Combretum species around Africa as alternative medicine: Ethnopharmacological and ethnobotanical importance

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ABSTRACT
Herbal medicine is a form of medicine that has been extensively exploited in traditional medicine, and its therapeutic potential is accepted. Combretum is one of the most frequently happening genera in the African and Asia tropical and subtropical areas; some are widely used in African herbal medicine due to their ethnopharmacological properties. Numerous species of this plant have been used and expended owing to high pharmaco-constituents following their phytochemical screening and evaluations. The recent incidence of multidrug-resistant strains and reduced receptiveness to antibiotics has raised serious anxiety in health delivery and the need for an urgent search for new antibiotics mediators from nature. A countless number of natural substances have resulted from the Combretum species as medicine and are utilized traditionally for the management of bacteriological infection. The plants have received comprehensive documentation as a good cradle of natural constituents that can be categorized into four groups following their biosynthetic source: alkaloids, terpenoids, polyketides, and phenylpropanoids. The study deals with the ethnobotanical and pharmacological significance of the Combretum species for treating numerous ailments and diseases.

INTRODUCTION
Communicable ailments are significant sources of morbidity and death universally, notably in developing countries, accounting for about 50% of diseases in countries with low healthcare facilities and as much as 20% of mortality rates in industrialized countries (Khalil et al., 2020; Motsumi et al., 2020; Mtunzi et al., 2017a; Ntshanka et al., 2020). Despite the high level of innovation and antibiotic application in microbiology, the intermittent occurrences of epidemics caused by drug-resistant microbes and the emergence of unknown disease-causing microorganisms pose a significant threat to healthcare (Abubakar, 2010; Nguedia and Shey, 2014; Silber et al., 2016).

The development of resistant strains to some antibiotics has complicated the management of infectious diseases, given that drugs are only effective against one-third of existing ailments (Fankam et al., 2015; Sahu et al., 2014). Microbial drug resistance became persistent because of drug abuse and misuse of antibiotics. Most drugs are ineffective against diseases for which they had previously been misused. This results in resistant pathogens becoming virulent, increasing the risk of complications and death (Fankam et al., 2015; Nguedia and Shey, 2014; Sampedro et al., 2009). Most drugs are discovered from biological natural resources, and natural yields from microbes have been the major cradle of...
antibiotic delivery. With the cumulative approval of herbal medicine as a substitute form of healthcare, the selection of herbal plants for bioactive constituents has become a very imperative aspect of the health system because they serve as a valuable cradle of innovative antibiotic exemplars (Khan et al., 2022; Sabo and Knezevic, 2019; Serralheiro et al., 2020). Antibiotics derived from fungi or living organisms are produced industrially using a fermentative process (Alfadil et al., 2014; Silber et al., 2016; Wright et al., 2014).

The predominance of other diseases like hematological and autoimmune disorders, human immunodeficiency virus (HIV) infection, cancer, and important immune system dysfunction may cause symbiotic microbes to change to pathogens under definite circumstances, typically called opportunistic contamination. Opportunistic pathogens consist of fungi, viruses, protozoa, and bacteria, taking advantage of immunocompromised patients and displaying new health challenges worldwide. Opportunistic diseases involve diminishing host defenses, occurring because of genetic deficiencies, introduction to antibiotics, and immunosuppressive substances or due to communicable diseases possessing immunosuppressive properties (Nagata et al., 2011; Ntshanka et al., 2020; Ryan and Ray, 2004; Yang et al., 2013).

Some chemotherapeutic mediators presently used are noxious with accompanying antagonistic side effects. Hence, there is a general necessity for novel chemotherapeutic mediators against several disease pathogenetiologies that are exceedingly resourceful, have low toxicity, and exhibit minor ecofriendly impacts. Herbal medications have various traditional claims, such as managing infectious sources. Several extracts of plant species were established against hundreds of microbial strains via various in vitro models and some had good action pharmacological consequences (Bhat, 2014; Fankam et al., 2015; Khumalo et al., 2018; Luis et al., 2016; Motsumi et al., 2020; Npupela and Shey, 2014). However, a limited number of these herbal plant extracts have been screened in animal or human studies to regulate safety and efficiency. Natural products and their byproducts characterize about 50% of all drugs in clinical use (Cragg and Newman, 2013; Fankam et al., 2015; Khumalo et al., 2018; Lahlou, 2013).

Natural products from natural cradles like plants, animals, and microorganisms, dated before human antiquity, perhaps thousands of years (Ji et al., 2016; Khan, 2018). These products can be categorized into four diverse groups according to their biosynthetic derivation, polyketides, alkaloids, terpenoids, and phenylpropanoids (Bisht et al., 2021; Guo, 2017), and continue to offer novel chemical structures with high levels of biological activity (Guo, 2017; Khan, 2018; Moloney, 2016). The mechanisms underlying many biological properties have been ascribed to numerous types of propolis, including antitumor, anti-inflammatory, wound healing, antioxidant, antimicrobial, and immunomodulatory activities (Shaihk et al., 2016). Plants do produce potentially toxic substances aside production of beneficial phytochemicals; therefore, toxicity assays incorporation in the bioactivity evaluation of medicinal plants is very important in understanding their therapeutic effects ( Alam et al., 2018; Araújo et al., 2013; Cundell, 2014; Luis et al., 2016; Ntshanka et al., 2020; Shah et al., 2010; Verma, 2016). The Chinese traditional medicine community is the world’s largest medicinal plant user is, with more than 5,000 plants and plant products registered in their pharmacopeia (Ji et al., 2016).

Traditional medicine in South Africa supports using abundant plant species for the treatment or management as prophylaxis against several kinds of ailment (infectious and noninfectious) (Masoko et al., 2010, 2012; Mtnzni et al., 2017a, 2017b; Street and Prinsloo, 2013). In South Africa, medicinal species are being traded for usage in local medicines since most are from ethnopharmacological guides (De Wet et al., 2013; Mabona and Van Vuuren, 2013; Street and Prinsloo, 2013). The sustainable use and control of medicinal plants are of a significant contest to all shareholders. Parts of many medicinal plants, like the stem, bark, and roots, are being harvested and merchandized in an unmanageable routine that may lead to the augmented death of the tree that is the source of medication. Assessment and authentication of leaf extract bioactivity as a promising substitute for stem, roots, and bark use to afford a viable opportunity for safeguarding medicinal plants (De Wet et al., 2013; Street and Prinsloo, 2013). Herbal medicine is the most significant medicine for most people on planet earth, specifically those who do not have access to modern and expensive drugs. Interestingly, it has formed the foundation of every medicine, the mother of all remedies in modern days. The exploitation of medicinal plants as herbal medicine alongside their curative perspective is well documented (Alam et al., 2018; Bhat, 2014; Cundell, 2014; Motsumi et al., 2020; Mtnzni et al., 2017a, 2017b; Sabo and Knezevic, 2019; Street and Prinsloo, 2013). The World Health Organization estimates that populace about 80% residing in developing nations excessively practice traditional medicine (Elloff, 1998; Motsumi et al., 2020; Mtnzni et al., 2017a).

Medicinal plant therapies have also been featured conspicuously in the ailments treatment of production and domestic animals, and ethnoveterinary therapeutic practices remain an imperative aspect of animal healthcare in unindustrialized countries (Ji et al., 2016; Khan, 2018). Combretum species is featured conspicuously among the utilized medicinal plants in South African traditional medicine as agents for handling communicable diseases like diarrhea (Combretum imberbe Wawra, Combretum vendee A.E.van Wyk), malaria (Combretum ghasalense), stomach disorders (Combretum molle R. Br. ex G. Don.), and coughs [C. molle R. Br. ex G. Don., C. imbere Wawra, Combretum erythrophyllum (Burch.) Sond.] (Elloff et al., 2008; Mtnzni et al., 2017b; Ntshanka et al., 2020). Combretum erythrophyllum is a member of the Combretaceae family, generally used for venereal disease management (Van Wyk and Gericke, 2000). Root parts are used as a laxative, while dried and pulverized gum is applied to blisters (Venter and Venter, 1996).

The roots and bark decoctions of C. erythrophyllum are utilized to treat cough and unproductiveness and as an aphrodisiac (Ahmed et al., 2014; Mtnzni et al., 2017b). The leaves are used to treat cough and stomach pains, while the seeds, which have been reported to be poisonous, are used to remove intestinal worms in dogs (Van Wyk et al., 2009). Combretum erythrophyllum is commonly scattered in the Southern Africa region, most commonly found in South Africa along the coast in the Eastern Province, namely Zimbabwe, KwaZulu-Natal, Northern South Africa (Mpumalanga, Gauteng, Limpopo, and the eastern parts of Northwest regions), Swaziland, and Mozambique, and marginally into the eastern parts of Botswana (Silén et al., 2023).
Martini et al. (2004a) isolated seven different flavonoids from leaf extract C. erythrophyllum (Burch.) collected from a tree within the Pretoria National botanic gardens, South Africa, known to be antibacterial phenolic compounds which include four flavonols: rhamnocitrin (1), rhamnazin (2), 5,7,4′-trihydroxyflavonol (kaempferol) (3), and 7,4′-dihydroxy-5,3′-dimethoxyflavonol (quercetin-5,3′-dimethyl ether) (4); three flavones: 5,7,4′-trihydroxyflavone (5), 5,4′-dihydroxy-7-methoxyflavone (6), and 5-hydroxy-7, 4′-dimethoxyflavone (7) (Fig. 1). All compounds possessed good activity against Enterococcus faecalis and Vibrio cholera, with the minimal inhibitory concentration (MIC) value <100 µg/ml. Rhamnocitrin and quercetin-5,3′-dimethyl ether inhibited Shigella sonnei and Micrococcus luteus with a MIC value of 25 µg/ml (Martini et al., 2004a, 2004b; Mawoza and Ndove, 2015).

In literature, medicinal plants have presented interesting ethnopharmacological potentials as chemotherapeutic agents. The Combretum species has great prospects for the management of various infectious diseases (Eloff et al., 2008) and will have a vital relevance with economic benefit to the perfumery industry (Alam et al., 2018; Barrales-Cureno et al., 2021; Crovadore et al., 2012; Mohaddese, 2016; Sabo and Knezevic, 2019). Nevertheless, the tangible potential of Combretum has not been exploited to the fullest. Hence, this review has made an effort to present a comprehensive overview of the summary of earlier research data regarding ethnopharmacological properties, antimicrobial, antifungal, antioxidant, cytotoxicity activities, and other noteworthy effects of Combretum species as alternative medicine.

METHODS AND LITERATURE QUEST

An epistemological paradigm grounded in a qualitative research approach was utilized for this study. The study seeks to explain, clarify, define, elucidate, and expand more on the understanding of the ethnopharmacological potentials of medicinal plants concerning Combretum species as chemotherapeutic agents for drug discovery.

Available reports and references on the medicinal plant species were accessed from published scientific peer-reviewed journals, books, short communications, reports from national, regional, and international organizations and institutions, theses, conference papers, and other materials. International online databases, including ISI Web of Science, SCOPUS, EBSCO, MEDLINE (National Library of Medicine), chemical abstracts service, Science Direct, SCIMAGO, ProQuest, EMBASE, and Google Scholar, were utilized for literature search using precise search terms. Selected keywords were used but not limited to Combretum species, ethnopharmacological promises, properties of the Combretum genus, phytochemicals, pharmacological, antibiotics, medicinal plants, biological assays, chemical constituents, chemotherapeutic agents, traditional medicine, and traditional uses of medicinal plants of about 600 studies and research articles consulted, articles from 1970 to 2022.

Snowball sampling technique was used in this study, followed by content and semantic analysis of data collected from the literature for systematic documentation of the biological, pharmacological, and traditional uses of medicinal plants: Combretum species around Southern Africa region as alternative medicine.

RESULTS AND DISCUSSION

Combretaceae family

Combretaceae hosts more than 600 species (Komape et al., 2014; Zhang et al., 2020). Combretum is among the most frequently occurring genera of Combretaceae in tropical and subtropical areas of Africa and Asia. Due to their ethnopharmacological properties, some of these genera are widely used in African traditional medicine (Chukwujeaku and van Staden, 2016; Gumisiriza et al., 2021). The different fragments of the Combretum species are broadly used to treat numerous diseases (Ares et al., 2006; Eloff et al., 2008; Mtnui et al., 2017b). The species of Combretum, generally known as the forest bushwillow tree (C. kraussii Hochst.), is medium to large in size and is found in the eastern part of South Africa, Swaziland, and Southern Mozambique (Chukwujeaku and van Staden, 2016; Zhang et al., 2020). Combretum kraussii Hochst. is often used as herbal medicine to treat eye infections and wounds and serves as a blood tonic and an appetite stimulant. It can also act as antiseptic and antidiuretic agent, (Chukwujeaku and van Staden, 2016; Quattrocchi, 2012).

Therapeutic potentials of Combretum species

Combretum species as an antioxidant agent

An important development that produces free radicals in living systems, substances, and even in food is referred to as oxidation (Barku et al., 2013). Oxidation is also the chemical reaction involving electron transfer from the electron-rich to the electron-deficient entity (Poljsak et al., 2021). The electron-scave molecule is labeled an oxidizer or oxidizing agent. Enzymes such as hydroperoxidase and catalase translate hydroperoxides and hydrogen peroxide (H₂O₂) to nonradical forms and perform natural antioxidants' role in the human body (Ofoedu et al., 2021). The prescribed oxidation state refers to the postulated charge an atom has if all bonds to other atoms of different elements are completely ionic. It is generally epitomized by integers that can either be zero, positive, or negative (Norman and Pringle, 2022).
Free radicals are reactive species containing unpaired electron that attacks macromolecules, including protein, lipid, and DNA. Free radicals are the products of natural human metabolism. Varieties of endogenous free radicals destroying antioxidants exist in the body, while others are obtained from dietary sources like vegetables, fruits, and teas. At present, accessible synthetic antioxidants like gallic esters, butylated hydroxytoluene, butylated hydroxyanisole, and tertiary butylated hydroquinone are assumed to bring about or hasty negative health consequences (Mongalo et al., 2012).

Antioxidants preclude oxidative impairment of cells, biomolecules, and reactive oxidative species oxidative species (ROS)-induced illnesses by reacting with free radicals, destroying free radicals, and chelating free catalytic metals (Pizzino et al., 2017). Antioxidant consumption possesses numerous health benefits, including oxidative damage associated with free radical damage and its role in diseases (Ejidike et al., 2019). Antioxidant nutrients, either endogenous or exogenous, natural or synthetic, can search for free radicals in the system and neutralize them before they further damage the body cells (Mandal et al., 2022; Medrano-Macias et al., 2022; Poljsak et al., 2021). Antioxidants are important constituents in the human body that safeguards it from impairment caused by oxidative stress induced by free radicals (Ejidike and Ajibade, 2015; Poljsak et al., 2021). There is emerging interest in the exploration of the antioxidant activities of secondary metabolites from medicinal species to compounds with greater potency and lower toxicities than the presently accessible synthetic ones (Medrano-Macias et al., 2022; Motsumi et al., 2020; Mtnunzi et al., 2017a; Ntshanka et al., 2020; Poljsak et al., 2021).

Recent epidemiological evaluations have revealed that many antioxidant compounds possess antibacterial, anticarcinogenic, anti-inflammatory, antiviral, antitumor, antiatherosclerotic, or antimutagenic activities to a bigger or smaller extent (Owen et al., 2000; Verma, 2016). The antioxidant perspective of natural plant products is attributable to several compounds such as phenols and flavonoids, which have a distinct mechanism of action. Consequently, one antioxidant compound was sequestered from *C. erythrophyllum* and is 5-hydroxy-7,4′-dimethoxyflavone but exhibited the weakest activity (Martini et al. 2004a, 2004b). Oxidative stress is the inequality between the generation and eradication of ROS or reactive nitrogen species (RNS) in support of ROS (Ejidike and Ajibade, 2015; Poljsak et al., 2021; Zhang et al., 2009). Oxidative stress is proficient in triggering cells to lose their function and structure and ultimately cause cell dysfunction. ROS/RNS can be produced within the airway epithelial cells in answer to proinflammatory cytokines like tumor necrosis factor-alpha (TNF-α) (Ejidike and Ajibade, 2015; Lü et al., 2010; Mandal et al., 2022; Medrano-Macias et al., 2022; Poljsak et al., 2021).

ROS and RNS perform various functions, including regulation of gene expression (Mandal et al., 2022) and stimulation of apoptosis (Huang and Zhou, 2021). The manufacture of ROS/RNS might have very detrimental effects and is neutralized by the antioxidant fortifications under standard circumstances in healthy people (Mandal et al., 2022; Medrano-Macias et al., 2022). Oxidative stress arises when there is a variation of balance in support of ROS/RNS and may happen in several situations, like in infection or malnutrition with deficient micronutrients to achieve the requirement for antioxidant defenses (Ejidike and Ajibade, 2015; Mandal et al., 2022; Medrano-Macias et al., 2022). It has been recognized that oxidative stress is among the chief contributory elements of various chronic and deteriorating ailments initiators comprising cancer, ischemic heart disease, atherosclerosis, diabetes mellitus, ageing, immunosuppressant, and neurodegenerative illnesses (Ejidike and Ajibade, 2015; Malekmohammad et al., 2019; Poljsak et al., 2021).

**Combretum species as an antimicrobial and antiviral agent**

Antimicrobial-resistant strains are the major causes of copious clinical problems (Fennel et al., 2004; Gangoué-Piéboji et al., 2009) and have increased the world’s mortality rate (Ejidike and Ajibade, 2015; Motsumi et al., 2020; Mtnunzi et al., 2017a, 2017b; Ntshanka et al., 2020). The resistance built by pathogenic against antibiotics has brought about great interest and the quest for novel antimicrobial drugs/agents from nature (Bouzidi et al., 2016; Dorman and Deans, 2000; Ejidike and Ajibade, 2015; Liouane et al., 2010). The unethical usage of antibiotics has brought about their resistance to bacterial strains (Martini and Eloff, 1998). Plants are an imperative basis for the growth of new chemotherapeutic agents, given that they are made up of potentially useful constituents (Barku et al., 2012). Since time immemorial, traditional plants have been used to prepare drugs, thus acting as a good source of medicine. Moreover, *Combretum* species have been shown to exhibit potential activities as antibacterial and antiviral agents (Adamu et al., 2005; Filho et al., 2015; Fyhrquist et al., 2006; Katerere et al., 2003; Maregesi et al., 2007; Martini et al., 2004a, 2004b; Martini and Eloff, 1998; Masika and Afolayan, 2002; Masoko et al., 2007, 2010; Mawoza and Ndove, 2015; McGaw et al., 2000; Ntshanka et al., 2020; Olukoya et al., 1993).

Different components of the *Combretum* plants have been utilized in the native system of medicine for the management of several human ailments ranging from ulcers, wounds, cholera, and snakebite to abdominal disorders (Begum et al., 2002; Maregesi et al., 2007; Masoko et al., 2010; Mawoza and Ndove, 2015). The leaves, stems, roots, and flower parts of *Combretum* species have been used traditionally for the treatment of neuralgia, throat contagions, wounds, eruptions, and a varied range of skin diseases like rashes, ringworm, and ulcers (Eloff et al., 2008; Masoko et al., 2007, 2010); treatment of related bacterial infections and diseases including pneumonia, chest infections, syphilis, diarrhea, coughs, and colds (Ahmed, 2012; Ahmed et al., 2014; Dawe et al., 2013; Fyhrquist et al., 2006; Gathirwa et al., 2011; Komape et al., 2014; McGaw et al., 2001; Ntshanka et al., 2020); treatment of digestive infections, bleeding, and throat contagions (Dimitrova et al., 2015; Hsouna and Hamdi, 2012); and also menopausal and menstrual complications, breast congestion, cellulite, and fluid retention (Pietrovsksy et al., 2006; Saraswathi et al., 2011). The leaf extracts have also been reported to treat childhood diseases like measles, chickenpox, and mumps (Brendler and Van Wyk, 2008). The following species have prominently featured as agents for treating contagious diseases: *C. imberbe, C. vendee* against diarrhea; *C. ghasalense* Engl. & Diels against malaria;
Ethnobotanical use

**Combretum adenogonium Steud. ex A. Rich.**

Four-leaved bushwillow

Leaves and stems are used for anti-inflammatory, hepatitis, arterial hypertension, and urinary infection. Aqueous stem bark powder is taken as an antiabortion solution. A decoction of the roots is used as a bath for children with convulsions.

Plant parts are utilized for the management of cough, leprosy and snakebite, diarrhea, malaria, aphirosis, syphilis, long-lasting wounds, poisoned wounds, and fungal infection of the scalp (Batawila et al., 2005; Fyrquist et al., 2006).

**Combretum albopunctatum Suesseng (Ciliatipetala Engl. & Diels)**

Thicket-forming shrub

Hexane, acetone, methanol, and dichloromethane leaf extracts possess antibacterial properties and antioxidant activities. Also, they are used in the wound healing process (Masoko and Eloff, 2007).

Aqueous roots are squashed and the juice is ingested for the management of snakebite. Methanol, hexane, ethanol, and aqueous leaf extracts are used as preventives for abdominal disorders, while the stem bark serves for conjunctivitis (Aderogba et al., 2012; Fyrquist et al., 2006; Katerere et al., 2012; McGaw et al., 2000; Olukoya et al., 1993).

**Combretum apiculatum Sond. ssp. apiculatum**

Red bushwillow

Water and ethanol leave and stem extracts have been used to treat earache, headache, fever, toothache, backache, and menstrual pains (Eloff, 1998; Olukoya et al., 1993).

**Combretum bracteatum (Laws.) Engl. & Diels**

Hiccup-nut

Water extracts of dried stems exhibited antimicrobial activity with a zone of inhibition value of 5–9 mm at 0.33 g/ml (Eloff, 1998).

**Combretum chebulicosum (Ciliatipetala Engl. & Diels)**

Stem bark

Methanolic extract of the stem barks exhibited *Clostridium chauvoei* (Jakati strain) neuraminidase activity inhibition at 100–1,000 μg/ml with an estimated LC50 value of 150 μg/ml (Useh et al., 2004).

Extracts from the root, leaf, and stem bark have the potential as antibacterial, antifungal, and antiproflligative agents (Fyrquist et al., 2006; Maregesi et al., 2007).

**Combretum chebula Chebula (Ciliatipetala Engl. & Diels)**

Dried fruit

Phenolic compounds, namely, three (3)-flavonoids and two (2)-cyclobutane chalcone dimers: rel-1β-(4,6-dihydroxy-2-methoxy)-benzoyl-rel-(3β,4α)-diphenylcyclobutane, rel-(1α,2β)-Di-(2,6-dimethoxy-4-hydroxy)-benzoyl-rel-(3α,4β)-diphenylcyclobutane, 5-Hydroxy-7-methoxy flavanone (alpinetin), 5,7-dihydroxyflavonone (pinocembrin), 4',6-dihydroxy-2'-methoxylvhalcone (cardamomin) (Katerere et al., 2004).

Two phytoestrogens: stigmasterol and β-sitosterol (Maima et al., 2008).

**Combretum chebulosum (Combretum Egidjike)**

Roots

Hexane, acetone, methanol, and aqueous root extracts possess antibacterial and antioxidant activities. Also, they are used in the wound healing process (Masoko and Eloff, 2007).

A strong antioxidant activities was demonstrated by Kaempferol and Quercetin and had with EC50 values of 47.36 ± 0.03 and 11.81 ± 85 μM respectively.

Water extract by Microdilution assay revealed that *Staphylococcus aureus* and *Bacillus subtilis* possessed MIC = 0.39 mg/ml (Olukoya et al., 1993).

**Combretum chinense Sond.**

Root

Water and ethanol root extracts exhibited antioxidant activity with a zone of inhibition value of 5–9 mm at 0.33 g/ml (Eloff, 1998).

**Combretum limpho Fisch. & C. A. Rich.**

Root, leaf, and stem bark

Phenolic compounds, namely, three (3)-flavonoids and two (2)-cyclobutane chalcone dimers: rel-1β-(4,6-dihydroxy-2-methoxy)-benzoyl-rel-(3β,4α)-diphenylcyclobutane, rel-(1α,2β)-Di-(2,6-dimethoxy-4-hydroxy)-benzoyl-rel-(3α,4β)-diphenylcyclobutane, 5-Hydroxy-7-methoxy flavanone (alpinetin), 5,7-dihydroxyflavonone (pinocembrin), 4',6-dihydroxy-2'-methoxylvhalcone (cardamomin) (Katerere et al., 2004).

Two phytoestrogens: stigmasterol and β-sitosterol (Maima et al., 2008).

**Combretum malabaricum (Combretum Egidjike)**

Root

1,3; 2,3; 4,5; 9,10-Dihydro-3,6,7-trimethoxy-2,5-dihydrobenzenes (Letcher and Nhamo, 1971).

**Combretum ovale (Combretum Egidjike)**

Leaf

5-Hydroxy-3,4′-dimethoxybibenzyl; 4′,5-dihydroxy-3,5-dimethoxybibenzyl; 4′-hydroxy-3,4,5-trimethoxybibenzyl (Katerere et al., 2012).

Nigacheligoside F1; β-D-glucopyranosyl-3β,19α-dihydroxy-2α,3α,6α,8α-tetrahydroxyolean-12-en-28-oate; Chebuloside II; β-D-glucopyranosyl 2α,3α,6α,8α-tetrahydroxsolan-12-en-28-oate; 1,2-di-O-α-linolenoyl-3-O-β-D-galactopyranosyl-sn-glycerol; 1,2-di-O-α-linolenoyl-3-O-[α-D-galactopyranosyl-(1→6)-O-β-D-galactopyranosyl]-sn-glycerol (Ntchatcho et al., 2009).

**Combretum obovatum Sond.**

Root, leaf, and stem bark

Phenolic compounds, namely, three (3)-flavonoids and two (2)-cyclobutane chalcone dimers: rel-1β-(4,6-dihydroxy-2-methoxy)-benzoyl-rel-(3β,4α)-diphenylcyclobutane, rel-(1α,2β)-Di-(2,6-dimethoxy-4-hydroxy)-benzoyl-rel-(3α,4β)-diphenylcyclobutane, 5-Hydroxy-7-methoxy flavanone (alpinetin), 5,7-dihydroxyflavonone (pinocembrin), 4',6-dihydroxy-2'-methoxylvhalcone (cardamomin) (Katerere et al., 2004).

Two phytoestrogens: stigmasterol and β-sitosterol (Maima et al., 2008).
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<th>Combretum species</th>
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</table>
| **Combretum caffrum** (Eckl. & Zeyh.) Kuntze | Eastern Cape bushwillow | Alcohol and aqueous bark, leaf, and stem extracts are used as an all-purpose tonic for the manufacture of general well-being; roots decoctions are included in the bath water before bedtime for the treatment of body pains (Masika and Afolayan, 2002; Masoko and Eloff, 2007; Masoko *et al*., 2007; Pettit *et al*., 1989). | The methanol extract was active against gram-negative bacteria, while acetone, methanol, hexane, and stem-water fractions and bark exhibited antimicrobial activity against gram (+ve) bacteria and a few fungal pathogens (Masika and Afolayan, 2002). Tetrachloromethane, trichloromethane, and dichloromethane fractions of dried, stem, fruit, leaf, twig, and methyl chloride root extract have exhibited in vitro antitumor activity against murine-P388 lymphocytic leukemia; immature astrocytoma 224c glioma cell (Pettit *et al*., 1995, 1999). Ethanol and crude extracts of fresh shoot bark have shown striking and dose-dependent larvicidal properties on the last larvae of the yellow fever mosquito. Different leaf extracts have exhibited weak in vitro antifungal and anthelmintic activities. Aqueous root and stem bark extracts have shown antimicrobial activity against *Proteus mirabilis* (Adamu *et al*., 2003; Katerere *et al*., 2003, 2012; Marquandt *et al*., 2020; Masoko *et al*., 2007). | Combretastatins: A-1, A-2, A-3, A-4, B-1, B-2, B-3, and B-4 were isolated from the wood (Pettit *et al*., 1989, 1995, 1999). Triterpenoids in the leaves (Rogers and Coombes, 1999). Stilbenoids combretastatins A and B and phenanthrenes (Katerere *et al*., 2003). 9,10-Dihydro-3,6,7-trimethoxy-2,5-phenanthrenediol (Katerere *et al*., 2012). Two bibenzyls: 5′-hydroxy-3,4,4′,5-tetramethoxybibenzyl; 1a,3′-dihydroxy-3,4,4′,5-tetramethoxybibenzyl (Katerere *et al*., 2012). Four flavonols: kaempferol, rhamnazin, 5,3′-dimethylether, quercetin, and rhamnocitrin, 3-Oxo-cycloart-1,11,24-trien-23,21-olide (Eloff, 1998). |}

| **Combretum collinum** Fresen. | Kalahari bushwillow | The stem bark powder mixture coupled with porridge or addition in tea is used to counter rectal collapse. Roots and leaves decoctions are consumed for the management of malaria. Root maceration or decoction is ingested to treat gonorrhrea, female sterility, and pyromositis. The juice extract from the roots is applied externally to toothache, snakebite wounds, and syphilitic sores (Adamu *et al*., 2003; Katerere *et al*., 2003, 2012; Marquandt *et al*., 2020; Masoko *et al*., 2007). | Extracts exhibited antimicrobial activities against *Escherichia coli*, *S. aureus*, *Candida albicans*, *Mycobacterium fortuitum*, and *Vibrio vulgaris* (Katerere *et al*., 2012). | Isolated compounds had MIC values of <200 µg/ml against *Pseudomonas aeruginosa*, *S. aureus*, *E. faecalis*, and *E. coli*. Rhamnocitrin and rhamnazin demonstrated robust antioxidant activity with prospective anti-inflammatory activity. Microdilution assay of dried leaf acetone extract exhibited an LC_{50} of 1.50 mg/ml on *S. aureus*, *P. aeruginosa*, and *E. faecalis*, while 0.8 mg/ml was observed for *E. coli* (Eloff, 1998). The toxicity level of *C. erythrophyllum* (Burch.) crude extract and portions investigated in Vero monkey kidney cells stretched from 34 to 223 mg/ml (Munzi *et al*., 2017b). Extracts of chloroform, hexane, butanol, acetone, and carbon tetrachloride solvents have revealed antibacterial activities against *E. coli*, *P. aeruginosa*, *E. faecalis*, *S. aureus* at different concentrations (Eloff, 1998; Martini and Eloff, 1998). | Four flavonols: kaempferol, rhamnazin, 5,3′-dimethylether, quercetin, and rhamnocitrin, Three flavones: genkwanin, apigenin, and 5-hydroxy-7,4′-dimethoxyflavone (Martini *et al*., 2004a, 2004b). |}

| **Combretum erythrophyllum** (Burch) Sond. | River bushwillow | The roots are used to treat venereal disease. Coughs and stomach pains have been cured using the leaf extract. Poisonous seeds are used for dogs′ intestinal worms purgative. Management of cough and unproductiveness, as well as an aphrodisiac, has been achieved using elixir from roots and bark (Aderogba *et al*., 2012; Arnold and Gulimian, 1984; Marini and Eloff, 1998; Munzi *et al*., 2017a, 2017b; Schwikkard *et al*., 2000; Van Wyk and Van Wyk, 1997). | The toxicity level of *C. erythrophyllum* (Burch.) crude extract and portions investigated in Vero monkey kidney cells stretched from 34 to 223 mg/ml (Munzi *et al*., 2017b). Extracts of chloroform, hexane, butanol, acetone, and carbon tetrachloride solvents have revealed antibacterial activities against *E. coli*, *P. aeruginosa*, *E. faecalis*, *S. aureus* at different concentrations (Eloff, 1998; Martini and Eloff, 1998). | Four flavonols: kaempferol, rhamnazin, 5,3′-dimethylether, quercetin, and rhamnocitrin, Three flavones: genkwanin, apigenin, and 5-hydroxy-7,4′-dimethoxyflavone (Martini *et al*., 2004a, 2004b). |}

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<th>Biological activity</th>
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<tbody>
<tr>
<td><em>Combretum</em></td>
<td>Four-leaved</td>
<td>Root decoctions are ingested to manage syphilis, cough, and leprosy. Cleansing of</td>
<td></td>
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<td>fragans F. Hoffm.</td>
<td>bushwillow</td>
<td>chronic wounds was achieved using leaf decoctions. Methanolic extracts of the</td>
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<td></td>
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<td>bark and stem have been used to treat blackleg in animals (Dawe et al., 2016;</td>
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<td>Maima et al., 2008; Useh et al., 2004).</td>
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<tr>
<td><em>Combretum</em></td>
<td>Lianas woody</td>
<td>Root-water decoction has been utilized locally as a management against hepatitis</td>
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<tr>
<td>griffithii</td>
<td></td>
<td>Bark, root, stem, and leaf decoction extracts have been used for malarial cough</td>
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<tr>
<td>Van Heurck &amp; Müll.</td>
<td></td>
<td>treatment (Moosophon et al., 2011).</td>
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<td>Arg.</td>
<td></td>
<td>Leave and root decoction extracts are used to manage diarrhea and cough. Ashes</td>
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<td><em>Combretum</em></td>
<td>Leadwood</td>
<td>of wood are used as toothpaste (Eloff et al., 2008).</td>
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<tr>
<td>imberbe</td>
<td></td>
<td>Root infusion was used to treat schistosomiasis; root maceration was used to</td>
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<tr>
<td>Wawra</td>
<td></td>
<td>treat stomach aches; infertility in women for gynecological complaints (McGaw et al.,</td>
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<td>2001; Roy et al., 2014a).</td>
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<tr>
<td><em>Combretum</em></td>
<td>Forest</td>
<td>Aqueous bark, root, and leave extracts are used for fever, sawdust irritants,</td>
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<td>kraussii Hochst.</td>
<td>bushwillow</td>
<td>antiseptic, anti-diuretic, and inflammation. Also, they are used for body pain</td>
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<td></td>
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<td>by bathing in the root powder decoction (Masoko et al., 2007; McGaw et al., 2001).</td>
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</table>

Root extracts exhibited antibacterial activity against *Shigella boydii*, *Klebsiella pneumonia*, and *S. aureus* (Chhabra et al., 1984).

Stem bark fractions have shown *C. chauvoei* neuraminidase inhibition, significant for handling blackleg in sheep, cattle, and other ruminants (Maima et al., 2008).

Methanol extract of the stem has displayed cytotoxicity against oral human epidermal carcinoma cell lines (LC50 = 2.8 μg/ml) and antimycobacterial assay with MIC 3.13 μg/ml (Moosophon et al., 2011).

Five pentacyclic triterpenoids have displayed activities against *A. celli* and *S. aureus* (Angeh et al., 2007a).

Pentacyclic triterpenes, glycosides based on imberbic acid and glycoside derivatives of hydroxyimberbic acid exhibited bacterial activities against *S. aureus* and *M. fortuitum* (Kairewe et al., 2003; Rogers, 1988).

MeCl2 extract of the leaf exhibited antibacterial action against *S. aureus* (MIC = 2.5 μg/ml) by microplate serial dilution method (Angeh et al., 2007a).

MeOH, hexane, MeCl2 and acetone extracts of the leaf have demonstrated antifungal activity against *A. fumigates*, *C. albicans*, *A. fumigates*, *M. canis*, and *S. schenckii* by microdilution assay (Masoko et al., 2007).

Acetone extract of the dried leaf has been used for in vitro nematocidal activity via egg hatching and larval growth of *H. contortus-Lethal* (Ademola and Eloff, 2010).

Acetone extract of the dried leaf has been used for in vitro nematocidal activity via egg hatching and larval growth of *C. elegans* (Angeh et al., 2007a).

Aqueous bark, root, and leave extracts are used for fever, sawdust irritants, antiseptic, anti-diuretic, and inflammation. Also, they are used for body pain by bathing in the root powder decoction (Masoko et al., 2007; McGaw et al., 2001).

Microdilution assay of dried leaf hexane, acetone, MeOH, and MeCl2 extracts have exhibited antifungal activities on *A. fumigates* with MIC values of 2.5, 1.25, 0.64, 0.16, and 2.5 mg/ml, respectively (Masoko et al., 2007; McGaw et al., 2001).
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<tbody>
<tr>
<td><em>Combretum leprosum</em> Mart.</td>
<td>Semideciduous tree</td>
<td>Aerial parts such as stems, leaves, flowers, and roots decoctions, and alcoholic extracts have been utilized as hemostatics and sedative agents for wound treatment during uterine bleeding.</td>
<td>Ethnolic extract from flower parts induced antinociception in different prototypes of chemical and thermal pain in mice (Pietrovska et al., 2006).</td>
<td>Pentacyclic triterpene 3β, 6β, 16β-trihydroxylup-20(29)-ene, (Longhi-Balbinot et al., 2009, 2011; Teles et al., 2015).</td>
</tr>
<tr>
<td><em>Combretum micranthum</em> G. Don</td>
<td>Bushy shrub or creeper</td>
<td>Aqueous extracts of diverse parts have been used as traditional remedies for treating numerous inflammatory infections (Facundo et al., 2005; Moraes et al., 2016; Nunes et al., 2009; Teles et al., 2015).</td>
<td>Bark extract on isolated arterial rings from different animals caused relaxations (Filho et al., 2015).</td>
<td>Cycloartanes, triterpenes (arjunolic and molic acid, and 3β, 6β, 16β-trihydroxylup-20(29)-ene), and flavonoids (3-O-methylquercetin, and quercetin) (Facundo et al., 1993).</td>
</tr>
<tr>
<td><em>Combretum nubeculeum</em> J.D. Carr &amp; Retief</td>
<td>Maputaland bushwillow</td>
<td>Leaf infusions are ingested against cold, colic, vomiting, fever, and gastrointestinal complications.</td>
<td>Aqueous extracts of leaves possess bactericidal potentials against <em>K. ozaenae</em>, <em>S. dysenteriae</em>, and <em>S. Paratyphi B</em> (Karou et al., 2005).</td>
<td>Polyphenols exhibiting antioxidative properties (Karou et al., 2005).</td>
</tr>
<tr>
<td><em>Combretum molle</em> R. Br. ex G. Don.</td>
<td>Velvet bushwillow</td>
<td>Roots decoction as anthelmintic and for washing and treatment of wounds. Aqueous ethanol, chloroform, and methanol extracts have been used for the treatment of microbial attacks.</td>
<td>Hypoglycemic activity has been observed for the leaves water extracts by stimulation of diabetes mellitus type 1 and 2 by allowing in rats at doses: 100, 200, or 400 mg/kg (p.o.) (Chika and Bello, 2010).</td>
<td>4-Hydroxyproline betaine (Ogan, 1972).</td>
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<td></td>
<td></td>
<td>Aqueous extracts of various plant parts have been used to treat malaria and bronchitis (Chika and Bello, 2010; De Morais Lima, 2012; Marquardt et al., 2020).</td>
<td>Activity against <em>B. subtilis</em> and <em>S. aureus</em> was displayed by the leaf extracts (Gaidamashvili and Van Staden, 2002).</td>
<td>3′,4′,5,7-Tetrahydroxyflavan; homoorientin; 2′′-O-galloylisovotexin; 3′,4′,5′,7-pentahydroxyflavan; orientin; 2′′-O-galloylmyricetin; myricetin-3-O-glucoside; 2′′-O-galloylohomoorientin; Isovitexin; Kinkeloid Al–D2 (Welch, 2010).</td>
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<td>Roots decoction is utilized as an aphrodisiac for the treatment of venereal syndrome and to purge patients of duodenal worms and microbial treatment (Gaidamashvili and Van Staden, 2002; McGaw et al., 2001).</td>
<td>Isolated lectin-like proteins for COX exhibited in vitro COX-1 activity with 72% inhibition (Gaidamashvili and Van Staden, 2006).</td>
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<td>The powdered root part is used as a wound dresser. Elixirs of the roots are used for leprosy, hookworm, fever, snakebite, general body swelling, stomach pains, and abortion (Fyhrquist et al., 2006; Masoko and Ellof, 2007; Ntshanka et al., 2020; Suleiman et al., 2013).</td>
<td>Leaf extracts were found to be effective against <em>E. faealis</em> (Ellof, 1998, 1999; Pegel and Rogers, 1985).</td>
<td>Lectins from leaf extracts (Gaidamashvili and Van Staden, 2002).</td>
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<tbody>
<tr>
<td><em>Combretum nigricans</em> Lepr.</td>
<td>Fairly tall tree in the tiger bush</td>
<td>Aqueous leaf extracts are used to treat stomach problems and as an expectorant. Also, used for the management of innumerable infections such as conjunctivitis, cutaneous, rheumatism, and icterus (Fyhquist et al., 2006; Simon et al., 2003).</td>
<td>Methanolic fraction of the fresh leaves inhibited the development of human tumor cell lines: bladder (J82), colon (HCT-15), non-small-cell lung (A549), and glioblastoma (U-373), cancer models (Jossang et al., 1996; Simon et al., 2003).</td>
<td>1α-Acetoxy-20,24-epoxy-25-hydroxy-dammar-3-one; arjungenin; arjunglucoside; (U-373), cancer models (Jossang et al., 1996).</td>
</tr>
<tr>
<td><em>Combretum padoides</em> Engl. &amp; Diels</td>
<td>Thicket bushwillow</td>
<td>Aqueous leaves and root extracts are utilized to treat conjunctivitis, snakebites, gastrointestinal complications, bloody diarrhea, and wounds, to eliminate hookworms, and as antimalarial (Ahmed et al., 2014; Fyhquist et al., 2006; Gathirwa et al., 2011; McGaw et al., 2001).</td>
<td>Microdilution assay of dried leaves of acetone, hexane, MeCl, or MeOH extracts have exhibited antifungal activities against A. fumigates, S. schenkii, M. canis, C. neoformans, and C. albicans with MIC stretching from 0.02 to 2.5 μg/ml (Masoko et al., 2007).</td>
<td>1α,23-β-Dihydroxy-12-oleanen-29-oic acid; 23-β-0-α-4-acetylrhamnopyranoside; 2,6,7-Trihydroxy-3,4-dimethoxyphenanthrene; 2,6,7-trihydroxy-3,4-dimethoxyphenanthrene (Angeh et al., 2007b).</td>
</tr>
<tr>
<td><em>Combretum psidioides</em> Welw.</td>
<td>Peeling bushwillow</td>
<td>Mixtures are used for coughs, chest problems, and pain treatment in the spinal cord, and root infusion is applicable. Aqueous leaves and root extract have been used for treating diarrhea, back pain, rheumatic pain, muscle pain, malaria, and derma.</td>
<td><em>In vitro</em> cytotoxicity potentials against T24 bladder, MCF7 breast, and HeLa cervical cancer (LC50 = 25 μg/ml) have been observed for methanolic extracts of dried stem bark, fruit, and root (Fyhquist et al., 2006; Nopsiri et al., 2014). Aqueous, EtOH (95%), EtOAc, and Pet ether extracts of root bark have displayed <em>in vitro</em> antimalarial activity against <em>P. falciparum</em> by microdilution assay (IC50 for drugs: 6.5–39.0 μg/ml (Gessler et al., 1994))</td>
<td>1α,23-β-Dihydroxy-12-oleanen-29-oic acid; 23-β-0-α-4-acetylrhamnopyranoside; 2,6,7-trihydroxy-3,4-dimethoxyphenanthrene; 2,6,7-trihydroxy-3,4-dimethoxyphenanthrene (Avagyan et al., 2007b).</td>
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<td>Hot water elixirs of roots and leaf extracts; or powdered fresh or dried leaves mixed with maize porridge (Ugali) have been used to manage diarrhea and edema (Fyhquist et al., 2006, 2020; Gessler et al., 1994).</td>
<td>Crude methanol extract; its CHCl3, and butanol portions have exhibited development inhibitory activity against <em>Mycobacterium smegmatis</em> with MIC values stretching from 625 to 2,500 μg/ml (Fyhquist et al., 2020).</td>
<td>2,3,6,7-Trihydroxy-3,4-dimethoxyphenanthrene; 7-hydroxy-2,3,4,6-tetramethoxyphenanthrene; 2,6,7-trihydroxy-3,4-dimethoxyphenanthrene; 2,3,6,7-tetramethoxy-9,10-dihydrophenanthrene; 2,7-dihydroxy-3,4,6-trimethoxyphenanthrene; 7-hydroxy-2,4,6-trimethoxy-9,10-dihydrophenanthrene; 7-hydroxy-2,4,6-trimethoxyphenanthrene (Kovacs et al., 2008).</td>
</tr>
</tbody>
</table>

Continued
Combretum species

Common name

Combretum quinqueloratum Kurz.

Ethnobotanical use

Shrub or small tree

Crushed stem decoction is applied externally as a fomentation.

The sap is rubbed onto the forehead to lessen fever.

The flowers are chewed to reinforce gums and strengthen the teeth.

The plant is reaped from the wild for indigenous medicinal use.

Biological activity

Three triterpenes: 6β-hydroxyhovenic acid, lupane type, 2α,6β-dihydroxybetulinic acid, and an oleanane type, 6β-hydroxyarjunic acid (Adnyana et al., 2000a, 2001a).

The seeds methanolic extract of C. quinqueloratum has exhibited effective hepatoprotective activity against TNF-α (Adnyana et al., 2000a, 2001a; Toume et al., 2011).

Ethanolic extract of the dried leaf via Agar disc diffusion method showed MIC: <0.125 mg/ml and zone of inhibition 10.0 ± 0.5 mm against S. aureus (Masengu et al., 2014).

Three fractions of the leaves of C. quinqueloratum, fractions I and II were collected as well as a control (Adnyana et al., 2000a, 2001a).

Seeds methanolic extract of C. quinqueloratum has exhibited antioxidative potentials. The antioxidant potentials gave an ABTS and DPPH radical scavenging capacity with IC₅₀ values of 76.62 ± 0.0040 and 5.16 ± 0.0169 μg/ml, respectively (Adnyana et al., 2001a).

The Aqueous extract of the roots and leaf has been utilized to cure bacterial-related contaminations and oxidize-related diseases such as pneumonia, syphilis, chest, diarrhea, coughs, and colds (Ahmed, 2012; Dawe et al., 2013; Komape et al., 2014).

Methanolic extract of the leaf part showed DPPH radical scavenging potential (Lwal et al., 2016).

Bioactive compounds isolated

(16r)-16-O-α-L-arabinofuranosyl-3β-hydroxymansumbin-13(16)-29-sic acids, (16r)-16-O-α-L-arabinofuranosyl-3β-hydroxydammar-24-dien-28-oic acid and (16r)-16-O-α-L-arabinofuranosyl-3β-hydroxydammar-24-dien-28-oic acid methyl ester; 4β,14α-dimethyl-5α,12,19-dien-28-oic acid β-d-glucopyranosyl; 5,7,3′,5′-tetrahydroxy-3,4′-dimethoxyflavone; 28-O-β-d-glucopyranosyl-6β,23-dihydroxytormentic acid (Adnyana et al., 2000a, 2001a; Toume et al., 2011).

Nine new, combretane-type, a-amyrantric acid methyl ester; 4β,14α-dimethyl-5α,12,19-dien-28-oic acid β-d-glucopyranosyl; 3′-O-[α-D-galactopyranosyl(1→2)]-α-D-glucose; 5,7,3′,5′-tetrahydroxy-3,4′-dimethoxyflavone; 28-O-β-d-glucopyranosyl-6β,23-dihydroxytormentic acid (Adnyana et al., 2000a, 2001a; Toume et al., 2011).

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<td>Combretum quinqueloratum</td>
<td>Shrub or small tree</td>
<td>Crushed stem decoction is applied externally as a fomentation. The sap is rubbed onto the forehead to lessen fever. The flowers are chewed to reinforce gums and strengthen the teeth. The plant is reaped from the wild for indigenous medicinal use.</td>
<td>Three triterpenes: 6β-hydroxyhovenic acid, lupane type, 2α,6β-dihydroxybetulinic acid, and an oleanane type, 6β-hydroxyarjunic acid.</td>
<td>(16r)-16-O-α-L-arabinofuranosyl-3β-hydroxymansumbin-13(16)-29-sic acids, (16r)-16-O-α-L-arabinofuranosyl-3β-hydroxydammar-24-dien-28-oic acid and (16r)-16-O-α-L-arabinofuranosyl-3β-hydroxydammar-24-dien-28-oic acid methyl ester; 4β,14α-dimethyl-5α,12,19-dien-28-oic acid β-d-glucopyranosyl; 5,7,3′,5′-tetrahydroxy-3,4′-dimethoxyflavone; 28-O-β-d-glucopyranosyl-6β,23-dihydroxytormentic acid.</td>
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<tr>
<td>Combretum woodii Dümmer</td>
<td>Large-leaved forest bushwillow</td>
<td>Leaves and barks extracts are used to manage chest complaints/pains, and microbial infections (Eloff et al., 2005; Masoko and Eloff, 2007; McGaw et al., 2001).</td>
<td>Combretastatin B5 showed a MIC = 16 µg/ml against <em>S. aureus</em>, while 1.25 µg/ml was observed against <em>E. faecalis</em> and <em>P. aeruginosa</em> (Eloff et al., 2005). Aqueous, acetone, and AcOEt leaf extracts using radioactivity bioassay have exhibited <em>in vitro</em> COX-1 inhibition; and <em>in vitro</em> anthelmintic against larvae of <em>C. elegans</em> var. Bristol at concentrations of 0.5 and 1 µg/ml (McGaw et al., 2001). Ethyl acetate fraction demonstrated an average MIC of 50 µg/ml against <em>E. coli</em>, <em>P. aeruginosa</em>, <em>E. faecalis</em>, <em>S. aureus</em>, acetone, and methylene dichloride fractions with MIC = 140 µg/ml. Fractions of acetone and methylene dichloride gave a total activity of 1,279 and 1,309 ml/g (Eloff et al., 2005). Acetone, DCM, and methanol elixirs demonstrated antioxidant activity after sparging chromatograms with DPPH (Masoko and Eloff, 2007).</td>
<td>Combretastatin B5; A stilbene; bibenzyl (Eloff et al., 2005).</td>
</tr>
<tr>
<td>Combretum yunnanense Exell</td>
<td>Forests, sparse woods</td>
<td>Sequestered compounds from the ethanolic leaves extract and stems have displayed cytotoxicity <em>in vitro</em> against five human cancer cell lines: SMMC-7721, MCF-7, A-549, SW480, and HL-60 (Wang et al., 2011).</td>
<td>Acetone leaf extracts possess some antibacterial potential (Eloff, 1999). <em>Bacillus subtilis</em> and <em>E. coli</em> by agar disc diffusion method exhibited MIC = less than 0.125 mg/ml and MIC = less than 0.004 mg/ml, respectively, with inhibition zone (18.5 ± 0.5 mm). <em>Candida albicans</em> (MIC: 0.03 mg/ml) (Masengu et al., 2014). Methanolic extracts of root and fruits exhibited <em>in vitro</em> cytotoxicity on MCF7 breast cancer cells with LC&lt;sub&gt;50&lt;/sub&gt; value of 25.00 µg/ml (Nopsiri et al., 2014).</td>
<td>Combretastatin B5; Combregenin, arjunogenin, arjunglucoside I, combreglucoside, betulinic acid, arjunic acid, arjunetin, asatic acid, ursoic acid, and maslinic acid (Wang et al., 2011). 2,4,4′-Trihydroxychalcone, 1-(2-methoxy-4-hydroxyphenyl)-3-(3-hydroxy-4-methoxyphenyl)-propane, eriodictyol, and combrequinone A–C (Wu et al., 2011). Combretol A–E; β-sitosterol; Scopoletin (Wang et al., 2011). 4-(α-Rhamnopyranosyl)ellagic acid; ellagic acid; 4-(4′′-O-acetyl-α-rhamnopyranosyl)ellagic acid (Asami et al., 2003). Arcapitin A (Facundo et al., 2008). Oleanolic acid; terminolic acid; 6β-hydroxymaslinic acid; 2α,3β-dihydroxyurs-12-en-28-oic acid; methylsumaresinolate (Ahmed, 2012; Runyoro et al., 2013). Maslinic acid (Runyoro et al., 2013).</td>
</tr>
<tr>
<td>Combretum zeyheri Sond.</td>
<td>Large-fruit bushwillow or Raasblaar</td>
<td>Inhalation of the burnt leaves smokes for the cure of coughs. Colic is alleviated with the unpleasant-tasting water extracts of dried pulverized and root infusion leaves. Also, for the treatment of bloody diarrhea (Ahmed, 2012; Roy et al., 2014a).</td>
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C. molle against stomach disorders; C. molle, C. imberbe, and C. erythrophylum against coughs (Eloff et al., 2008).

The medicinal benefits of Combretum species lie in some vital chemical constituents responsible for certain physiological and drug development (Ademola and Eloff, 2010; Moraes et al., 2016; Roy et al., 2014a, 2014b). Combretum species possess antimicrobial activities (Adamu et al., 2005; Katerere et al., 2003; Masika and Afolayan, 2002; Olukoya et al., 1993). Chemicals constituents from Combretum stem bark are rich in flavonoids, triterpenoids, phenanthrenes and their derivatives, diarylpropanes, and stilbenoids and their derivatives. Isolates or extracts from this class of species have shown several bioactivities, including antibacterial, antifungal, antidiabetic, antihyperglycemic, cytotoxicity, and inhibitory activities, against different human tumor cell lines, anti-inflammatory, antimalarial, anti-snake venom, and anti-HIV/AIDS properties. Also, they have been used for the management of diverse infirmities and diseases (Aderogba et al., 2012; Facundo et al., 1993; Katerere et al., 2012; Kgate, 2007; Longhi-Balbinot et al., 2009, 2011; Sabo and Knezevic, 2019; Welch, 2010). The species of Combretum has featured conspicuously as an agent for handling infectious diseases as exemplified in Table 1.

**Evidence for medical efficacy of Combretum species**

Phytochemical investigations to determine the medical efficacy of Combretum, the most widespread genus of Combretaceae, has paved the way several constituents comprising flavonoids, triterpenoids, phenanthrenes and their derivatives, diarylpropanes, and stilbenoids and their derivatives. Isolates or extracts from this class of species have shown several bioactivities, including antibacterial, antifungal, antidiabetic, antihyperglycemic, cytotoxicity, and inhibitory activities, against different human tumor cell lines, anti-inflammatory, antimalarial, anti-snake venom, and anti-HIV/AIDS properties. Also, they have been used for the management of diverse infirmities and diseases (Aderogba et al., 2012; Ares et al., 2006; Belkaid and Hand, 2014; Chika and Bello, 2010; Dawe et al., 2013; De Morais Lima et al., 2012; Kenvoufo et al., 2008; Khumalo et al., 2018; Masoko et al., 2007; Motsumi et al., 2020; Nagata et al., 2011; Uzor and Osadebe, 2016). Antidiabetic activity through adenosine monophosphate-activated protein kinase activation by quercetin from flower extracts of C. lanceolatum has been reported (Dechandt et al., 2013). Anti-candidiasis agents from African Tanzanian plant: C. zeyheri (Runyoro et al., 2013), while lignin derivative from C. alfredii (Bai et al., 2016). Combretum species have also shown great potential as sources of various secondary metabolites. Metabolites and their related endophytic fungus Nigrospora oryzae as proof of a metabolic conglomerate from C. dolichopetalum have been reported by Uzor et al. (2015).

Studies on the antioxidant, antibacterial, cytotoxicity, and antifungal potentials of solvent-to-solvent fractionations of C. erythrophylum (Burch.) leave elixirs revealed that Combretum species are nontoxic for usage in traditional medicine for the management of infectious and stress-related diseases (Mtuoni et al., 2017b). Methanolic extract of the C. adenognonum Steud. ex A. Rich stem barks inhibited C. chauvoei (Jakari strain) neumaminidase activity as reported by Ushe et al. (2004) at 100–1,000 μg/ml with an estimated LC50 value of 150 μg/ml. Extracts from the stem bark, root, and leaf have the potential as antibacterial, antifungal, and antiproliferative agents (Fyhrquist et al., 2006; Maregesi et al., 2007). Ethanolic stem bark, root, and leaf elixirs have displayed antioxidant by microdilution methods, an anti-HIV-1 protease with LC50 value of 24.7 and 26.5 μg/ml for root and stem bark extracts, respectively, and cytotoxic activities using brine shrimp’s lethality assay (Mushi et al., 2012).

Acetone elixir of Combretum mole stem bark had inhibited the evolution of Mycobacterium Tuberculosis typus humanus (ATCC 27294) (Asres et al., 2001), inhibits HIV-1 reverse transcriptase (Bessong et al., 2005). Aqueous-methanol stem bark elixir of C. mole has exhibited anthelmintic activity in infected lambs with H. contortus via faecal egg count reduction test (Simon et al., 2012; Suleiman et al., 2013). Interestingly, powdered and decoctions of C. mole root part have been used as a wound dresser for treatments of leprosy, fever, snake bite, stomach pains, all-purpose body swelling, hookworm, and abortion. While the activities of this C. mole associated with bioactive compounds such as hydrolysable tannin and punicalagin demonstrated antimycobacterial properties (Asres et al., 2001). Compounds such as malasinic acid, ursoic acid; combretastatin B5-O-2’-beta glucopyranoside, corosolic acid, arjunolic acid, combretastatin B1-O-2’-beta glucopyranoside (Ahmed, 2012) isolated from C. vendee A.E. van Wyk have exhibited antimicrobial and antifungal activities (Ahmed et al., 2006; Suleiman et al., 2010); antiradical activity with the EC50 of lesser or analogous to the control (Ahmed, 2012).

**CONCLUSION**

The reports detailed in this review advocate using medicinal plants as alternative medicine. Combretaceae species have displayed a broad spectrum of ethnopharmacological potentials for treating infectious diseases, exhibits significant antimicrobial and antifungal potentials against varieties of bacterial and fungal species, respectively, and also exhibit good antioxidant, anti-inflammatory, antimalarial, antituberculosis, antidiarrhoea, cytotoxicity, anthelmintic, antischistosomal, COX-1 inhibition, and HIV-1 integrase inhibition. Phytochemical constituents of the species are great prospective agents for averting and treating many related oxidative stress diseases. Even though the oils from some of these species have not been harnessed as a fragrance in the perfumery, food, and beverage industry; the oils and active compounds may also possess great potential for protecting food and cosmetics from microbial spoilage. Hence, medicinal plants can be seen as an alternative to medicine if properly used as prescribed or as a precursor for synthesizing chemotherapeutic agents for disease control. Concerning the above investigation, it is evident that Combretaceae species contain bioactive compounds such as triterpenoids, glycosylated triterpenes, and phytochemical constituents of biological importance. Given these outstanding values, few pharmacological and phytochemical analyses have been conducted. Hence, it will greatly benefit the health sector and medicinal chemistry if further research is encouraged and carried out toward identifying bioactive compounds and corroborating their medicinal and pharmacological properties. Areas of research in the economy, domestication, and proliferation, as well as quality control and procedures for sustainable utilization of these plant species as future potential antibiotic and chemotherapeutic agents, should be prioritized. This should be a priority for researchers and
stakeholders as these plants can increase the well-being of the populace who finds solace in them.

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