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Review Article

Ethnomedicinal Applications, Phytochemical Constituents and Pharmacological Activities of *Combretum zeyheri* Sond

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Abstract

Combretum zeyheri Sond. has several ethnomedicinal applications in tropical Africa, some of them known since prehistoric times. The current study reviewed the ethnomedicinal applications, phytochemical and pharmacological properties of *C. zeyheri*. A search for literature on the ethnomedicinal applications, phytochemical and pharmacological properties of *C. zeyheri* was conducted by systematically searching the scientific databases such as PubMed®, ScienceDirect®, Web of Science, Google Scholar, SpringerLink®, SciELO and Scopus®, as well as pre-electronic literature sources such as book chapters, books and other scientific publications obtained from the university library. This study showed that the bark, leaves, roots and root bark of *C. zeyheri* are used as ethnoveterinary medicine and as traditional medicine against menstrual problems, bleeding nose, infertility in women, sores, wounds, skin infections, eye problems, respiratory infections and gastrointestinal problems. The phytochemical assessment of *C. zeyheri* revealed that it contains phospholipids, fatty acid amides, glycosides, flavonoids, cholesterol, amines, amino acids, phenols, alcohols, triterpenoids and alkaloids. Ethnopharmacological assessments showed that the crude extracts and phytochemical compounds isolated from the species have anticholinesterase inhibition, antibacterial, antimycobacterial, antifungal, anti-inflammatory, antioxidant, antitrypanosomally and cytotoxicity activities. The ethnopharmacological properties of *C. zeyheri* documented in this review will assist in understanding the therapeutic relevance and potential of the species in the discovery of novel plant-based health products required to manage both animal and human health-related ailments or diseases.

Key words: Bush willow, combretaceae, *Combretum zeyheri*, indigenous knowledge, *materia medica*

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Combretum zeyheri Sond. (Fig. 1) is a member of the Combretaceae family, commonly known as the white mangrove, Indian almond or bush willow family. *Combretum zeyheri* is a multipurpose species widely used as ethnoveterinary medicine throughout its distributional range in tropical Africa¹⁻³. In Namibia and South Africa, the leaf decoction of *C. zeyheri* is usually instilled into the inflamed eyes of cattle and sheep or sometimes rubbed around the eyes of the animals as an ointment for inflamed eyes⁴. In Zimbabwe, the bark, leaf or root decoction of *C. zeyheri* is used as ethnoveterinary medicine against constipation, diarrhea, fertility problems and intestinal worm infestations⁵. *Combretum zeyheri* is also a valuable medicinal plant species used by the majority of the cultural groups in South Africa and the species has been incorporated into the traditional *materia medica* of this country^{6,7}. *Combretum zeyheri* is therefore included in two South African encyclopedias, namely, "Medicinal and magical plants of Southern Africa: An Annotated Checklist"⁸ and "medicinal plants of South Africa"⁹. These two monographs document the botanical descriptions of medicinal plants included in South African *materia medica*, the plant parts used, medicinal applications, preparation, dosage, active ingredients and pharmacological properties of the species^{8,9}. *Combretum zeyheri* is also an important fodder species in tropical Africa, with its bark, leaves, fruits and shoots being palatable and browsed by livestock and game, particularly during the dry periods, with protein content ranging from 11.3% to 16.5%¹⁰. *Combretum zeyheri* is an attractive shrub or tree which is popular as an ornamental and/or shade plant in private gardens,

tolerating frost and moderate drought and also cultivated to fill large open spaces¹⁰. The gum that exudes from damaged stems of *C. zeyheri* is edible and its roots are used to weave baskets, funnel-shaped fishing traps, initiation necklaces and wedding bands¹¹. In Zambia, the long roots of *C. zeyheri* are used to thrash and loosen the edible part of crop grains¹² and honeybees often collect nectar and pollen from *C. zeyheri*¹¹. The leaves of *C. zeyheri* produce a yellow dye which is used to dye cloth and the species is also of considerable religious importance³. *Combretum zeyheri* wood is considered to be one of the most important and best quality firewood as it burns slowly with intense heat, little smoke and makes good charcoals¹³. The wood of *C. zeyheri* is yellow, hard, heavy, strong, compact and termite and borer-proof and makes a useful general-purpose timber¹⁴. Therefore, *C. zeyheri* is widely used throughout its distributional range as a source of building materials for houses, livestock enclosures, fencing posts and handles of agricultural implements¹⁰. The presence of extensive stands of *C. zeyheri* is regarded as an indicator of sourveld by the cattle farmers¹⁰. Therefore, this article reviews the importance of *C. zeyheri* in ethnomedicine with a holistic approach that includes its botany, chemical constituents, as well as its pharmacological properties.

MATERIALS AND METHODS

A search for available information on the ethnobotanical uses, chemical constituents and nutritional properties of *Combretum zeyheri* was conducted by systematically searching the scientific databases such as PubMed®, ScienceDirect®, Web of Science, Google Scholar, SpringerLink®, SciELO and Scopus®, as well as pre-electronic



Fig. 1(a-b): *Combretum zeyheri*, (a) Entire plant in fruit and (b) Branch showing leaves and fruits

(Photos from the database Global Biodiversity Information Facility (GBIF) taken by A Pieter (<https://www.gbif.org/species/3698630>, retrieved on 19 March, 2025)

literature sources such as book chapters, books and other scientific publications obtained from the university library. The search was conducted from July, 2024 to January, 2025 using the following keywords: "*Combretum zeyheri*", "Biological activities of *Combretum zeyheri*", "Pharmacological properties of *Combretum zeyheri*", "Ethnobotany of *Combretum zeyheri*", "Medicinal uses of *Combretum zeyheri*", "Ethnoveterinary medicine applications of *Combretum zeyheri*", "Phytochemistry of *Combretum zeyheri*" and "Traditional uses of *Combretum zeyheri*". The search covered publications from 1962 to 2024, a long period to capture literature on the medicinal, ethnoveterinary medicine applications, phytochemical and pharmacological properties of *C. zeyheri*.

Botanical description of *Combretum zeyheri*: 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), who used it in reference to an unknown plant^{10,11,15}. The name was also reused by the Swedish botanist Pehr Löfving (31 January, 1729 - 22 February, 1756) for the *Combretum* genus^{10,11,15}. The specific name "*zeyheri*" is in honor of Karl Ludwig Philipp Zeyher (2 August, 1999 to 13 December, 1958), a German botanist and insect collector, who collected the type specimen of *C. zeyheri* in Magaliesberg in South Africa in 1835¹¹. The common name 'bush willow' indicates a superficial resemblance of the species to willows, that is, species belonging to the genus *Salix* L. (family Salicaceae), but "bush willows" and "willows" are not closely related to each other¹¹. Other common names of the species include "large-fruited bush willow", "large-fruited combretum" and "Zeyher's bush willow"^{11,14}. The synonyms of *C. zeyheri* Sond. include *C. antunesii* Engl. and Diels, *C. braggae* Engl., *C. calocarpum* Gilg ex Suess., *C. dilembense* De Wild., *C. glandulosum* F. Hoffm., *C. lopolense* Engl. and Diels, *C. megalocarpum* Brenan, *C. oblongum* F. Hoffm., *C. odontopetalum* Engl. and Diels, *C. platycarpum* Engl. and Diels, *C. rupicola* Engl. and Diels, *C. sankisiense* De Wild., *C. sinuatipetalum* De Wild., *C. teuszii* Engl. and Diels, *C. tinctorum* Welw. ex M.A. Lawson and *C. zeyheri* Sond. var. *seineri* Engl.¹⁶⁻¹⁹

Combretum zeyheri is a small to medium-sized deciduous tree reaching 10 m height, often spreading with a single or several stems^{11,14} (Fig. 1a). The bark of young trees is grey-brown, fairly smooth but later becomes rough and mottled, sometimes peeling in small flakes and branchlets with minute whitish hairs. The leaves

are simple, usually opposite or sometimes in whorls, elliptic to oblong in shape, young leaves covered with soft hairs, but when mature, almost hairless and leathery. The leaf apex and base are broadly tapering to rounded with entire margins, often waxy, light to medium dull green above and yellowish green below, with principal lateral veins raised below. The flowers are small, yellowish-green in colour, which occur in axillary spikes and appear before or with the formation of new leaves. The fruits are large, winged, pale green in colour when young, drying to pale brown or straw-colored (Fig. 1b), conspicuous, remaining on the tree until the leaves have fallen¹⁴. *Combretum zeyheri* has been recorded in Angola, Botswana, the Democratic Republic of Congo (DRC), Eswatini, Kenya, Malawi, Mozambique, Namibia, South Africa, Tanzania, Zambia and Zimbabwe (Fig. 2). *Combretum zeyheri* has been recorded from low to higher altitudes in woodland, wooded grassland, bushveld and common on serpentine-derived soils, rocky hillsides, sometimes along rivers and stream and tolerating a wide range of soils. *Combretum zeyheri* has been recorded on poor, sandy, gravelly soils, acidic soils, sandy dunes and often on stony hill slopes at an altitude ranging from 45 m to 1600 m above sea level¹⁶.

Ethnomedicinal applications of *Combretum zeyheri*:

Combretum zeyheri is used as a source of traditional medicines in Angola, South Africa, Namibia, Tanzania, Eswatini, Zambia, Mozambique and Zimbabwe, 57.1% of the countries where the species is indigenous (Table 1). In South Africa, the leaves, roots and stem bark of *C. zeyheri* are sold in informal herbal medicine markets as sources of traditional medicines²⁰. The traditional medicines prepared from the bark, leaves, roots and root bark decoction or infusion of *C. zeyheri* are used to treat and manage 55 human diseases and ailments (Table 1). The main ailments and diseases treated by *C. zeyheri* extracts (Fig. 3) include the use of bark, leaf, root or root bark extracts as embrocation's, poison antidote and traditional medicine against hemorrhoids, toothache, body pains, bleeding nose, menstrual problems, infertility, skin infections, sores and wounds, eye problems, respiratory infections and gastro-intestinal problems. In Namibia, the leaves or roots of *C. zeyheri* are combined with those of *Ochna pulchra* Hook. (Ochnaceae family), alternatively, the leaves or roots are mixed with those of *Burkea africana* Hook. (Fabaceae family), *Diospyros chamaethamnus* Mildbr. (Ebenaceae family) and *O. pulchra* and taken orally as remedy for malaria²¹. In Zambia, the leaves and stems of *C. zeyheri* are mixed with roots of *Manihot esculenta* Crantz (Euphorbiaceae family) and applied topically as remedy for smallpox^{14,22}.



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

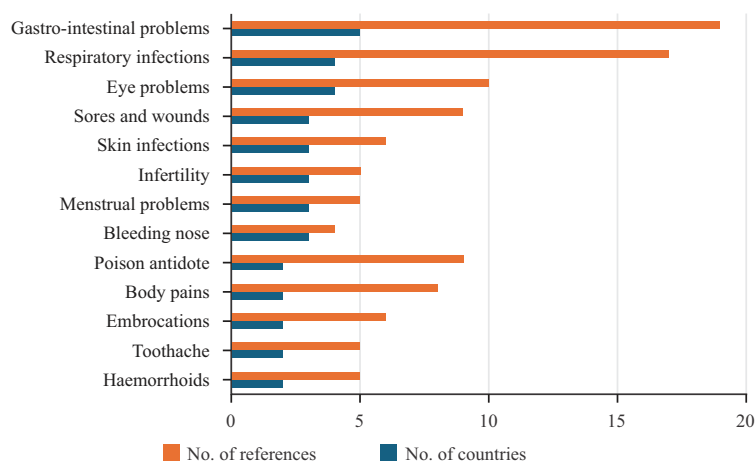


Fig. 3: Main diseases and ailments treated and managed using *Combretum zeyheri* extracts

Table 1: Medicinal uses of *Combretum zeyheri*

Medicinal use	Parts used	Country	Reference
Mono-therapeutic applications			
Anaemia	Bark, leaf or root infusion taken orally	Tanzania	Augustino <i>et al.</i> ²³ and Moura <i>et al.</i> ²⁴
Anal eczema	Bark, leaf or root decoction applied topically	Tanzania	Augustino <i>et al.</i> ²³ and Moura <i>et al.</i> ²⁴
Baby delivery	Root infusion taken orally	Tanzania	Moura <i>et al.</i> ²⁴ and Luoga <i>et al.</i> ²⁵
Bilharzia	Bark, leaf or root infusion taken orally	Tanzania	Quattrocchi ¹³ , Silén <i>et al.</i> ²² , Hedberg <i>et al.</i> ²⁶ , Fyhrquist <i>et al.</i> ²⁷ and Kokwaro ²⁸
Bleeding nose (epistaxis)	Root powder sniffed	Eswatini, South Africa and Zimbabwe	Venter and Venter ¹⁰ , Palgrave ¹⁴ , Silén <i>et al.</i> ²² and Gelfand <i>et al.</i> ²⁹
Body pains (backache and neck pains)	Bark, leaf or root decoction applied topically	South Africa and Tanzania	Quattrocchi ¹³ , Venter and Venter ¹⁰ , Palgrave ¹⁴ , Augustino <i>et al.</i> ²³ , Moura <i>et al.</i> ²⁴ , Hedberg <i>et al.</i> ²⁶ , Fyhrquist <i>et al.</i> ²⁷ and Kokwaro ²⁸
Cancer	Leaf or root infusion taken orally	Tanzania	Moura <i>et al.</i> ²⁴ and Fyhrquist <i>et al.</i> ²⁷
Cleanse blood	Bark infusion taken orally	South Africa	Grace <i>et al.</i> ³¹
Colic	Leaf decoction taken orally	South Africa	Quattrocchi ¹³
Dilated veins around the umbilicus (caput medusae)	Root infusion taken orally	Zimbabwe	Gelfand <i>et al.</i> ²⁹
Earache	Root infusion dropped into the ear	South Africa and Zambia	Gelfand <i>et al.</i> ²⁹
Embrocation's	Crushed leaves applied topically	South Africa and Zambia	Watt and Breyer-Brandwijk ⁶ , Hutchings <i>et al.</i> ⁷ , Venter and Venter ¹⁰ , Palgrave ¹⁴ , Gelfand <i>et al.</i> ²⁹ and Magwenzi <i>et al.</i> ³²
Eye problems	Leaf, powdered bark or root decoction applied topically	Angola, Mozambique, South Africa and Zambia	Watt and Breyer-Brandwijk ⁶ , Hutchings <i>et al.</i> ⁷ , Venter and Venter ¹⁰ , Palgrave ¹⁴ , Silén <i>et al.</i> ²² , Moura <i>et al.</i> ²⁴ , Gelfand <i>et al.</i> ²⁹ , Magwenzi <i>et al.</i> ³² , Ribeiro <i>et al.</i> ³³ and Siteo and van Wyk ³⁴
Gallstones	Bark decoction taken orally	South Africa	Hutchings <i>et al.</i> ⁷ , Venter and Venter ¹⁰ , Schmidt <i>et al.</i> ¹⁵ , Grace <i>et al.</i> ³¹
Gastrointestinal diseases (abdominal disorder, abdominal ulcers, diarrhea, dysentery and stomachache)	Bark, leaf or root decoction or infusion taken orally	Mozambique, South Africa, Tanzania, Zambia and Zimbabwe	Quattrocchi ¹³ , Watt and Breyer-Brandwijk ⁶ , Hutchings <i>et al.</i> ⁷ , van Wyk <i>et al.</i> ³⁵ , Fowler ¹² , Schmidt <i>et al.</i> ¹⁵ , Silén <i>et al.</i> ²² , Augustino <i>et al.</i> ²³ , Moura <i>et al.</i> ²⁴ , Hedberg <i>et al.</i> ²⁶ , Fyhrquist <i>et al.</i> ²⁷ , Siteo and van Wyk ³⁴ , Masoko and Eloff ³⁵ , Nicosia <i>et al.</i> ³⁶ and Shopo <i>et al.</i> ³⁷
Kokwaro <i>et al.</i> ²⁸ , Gelfand <i>et al.</i> ²⁹ , Fyhrquist <i>et al.</i> ²⁷ , Magwenzi <i>et al.</i> ³²			
Hemoptysis (vomiting blood)	Root infusion taken orally	Zimbabwe	Quattrocchi ¹³ and Gelfand <i>et al.</i> ²⁹
Hemorrhoids	Bark, leaf or root decoction taken orally	South Africa and Tanzania	Venter and Venter ¹⁰ , Palgrave ¹⁴ , Silén <i>et al.</i> ²² , Augustino <i>et al.</i> ²³ and Moura <i>et al.</i> ²⁴
Headache	Leaf or root decoction taken orally	South Africa	Palgrave ¹⁴ , Semenya and Maroyi ³⁸ , Semenya and Maroyi ³⁹ and Semenya and Maroyi ⁴⁰
Hernia	Root infusion taken orally	Tanzania	Moura <i>et al.</i> ²⁴ and Luoga <i>et al.</i> ²⁵
Infertility	Bark, leaf or root decoction taken orally	South Africa, Tanzania and Zimbabwe	van Wyk <i>et al.</i> ³⁵ , Augustino <i>et al.</i> ²³ , Moura <i>et al.</i> ²⁴ , Gelfand <i>et al.</i> ²⁹ Kacholi <i>et al.</i> ⁴¹
Kidney pains	Root powder taken orally	South Africa and Zimbabwe	Venter and Venter ¹⁰ and Gelfand <i>et al.</i> ²⁹
Lack of appetite	Root infusion taken orally	South Africa	Semenya and Maroyi ³⁹ and Semenya and Maroyi ⁴²
Malaria	Leaf or root decoction taken orally	Not specified	Quattrocchi ¹³

Table 1: Continue

Medicinal use	Parts used	Country	Reference
Menstrual problems	Powdered bark decoction taken orally	Angola, South Africa and Zambia	Watt and Breyer-Brandwijk ⁶ , Hutchings <i>et al.</i> ⁷ , Schmidt <i>et al.</i> ¹⁵ , Gelfand <i>et al.</i> ²⁹ and Magwenzi <i>et al.</i> ³²
Nausea	Bark, leaf or root decoction taken orally	Mozambique	Quattrocchi ³ and Nicosia <i>et al.</i> ³⁶
Poison antidote, scorpion and snake bite	Bark, leaf or root decoction applied topically	Mozambique and Tanzania	Quattrocchi ³ , Watt and Breyer-Brandwijk ⁶ , Silén <i>et al.</i> ²² , Augustino <i>et al.</i> ²³ , Moura <i>et al.</i> ²⁴ , Gelfand <i>et al.</i> ²⁹ , Magwenzi <i>et al.</i> ³² , Nicosia <i>et al.</i> ³⁶ , Mogha <i>et al.</i> ⁴³
Purgative	Bark infusion taken orally	South Africa	Grace <i>et al.</i> ³¹
Rectal prolapse	Bark, leaf or root decoction used as an enema	Tanzania	Augustino <i>et al.</i> ²³ and Moura <i>et al.</i> ²⁴
Respiratory infections (colds, cough, influenza, pneumonia and sore throat)	Bark, leaf, root or root bark decoction or infusion taken orally	Angola, Mozambique, South Africa and Tanzania	Quattrocchi ³ , van Wyk <i>et al.</i> ⁹ , Silén <i>et al.</i> ²² , Augustino <i>et al.</i> ²³ , Moura <i>et al.</i> ²⁴ , Hedberg <i>et al.</i> ²⁶ , Fyhrquist <i>et al.</i> ²⁷ , Kokwaro <i>et al.</i> ²⁸ , Gelfand <i>et al.</i> ²⁹ , Magwenzi <i>et al.</i> ³² , Masoko and Eloff ³⁵ , Nicosia <i>et al.</i> ³⁶ , Semenya and Maroyi ³⁸ , Semenya and Maroyi ³⁹ , Semenya and Maroyi ⁴⁰ , Semenya and Maroyi ⁴⁴ and Tchamba <i>et al.</i> ⁴⁵
Rheumatism	Bark, leaf or root decoction applied topically	Tanzania	Quattrocchi ³ , Hedberg <i>et al.</i> ²⁶ , Fyhrquist <i>et al.</i> ²⁷ , Kokwaro <i>et al.</i> ²⁸
Rituals	Bark, leaves or roots	Tanzania	Augustino <i>et al.</i> ²³
Sexually transmitted infections (gonorrhea, syphilis and venereal diseases)	Leaf decoction taken orally	South Africa	Quattrocchi ³ and van Wyk <i>et al.</i> ⁹
Skin infections (burns, candidiasis, leprosy and smallpox)	Leaf ointment applied topically	Namibia, South Africa and Zimbabwe	Quattrocchi ³ , Moura <i>et al.</i> ²⁴ , Gelfand <i>et al.</i> ²⁹ , Grace <i>et al.</i> ³¹ , Masoko and Eloff ³⁵ and Chinemana <i>et al.</i> ⁴⁶
Sores and wounds	Bark, leaf or root decoction applied topically	South Africa, Tanzania and Zimbabwe	Quattrocchi ³ , van Wyk <i>et al.</i> ⁹ , Silén <i>et al.</i> ²² , Augustino <i>et al.</i> ²³ , Moura <i>et al.</i> ²⁴ , Hedberg <i>et al.</i> ²⁶ , Fyhrquist <i>et al.</i> ²⁷ , Kokwaro <i>et al.</i> ²⁸ , Chinemana <i>et al.</i> ⁴⁶
Toothache	Bark, leaf or root decoction taken orally	Mozambique and Tanzania	Silén <i>et al.</i> ²² , Kokwaro <i>et al.</i> ²⁸ , Gelfand <i>et al.</i> ²⁹ , Magwenzi <i>et al.</i> ³² and Nicosia <i>et al.</i> ³⁶
Used in combination with other species			
Malaria	Leaves or roots mixed with <i>Ochna pulchra</i> Hook. (Ochnaceae family) and taken orally	Namibia	du Preez <i>et al.</i> ²¹
Malaria	Leaves or roots mixed with those of <i>Burkea africana</i> Hook. (Fabaceae family), <i>Diospyros chamaethamnus</i> Mildbr. (Ebenaceae family) and <i>O. pulchra</i> (Ebenaceae family) and roots of <i>Manihot esculenta</i> Crantz (Euphorbiaceae family) and applied topically	Namibia	du Preez <i>et al.</i> ²¹
Smallpox		Zambia	Palgrave ¹⁴ and Silén <i>et al.</i> ²²

Table 2: Phytochemical compounds identified from *Combretum zeyheri*

Phytochemical compound	Formula	Part	Reference
1-piperidinecarboxaldehyde	C ₈ H ₁₁ NO	Leaves	Manyawi <i>et al.</i> ⁴⁷
2α,3β-dihydroxyurs-12-en-28-oic acid	C ₃₀ H ₄₈ O ₄	Leaves	Runyoro <i>et al.</i> ⁴⁸
3-hydroxy-4-isopropylbenzyl alcohol 3-glucoside	C ₁₆ H ₂₄ O ₇	Leaves	Manyawi <i>et al.</i> ⁴⁷
3-O-rhamnosyl-5,7,2,3,5-pentahydroxyflavone	C ₂₁ H ₂₆ O ₁₂	Leaves	Chikafa <i>et al.</i> ⁴⁹
3-O-rhamnosyl-5,7,3,5-tetrahydroxyflavone	C ₂₁ H ₂₁ O ₁₁	Leaves	Chikafa <i>et al.</i> ⁴⁹
(3R,7R)-1,3,7-octanetriol	C ₈ H ₁₈ O ₃	Leaves	Manyawi <i>et al.</i> ⁴⁷
3,3'-Di-O-methyl-4-O-(n"-O-galloyl-β-D-xylopyranosyl) ellagic acid	C ₂₈ H ₂₂ O ₁₆	Roots	Fyhrquist <i>et al.</i> ⁵⁰
3',5,7-trihydroxy-3,4'-dimethoxyflavone	C ₁₇ H ₁₄ O ₇	Leaves	Mangoyi <i>et al.</i> ⁵¹
3,5,7,6 -tetrahydroxyflavanone	C ₁₅ H ₁₂ O ₆	Leaves	Chikafa <i>et al.</i> ⁴⁹
11-aminoundecanoic acid	C ₁₁ H ₂₃ NO ₂	Leaves	Manyawi <i>et al.</i> ⁴⁷
Ampelopsin glucoside	C ₂₁ H ₂₂ O ₁₃	Leaves	Chikafa <i>et al.</i> ⁴⁹
Apigenin glucoside	C ₂₁ H ₂₂ O ₁₀	Leaves	Chikafa <i>et al.</i> ⁴⁹
Cirsimaritin	C ₁₇ H ₁₄ O ₆	Leaves	Chikafa <i>et al.</i> ⁴⁹
Di-methyl-ellagic acid xyloside	C ₂₁ H ₁₈ O ₁₂	Roots	Fyhrquist <i>et al.</i> ⁵⁰
Gallic acid	C ₇ H ₆ O ₅	Roots	Fyhrquist <i>et al.</i> ⁵⁰
Hexagalloylglucose	C ₄₈ H ₃₆ O ₃₀	Roots	Fyhrquist <i>et al.</i> ⁵⁰
Hydroxysocaproic acid	C ₆ H ₁₂ O ₃	Leaves	Manyawi <i>et al.</i> ⁴⁷
Maslinic acid	C ₃₀ H ₄₈ O ₄	Leaves	Runyoro <i>et al.</i> ⁴⁸
Methyl-ellagic acid xyloside	C ₂₀ H ₁₆ O ₁₂	Roots	Fyhrquist <i>et al.</i> ⁵⁰
Nevadensin	C ₁₈ H ₁₆ O ₇	Leaves	Chikafa <i>et al.</i> ⁴⁹
Oleamide	C ₁₈ H ₃₅ NO	Leaves	Manyawi <i>et al.</i> ⁴⁷
Oleanolic acid	C ₃₀ H ₄₈ O ₃	Leaves	Runyoro <i>et al.</i> ⁴⁸
Palmitic amide	C ₁₆ H ₃₃ NO	Leaves	Manyawi <i>et al.</i> ⁴⁷
Phytosphingosine	C ₁₈ H ₃₉ NO ₃	Leaves	Manyawi <i>et al.</i> ⁴⁷
Protocatechuic acid	C ₇ H ₆ O ₄	Roots	Fyhrquist <i>et al.</i> ⁵⁰
Punicalagin	C ₄₈ H ₂₈ O ₃₀	Roots	Fyhrquist <i>et al.</i> ⁵⁰
Quinic acid	C ₇ H ₁₂ O ₆	Leaves	Chikafa <i>et al.</i> ⁴⁹
Sphinganine	C ₁₈ H ₃₉ NO ₂	Leaves	Manyawi <i>et al.</i> ⁴⁷
Terminolic acid	C ₃₀ H ₄₈ O ₆	Leaves	Runyoro <i>et al.</i> ⁴⁸
(-)-tortuosamine	C ₂₀ H ₂₆ N ₂ O ₂	Leaves	Manyawi <i>et al.</i> ⁴⁷
Ursolic acid	C ₃₀ H ₄₈ O ₃	Leaves	Runyoro <i>et al.</i> ⁴⁸

Ethnopharmacological properties of *Combretum zeyheri*

The leaves, roots and stems of *C. zeyheri* are rich in different classes of phytoconstituents belonging to phospholipids, fatty acid amides, glycosides, flavonoids, cholesterol, amines, amino acids, phenols, alcohols, triterpenoids and alkaloids⁴⁷⁻⁵⁴ (Table 2). Some of these phytochemical compounds may be responsible for the biological activities exhibited by *C. zeyheri*, which include anticholinesterase inhibition⁵², antibacterial^{53,54}, antimycobacterial^{50,55}, antifungal^{48,56-58}, anti-inflammatory^{52,59,60}, antioxidant^{35,52,59}, antitrypanosomal⁶¹ and cytotoxicity⁶¹ activities.

Anticholinesterase inhibition activities: Dzoyem and Eloff⁵² assessed the anticholinesterase inhibition properties of the acetone extract of *C. zeyheri* leaves using the acetylcholinesterase inhibition assay with eserine as a positive control. At a determined concentration of 500.0 µg/mL, the acetone extract demonstrated the anticholinesterase inhibitory properties of 63.5% and a dose-dependent half maximum inhibitory concentration (IC₅₀) average value of 398.6 µg/mL⁵².

Antibacterial activities: Anokwuru *et al.*⁵³ evaluated the antibacterial activities of the methanol extract of *C. zeyheri* leaves against *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Bacillus cereus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Escherichia coli*, *Shigella sonnei* and *Salmonella typhimurium* using the microdilution method with ciprofloxacin as a positive control. The extract exhibited activities against the tested pathogens with minimum inhibitory concentration (MIC) values ranging from 0.25 mg/mL to >3.0 mg/mL⁵³. Machingauta and Mukanganyama⁵⁴ evaluated the antibacterial activities of acetone, ethanol and methanol extracts of *C. zeyheri* leaves against *Acinetobacter baumannii* using the broth microdilution method. The extracts exhibited activities with an MIC value of 1000.0 µg/mL against the tested pathogen⁵⁴.

Antimycobacterial activities: Nyambuya *et al.*⁵⁵ evaluated the antimycobacterial activities of the alkaloid extract of *C. zeyheri* leaves against *Mycobacterium smegmatis* using the broth microdilution method with rifampicin as a positive control. The alkaloid extract exhibited activities against the pathogen

with an MIC value of 125.0 µg/mL⁵⁵. Fyhrquist *et al.*⁵⁰ evaluated the antimycobacterial activities of aqueous, butanol and chloroform extracts of *C. zeyheri* roots against *Mycobacterium tuberculosis* using the agar diffusion assay with rifampicin as a positive control. The extracts demonstrated antimycobacterial properties against the tested pathogen, with the zone of inhibition ranging from 14.0 mm to 23.0 mm⁵⁰.

Antifungal activities: Runyoro *et al.*⁴⁸ evaluated the antifungal activities of the phytochemical compound terminolic acid isolated from *C. zeyheri* leaves against *Candida albicans* strains MTCC 1637 and ATCC 90028 using the disk diffusion assay with amphotericin B and clotrimazole as positive controls. The phytochemical compound exhibited activities against the tested pathogens with MIC values ranging from 62.5 µg/mL to 125.0 µg/mL⁴⁸. Mapfunde *et al.*⁵⁶ evaluated the antifungal activities of the ethanol extract of *C. zeyheri* leaves against *Candida albicans* using the broth microdilution method with miconazole as a positive control. The extract exhibited activities against the tested pathogen with an IC₅₀ value of 16.0 µg/mL⁵⁶. Liu *et al.*⁵⁷ assessed the antifungal properties of methanol and ethanol extracts of *C. zeyheri* leaves against *Candida parapsilosis*, *Candida krusei* and *Candida albicans* using the colorimetric broth microdilution assay with itraconazole as a positive control. The extracts demonstrated activities against the tested pathogens, exhibiting MIC values ranging from 8.0 to 500.0 mg/L⁵⁷. Masoko *et al.*⁵⁸ assessed the antifungal properties of dichloromethane, hexane, methanol and acetone extracts of *C. zeyheri* leaves against *Aspergillus fumigatus*, *Candida albicans*, *Cryptococcus neoformans*, *Microsporum canis* and *Sporothrix schenckii* using the microdilution method with amphotericin B as a positive control. The extracts demonstrated activities against the tested pathogens, exhibiting MIC values ranging from 0.02 to 2.5 mg/mL⁵⁸.

Anti-inflammatory activities: Dzoyem and Eloff⁵² assessed the anti-inflammatory properties of the acetone extract of *C. zeyheri* leaves using the soybean lipoxygenase inhibition, viability of LPS-activated RAW 264.7 macrophage assay and the nitric oxide production method with indomethacin and quercetin as positive controls. The acetone extract demonstrated anti-inflammatory activities with anti-lipoxygenase activities showing 70.0% inhibition and an IC₅₀ value of 45.5 µg/mL at 100.0 µg/mL. The extract exhibited a dose-dependent inhibition of nitric oxide production⁵².

Chirisa and Mukanganyama⁵⁹ evaluated the anti-inflammatory activities of ethanol extract of *C. zeyheri* leaves in *in vitro* assay for Cyclooxygenase-1 (COX-1) inhibitors with indomethacin as a positive control. The extract demonstrated anti-inflammatory properties by exhibiting COX-1 inhibition of 97.0%⁵⁹. McGaw *et al.*⁶⁰ assessed the anti-inflammatory properties of ethyl acetate and acetone extracts of *C. zeyheri* leaves in an *in vitro* assay for cyclooxygenase inhibitors with indomethacin as a positive control. The extracts demonstrated anti-inflammatory properties by showing inhibition ranging from 75.0 to 91.0%⁶⁰.

Antioxidant activities: Masoko and Eloff³⁵ evaluated the antioxidant activities of acetone and methanol extracts of *C. zeyheri* leaves using 2,2-Diphenyl-1-Picrylhydrazyl (DPPH) free radical scavenging assay. The extract exhibited moderate antioxidant activities³⁵. Dzoyem and Eloff⁵² assessed the antioxidant properties of the acetone extract of *C. zeyheri* leaves using the DPPH, ferric reducing antioxidant power (FRAP) and 2,2'-Azino-bis (3-Ethylbenzothiazoline-6-Sulfonic Acid (ABTS) assays with trolox and ascorbic acid as positive controls. The extracts demonstrated antioxidant properties with IC₅₀ values of 3.5 µg/mL for DPPH, 4.6 µg/mL for ABTS and 96.0 µg/mL for FRAP⁵². Chirisa and Mukanganyama⁵⁹ evaluated the antioxidant activities of ethanol extracts of *C. zeyheri* leaves the DPPH and tetramethoxy azobismethylene quinone (TMAMQ) free-radical scavenging assays with ascorbic acid and gallic acid as positive controls. The extract exhibited antioxidant activities in both DPPH and TMAMQ assays with 100.0% of the radicals quenched at 21.0 µg/mL and 25.0 µg/mL µg/mL, respectively⁵⁹.

Antitrypanosomal activities: Nibret *et al.*⁶¹ assessed the antitrypanosomal properties of dichloromethane and methanol extracts of *C. zeyheri* bark using the quantitative colorimetric method via the oxidation–reduction indicator resazurin against *Trypanosoma brucei brucei* with diminazene aceturate as the positive control. The methanol and dichloromethane extracts demonstrated antitrypanosomal properties exhibiting IC₅₀ values of 87.5 µg/mL and 39.0 µg/mL respectively⁶¹.

Cytotoxicity activities: Nibret *et al.*⁶¹ evaluated the cytotoxicity activities of methanol and dichloromethane extracts of *C. zeyheri* bark against the human cancer cell line HL-60 cells using the quantitative colorimetric assay with diminazene aceturate as the positive control. The

methanol and dichloromethane extracts exhibited activities with IC₅₀ values of 156.0 µg/mL and 108.9 µg/mL respectively⁶¹.

CONCLUSION

The present review provides an overview of the ethnomedicinal applications of *C. zeyheri* extracts in tropical Africa, as well as its phytochemical and pharmacological properties. The importance of *C. zeyheri* as a medicinal plant species in addressing human and animal diseases in tropical Africa cannot be denied. The current review testifies that *C. zeyheri* is an integral part of the *materia medica* in Angola, South Africa, Namibia, Tanzania, Eswatini, Zambia, Mozambique and Zimbabwe, that is, 57.1% of the countries where the species is indigenous. Although preliminary ethnopharmacological research focusing on the active ingredients of the species and its pharmacological properties conducted so far, appear to show *C. zeyheri* as crucial and promising in addressing primary health care issues of both humans and animals, there is need for detailed studies focusing on toxicity and safety, mechanisms of action *in vivo* and clinical research aimed at corroborating the medicinal applications of the species.

SIGNIFICANCE STATEMENT

This study contributes to the existing traditional knowledge about ethnomedicinal applications, phytochemical and pharmacological properties of *C. zeyheri* that could be useful in bio-prospecting for new health-promoting and pharmaceutical products. Such basic information, including pharmacological screening, isolation and identification of pharmacologically active phytochemical compounds, toxicological properties of the crude extracts and active constituents and clinical studies of the species, is needed for the comprehensive primary health care system in tropical Africa. Therefore, future research on the species should focus on conducting detailed phytochemical and pharmacological studies and also evaluating toxicological properties, *in vivo* and clinical studies, as well as addressing the need for standardized quality control procedures for herbal medicinal products.

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