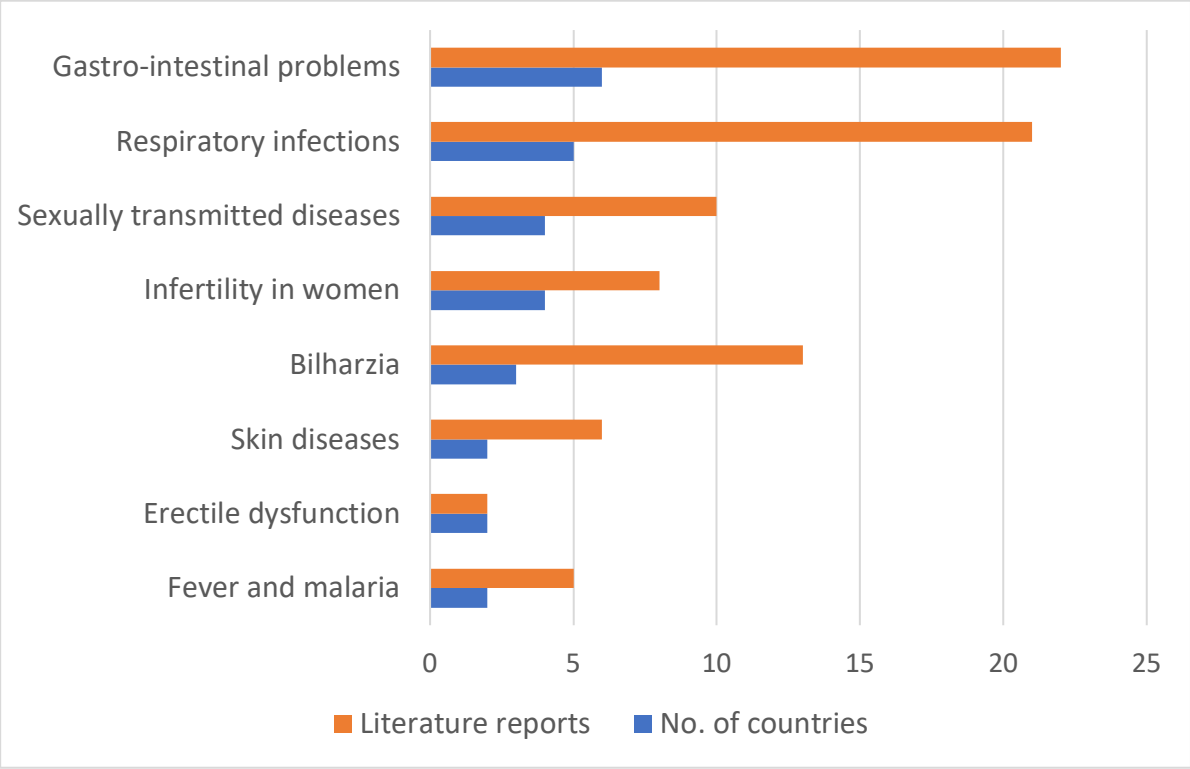

Figure 3. Main diseases and ailments treated and managed by *Combretum imberbe* in tropical Africa

Table 2. Phytochemical composition of *Combretum imberbe.*

Phytochemical compound	**Formula**	**Part**	**Reference**
1α,3β-hydroxyimberbic acid	$C_{30}H_{48}O_4$	Leaves	Katerere *et al.* 2003
1α,3β-hydroxyimberbic acid-23-O-α-ʟ-4-acetylrhamnopyranoside	$C_{38}H_{61}O_{10}$	Leaves	Katerere *et al.* 2003
1α,3β-hydroxyimberbic acid-23-O-α-ʟ-3,4-diacetyl-rhamnopyranoside	$C_{40}H_{62}O_{11}$	Leaves	Katerere *et al.* 2003
1α,3β-hydroxyimberbic acid-23-α-[ʟ-3,4-diacetyl-rhamnopyranosyl]-29-O-α-rhamnopyranoside	$C_{46}H_{72}O_{15}$	Leaves	Katerere *et al.* 2003
1-O-vanillin	$C_8H_8O_3$	Leaves and roots	Eiki *et al.* 2022
3,30-dihydroxyl-12-oleanen-22-one	$C_{30}H_{48}O_3$	Leaves	Angeh *et al.* 2007

4-hydroxy, 3-Methyl (3-Methylglutaconic acid)	$C_6H_{10}O_5$	Leaves and roots	Eiki *et al.* 2022
Caffeic acid	$C_9H_8O_4$	Leaves and roots	Eiki *et al.* 2022
Corilagin	$C_{27}H_{24}O_{18}$	Leaves and roots	Eiki *et al.* 2022
(-)-Epigallo (-)-epigallocatechin	$C_{22}H_{18}O_{11}$	Leaves and roots	Eiki *et al.* 2022
Gallic acid	$C_7H_6O_5$	Leaves and roots	Eiki *et al.* 2022
Gentesic acid	$C_7H_6O_4$	Leaves and roots	Eiki *et al.* 2022
β-Glucan	$C_{18}H_{32}O_{16}$	Leaves and roots	Eiki *et al.* 2022
Imberbic acid	$C_{30}H_{48}O_4$	Leaves	Roggers 1988, Rogers & Subramony 1988, Katerere *et al.* 2003, Anokwuru *et al.* 2022
Methylisothiazolinone	C_4H_5NOS	Leaves and roots	Eiki *et al.* 2022
Pantoprazole sodium	$C_{16}H_{14}F_2N_3NaO_4S$	Leaves and roots	Eiki *et al.* 2022
Pedunculin	$C_{18}H_{16}O_7$	Leaves and roots	Eiki *et al.* 2022
Pedunculagin	$C_{34}H_{24}O_{22}$	Leaves and roots	Eiki *et al.* 2022
Piscidic acid	$C_{11}H_{12}O_7$	Leaves and roots	Eiki *et al.* 2022
Punicalin	$C_{34}H_{22}O_{22}$	Leaves and roots	Eiki *et al.* 2022
alpha-D-Rhap-(1->3)-alpha-D-Rhap	$C_{18}H_{32}O_{13}$	Leaves and roots	Eiki *et al.* 2022
Stizolobat	$C_9H_9NO_6$	Leaves and roots	Eiki *et al.* 2022
Tachioside	$C_{13}H_{18}O_8$	Leaves and roots	Eiki *et al.* 2022
Theogallin	$C_{14}H_{16}O_{10}$	Leaves and roots	Eiki *et al.* 2022
L-Tryptophan	$C_{11}H_{12}N_2O_2$	Leaves and roots	Eiki *et al.* 2022
Ursolic acid	$C_{30}H_{48}O_3$	Leaves	Anokwuru *et al.* 2022

Antimycobacterial activities

Magwenzi *et al.* (2014) evaluated the antimycobacterial activities of ethanol extract of *C. imberbe* leaves against *Mycobacterium smegmatis* using the broth microdilution assay with rifampicin as a positive control. The extract exhibited activities with MIC value of 125.0 µg/ml (Magwenzi *et al.* 2014). Raidron *et al.* (2022) evaluated the antimycobacterial activities of organic extract of *C. imberbe* stem bark and twigs against the Mycobacterium tuberculosis H37Rv-GFP strain using the broth microdilution assay with rifampicin as a positive control. The extract exhibited activities against the tested pathogen with MIC values ranging from 47.2 µg/ml to 125.0 µg/ml (Raidron *et al.* 2022).

Antifungal activities

Masoko *et al.* (2007) evaluated the antifungal activities of hexane, acetone, methanol and dichloromethane extracts of *C. imberbe* 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 0.04 mg/ml to >2.5 mg/ml (Masoko *et al.* 2007). Masoko *et al.* (2010) evaluated the *in vivo* antifungal activities of acetone extract of *C. imberbe* leaves against *Sporothrix schenckii, Candida albicans, Microsporum canis* and *Cryptococcus neoformans* on wounds of immunocompromised Wistar rats. The extracts exhibited activities against the tested pathogens exhibiting MIC values ranging from 0.04 mg/ml to 2.5 mg/ml (Masoko *et al.* 2010). Mangoyi *et al.* (2012) evaluated the antifungal activities of ethanol extract of *C. imberbe* leaves against *Candida albicans* and *Candida krusei* using the broth dilution method with miconazole as a positive control. The extract exhibited activities against the tested pathogens with MIC values ranging from 0.31 mg/ml to 0.63 mg/ml (Mangoyi *et al.* 2012).

Anti-inflammatory activities

Eloff *et al.* (2001) evaluated the anti-inflammatory activities of acetone extract of *C. imberbe* leaves using the radiochemical cyclooxygenase bioassay against the sheep seminal vesicles. The extract demonstrated 89.0% inhibition of cyclooxygenase activity (Eloff *et al.* 2001). McGaw *et al.* (2001) evaluated the anti-inflammatory activities of acetone and ethyl acetate extracts of *C. imberbe* leaves in an *in vitro* assay for cyclooxygenase inhibitors with indomethacin as a positive control. The extract exhibited activities by showing inhibition ranging from 91.0% to 92.0% (McGaw *et al.* 2001). Angeh *et al.* (2007) evaluated the anti-inflammatory activities of the phytochemical compounds 1α,3β-dihydroxy-12-oleanen-29-oic and 1α,23-dihydroxy-12-oleanen-29-oic acid-3β-O-2,4-di-acetyl-l-rhamnopyranoside isolated from *C. imberbe* leaves by assessing the inhibition of 3α-hydroxysteroid dehydrogenase from the rat liver cytosol. The phytochemical compounds showed very strong inhibition of 3α-hydroxysteroid dehydrogenase with half maximal inhibitory concentration (IC_{50}) value of 0.3 µg/ml (Angeh *et al.* 2007).

Antioxidant activities

Masoko & Eloff (2007) evaluated the antioxidant activities of acetone and methanol extracts of *C. imberbe* leaves using 2,2-diphenyl-1-picryl hydrazyl (DPPH) free radical scavenging assay. The extract exhibited moderate antioxidant activities (Masoko & Eloff 2007).

Anti-proliferative activities

Angeh *et al.* (2007) evaluated the anti-proliferative activities of the phytochemical compounds 1α,3β-dihydroxy-12-oleanen-29-oic, 3,30-dihydroxyl-12-oleanen-22-one and 1α,23-dihydroxy-12-oleanen-29-oic acid-3β-O-2,4-di-acetyl-l-rhamnopyranoside isolated from *C. imberbe* leaves by assaying these on K-562 (DSM ACC 10) and L-929 (DSM ACC 2) cell lines. The phytochemical compounds showed anti-proliferative activities by exhibiting median growth inhibition (GI_{50}) values ranging from 8.7 µg/ml to 32.9 µg/ml (Angeh *et al.* 2007).

Antischistosomal activities

McGaw *et al.* (2001) evaluated the antischistosomal activities of water extract of *C. imberbe* leaves against schistosomules of the species *Schistosoma haematobium* with praziquantel as a positive control. The extracts exhibited activities at a MIC value of 12.5 mg/ml (McGaw *et al.* 2001).

Cytotoxicity activities

Angeh *et al.* (2007) evaluated the cytotoxicity activities of the phytochemical compounds 1α,3β-dihydroxy-12-oleanen-29-oic, 3,30-dihydroxyl-12-oleanen-22-one, 1,3,24-trihydroxyl-12-olean-29-oic acid and 1α,23-dihydroxy-12-oleanen-29-oic acid-3β-O-2,4-di-acetyl-l-rhamnopyranoside isolated from *C. imberbe* leaves by assaying these against HeLa (DSM ACC 57). The phytochemical compounds showed cytotoxicity activities by exhibiting median cytotoxic concentration (CC_{50}) values ranging from 10.5 µg/ml to 47.3 µg/ml (Angeh *et al.* 2007).

Conclusion

As outlined in the present review, *C. imberbe* is characterized by important and diverse traditional uses, phytochemical and pharmacological properties. To realize the full potential of *C. imberbe* as a medicinal plant species, there is need for detailed evaluations of phytochemical, pharmacological and toxicological properties of the species. Future studies should also focus on assessing safety, mechanisms of action of the species extracts and its phytochemical compounds *in vivo* and clinical research aimed at corroborating the traditional medical applications of *C. imberbe*. Such extensive research can make a valuable contribution to growing knowledge about *C. imberbe* and its active ingredients.

Declarations

List of abbreviations: CC_{50} - median cytotoxic concentration; DPPH - 2,2-diphenyl-1-picryl hydrazyl; GI_{50} - median growth inhibition; IC_{50} - half maximal inhibitory concentration; MIC - minimum inhibition concentration

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