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South African Medicinal Plants Used in the Treatment of Human Bacterial Infections: An updated Review

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Traditional medicine based on the use of medicinal plants plays an important role in the preservation of health and well-being of many people globally. Today herbal medicine application is progressively finding more significance especially with the acknowledgement of the challenges of antibiotic resistance. The aim of this review was to collect literature based on the traditional application of South African medicinal plant species used in South Africa to prevent and treat various pathogenic bacterial infections. The search was carried out using key electronic scientific databases including PubMed, Google Scholar, SpringerLink, ProQuest, Science Direct, Elsevier, BioMed Central. Other sources of literature included scientific articles, book chapters, dissertations, theses and websites. It was found that Bacillus spp., Escherichia coli, Staphylococcus aureus and Pseudomonas aeruginosa were the most frequently investigated bacterial pathogens which have developed resistance to most of the available standard antibiotics. Organic and aqueous extracts of many South African plants including Acacia karroo, Psidium guajava, Punica granatum, Eucomis autumnalis, Vernonia amygdalina and Cyathula uncinulata have demonstrated potent antibacterial efficacy against the aforementioned pathogens. This review exemplifies that South African medicinal plants have the potential to be considered as new leads for the development of antibacterial agents against resistant pathogens.

Keywords: Antibiotic resistance, Antimicrobials; Human bacterial infections; Medicinal plants; South Africa.

Medicinal plants play an important role in the preservation of health and well-being of many people and animals across the globe [1-2]. In the past, many people have relied on indigenous herbs with remedial actions for the prevention and treatment of infectious diseases [3]. There is a growing amount of literature on the use of medicinal plants and their benefits, across the world including South Africa [4-5].

According to ethnobotanical survey, South Africa has a strong history of traditional healing and anchors a rich biodiversity of more than 30 000 plant species [6-8]. However, over 4000 species are recognised to have ethnobotanical importance, with more than 3000 plants used for medicinal purposes [9-10]. Notably, more than 10% of the world's higher plant species of medicinal value grow in South Africa [7-8]. Furthermore, most

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of these plant species are native species while a few are exotic species which were accidentally or deliberately introduced to South Africa over the years [11].

The use of medicinal plants to treat vast diseases by inhabitants of Sub-Saharan Africa is enormous so that the traditional medicine has been understood as part of African culture [12]. According to researchers, medicinal plants have a myriad of diverse bioactive compounds with complex chemical profiles that contributes to their massive usage in the treatment and prevention of many diseases [7, 13, 14]. These diseases include, but not limited to, asthma, diabetes, cancer, food borne diseases, nosocomial infections, mental and gynaecological problems, hypertension as well as tuberculosis [4, 15, 16].

However, the majority of the diseases are caused by organisms of bacterial origin including but not limited to *Staphylococcus aureus, Escherichia coli, Mycobacterium tuberculosis, bacillus* spp., *Klebsiella* spp., *Streptococcus* spp. and *Pseudomonas* aeruginosa [15, 17]. Many scientific investigators have reported these bacterial pathogens of being resistant to a majority of the mainstream antibiotics design to kill them including those of last resort such as carbapenems, colistin, and tigecycline [18-20]. Due to this phenomenon, the frail are left with no other choice but to explore medicinal herbs as an alternative means to regain health [21-23]. [16], have reported the potential incorporation of traditional medicine with the Western counterparts as part of its primary healthcare approach in South Africa.

Scientific studies depicted that plants growing in South Africa have been used to remedy many bacterial infections including but not limited to diarrhoea, dysentery, skin and wound diseases, tuberculosis and pneumonia [17, 24-26]. Also, [10] recounts the historical systematic use of medicinal plants in South Africa to treat bacterial diseases and the progress that has been made which could lead to future exploration of these plants as new pharmaceuticals. Today, South Africa has a good documented record of medicinal plant use to cure infectious diseases including those of bacterial origin [17]. Therefore, the aim of the study was to report on South African medicinal plant used in the treatment of human bacterial infections.

MATERIALS AND METHODS

The search was carried out using key electronic scientific databases including PubMed, Google Scholar, SpringerLink, ProQuest, Science Direct, Elsevier, BioMed Central. Other sources of literature included scientific articles, book chapters, dissertations, theses and websites. The key words such as "medicinal plants", "antioxidants", "bacterial infections", "traditional medicines", "bioactive compounds", and "South Africa", were used to get the trimmed searches.

Parts of medicinal plants frequently used

It has been reported that the herbal preparations used during various treatments comes either from whole plant or from parts including the leaves, flowers, tubers, stems, roots, fruits and barks [27-28]. However, the parts of plants reported as frequently used in traditional medicine practices in South Africa includes but not limited to the ones listed below:

Bark

Tree barks are made of a hard outer layer of actively dividing living cells which functions to transport nutrients, acts as a physical barrier and protects the plant [29-30]. Some researchers have reported that the barks of most medicinal plants contain substantial amounts of bioactive substances necessary to prevent and cure a variety of infections [31-32]. According to [33], more than 30% of the woody plant bark used in the Limpopo province in South Africa have been reported to have high medicinal values. In South Africa, more than one third of the plant materials used in traditional medicine comes from the bark of plants [32, 34].

Leaf

The leaf of a plant is an important structure as it manufactures food that the plant needs for its growth and survival through the process of photosynthesis [35]. The leaf is also fused with green substances known as chlorophyll which absorbs sunlight that aids in the conversion of carbon dioxide and water to glucose needed for plant's growth [35]. However, some of the leaves used during traditional medicine practices are known to contain bioactive substances including the leaves of *Burkea Africana, Lippia javanica* and *Leucaena leucocephala* [36-38].

Root

Plants roots help to anchor the plant to a surface by creating resistance and helps to transport substances necessary for its growth from the soil to the rest of the plant [39]. In traditional medicine, the application of plant roots either independently or in combination with other plant parts is common as reported by [40-41]. Research has demonstrated that most roots of plants used in traditional medicine contains important phytochemicals [42-43]. Some of the plants that have their roots used as medicine includes but not limited to devil's claw root, stinging nettle root and ginseng [42, 44].

According to [41], most traditional healers are convinced that the roots and bulbs of plants or any part hidden beneath the earth contains higher healing powers than any other plant part. In line with this, a research by [40] found out that the roots and other under-ground parts of plants holds elevated concentrations of plant natural substances. According to an ethnobotanical survey conducted by [27-28], the roots and barks are the most used and preferred over other parts by the indigenous people. Furthermore [45], was in agreement with this and reported on similar findings that the bark and roots are the most favoured parts of plants used by the Tsonga people of Mpumalanga province in South Africa, as illustrated in Figure 1.

Antimicrobial ethno-medicinal plants used in South Africa

According to World Health Organisation, more than 60% of people depend on traditional medicine for the purpose of preventing and treating diseases [46]. This includes 80% of the populations from underdeveloped and developing countries including South Africa [45, 47]. The traditional application of medicinal plants as medicine is one of the key sources of health care in South Africa [16]. Additionally, South Africa is reputable for traditional healing using medicinal plants and it is estimated that over 27 million people in both townships and the rural communities prefer and rely on traditional medicine for their primary health care [9, 45, 48]. Of this, [16] reports that 72% of the population are the Black Africans including the Zulus, the Xhosa, the Bapedi, the Venda people, the Northern and the Southern Sotho people make use of traditional herbal medicine the most. A recent survey conducted by [16], on the use of natural plant products to treat human diseases in the Limpopo province of South Africa had similar findings. However, the remainder of the population including the Whites, mixed race, Indians and Chinese also use traditional medicine but at a lesser extent [49]. Numerous ethnobotanical surveys done in South Africa revealed that a significant amount of plant species are used as medicine especially in regions including KwaZulu-Natal and Limpopo to relieve symptoms of bacterial, fungal and viral infections as shown in Table 2 [5, 45, 50].

In addition, [27] reported on parts from one plant species frequently used during the preparation of natural product medicine than a mixture of species. However, it is logical to speculate that harvesting and using parts from one plant species especially the roots as medicine is not sustainable as the plant survival is endangered. This practice of overharvesting and exploitation can kill the plant resulting to devastating consequences including species extinction [51]. This is particularly true for slow-growing and protected species [50].

Table 1 below shows the various plant species used to treat human ailments, parts, methods of preparation, parts of the plants that are commonly used, traditional therapeutic uses, and the distribution of plant in South Africa.

Bacterial diseases treated with indigenous medicinal plants in South Africa

It is not new that people use medicinal herbs to treat common health problems [16, 58, 92]. Previously published ethnobotanical reports elucidates that some of the illnesses and/ infections commonly prevented or treated with local medicinal plants in South Africa includes, but not limited to, oral infections, heart and lung problems, sexually transmitted infections (STIs), diabetes mellitus, headaches, infertility, erectile disorder, skin problems, gastrointestinal infections including diarrhoea, Human Immunodeficiency Virus / Acquired Immune Deficiency Syndrome (HIV/ AIDS) and related infections, wounds, cancer, cardiovascular diseases, respiratory ailments including coughs and tuberculosis (TB), just to name a few [12, 16, 25, 28, 32,57-58].

According to past and resent research, South Africa has an elevated level of infectious diseases burden notably from bacterial origin [5, 93]; even though viral, protozoal and helminthic, as well as yeast infectious agents have also been reported [17, 94-96]. This is in consistence with the research by [93, 95,

[95], who reports that a larger proportion of the deaths in South Africa results from infectious diseases including tuberculosis, sexually transmitted infections (STIs) and diarrhoea.

Tuberculosis

The bacterium, *Mycobacterium tuberculosis* (TB) is the causative pathogen for tuberculosis which is problematic to the medical community and causes more than 1.5 million deaths in a year worldwide [89, 97]. In South Africa it is estimated that 28% of TB infection burden is due to HIV it its population, thus ranking fourth largest globally [98]. According to a review by [94], in the year 2013 alone South Africa recorded 860 TB cases per 100 000 people. It is worth noting that tuberculosis has been reported as the leading cause of death in South Africa [5, 65, 95].

A substantial number of studies have reported TB resistance to many pharmaceutical medications giving rise to multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) [95, 99-100]. However, plant natural material has been widely applied to treat TB infections due to the presence of its chemical constituents including alkaloids, glycosides, tannins, phenolics, xanthones, quinones, sterols and triterpenoids [30, 97, 101].

The Bapedi traditional healers in the Limpopo province use a variety of plants including *Psiadia punctulata* (DC.), Vatke and *Xerophyta retinervis* Baker to cure TB and its associated secondary infections [5]. The Jongilanga local community in Mpumalanga also apply medicinal plants to remedy conditions of cancer, TB and acne [45]. According to a research by [101], some herbs that are used by the inhabitants of the Free State Province to treat TB are active at very smaller concentrations and these includes *Dicoma anomala* (0.195 – 6.25 mg/ml), *Hermannia depressa* (0.78 – 1.56 mg/ml), *Senecio harveianus* (0.195 – 0.39 mg/ml) and *Lotononis lanceolate* (0.195 - 0.65 mg/ml).

Sexually transmitted infections (STIs)

Venereal diseases also called sexually transmitted infections (STIs) are mostly caused by bacterial pathogens including *Treponema pallidum* which causes syphilis, *Neisseria gonorrhoeae* which causes gonorrhoea and *Chlamydia trachomatis* which causes chlamydia infections [102-104]. However viral and parasitic pathogens have been reported to also cause STIs [76, 104]. It is estimated that in a year, in South Africa more than 11 million STI infections are recorded in the health registers [103, 105]. The misconceptions and stigma attached to STIs in South Africa cause most of the people to favour traditional homemade remedies using medicinal plants over hospitals and local clinics visits [105]. Apart from that, undesirable effects as well as resistance to most STI orthodox medications have been reported [103].

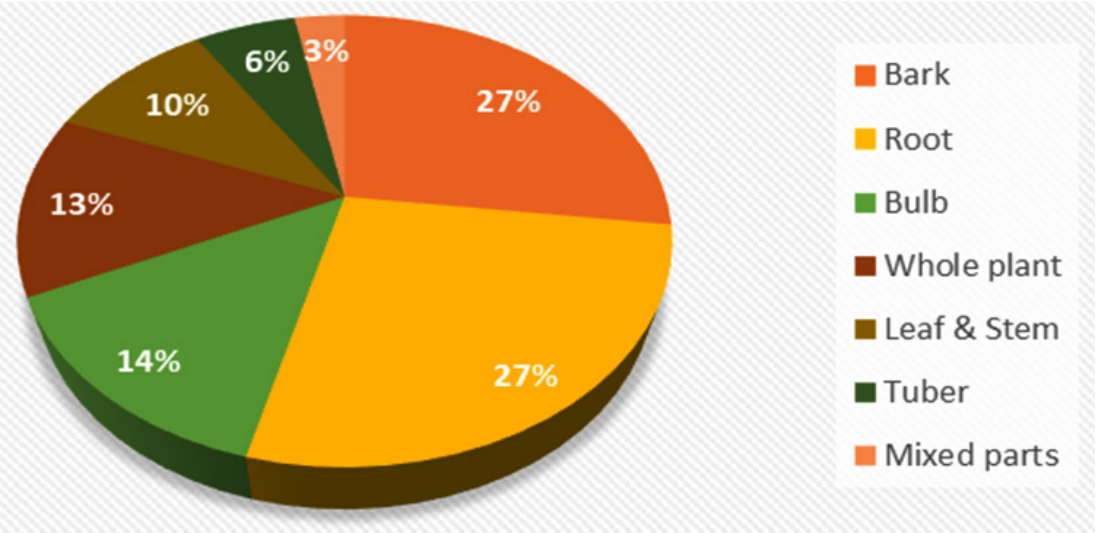

Fig. 1. Percentage of the parts of plants frequently used for preparing traditional medicines in South Africa. Adapted from Lall et al., (2018)

Table 1. Plants commonly used for medicinal purposes in South Africa to treat human ailments

Botanical name	Family	Common name	Plant parts used	Method of preparation	Traditional therapeutic uses	Distribution in South Africa (Exotic or Indigenous)	References
Acacia karroo Hayne = *Vachellia karroo* (Hayne) Banfi & Glasso [26, 41, 52- 53]	Fabaceae (Sub Family Mimosoideae)	Sweet thorn	Leaves Root Gum leaf decoction applied externally	Decoction	Oral thrush, mouth ulcers, diarrhoea, stomach ache, dysenteries, headache, eye infections, colds, wounds abscesses, STIs [26, 41, 52, 53]	Eastern Cape Mpumalanga (Indigenous)	26, 41, 52-53
Acorus calamus L.	Acoraceae	Sweet flag	Rhizome Stem	Decoction	Diarrhoea, ingestion, dysentery, worms, asthma	KwaZulu-Natal (Exotic)	54-55
Albizia adianthifolia (Schumanch.) W.Wight	Fabaceae	Flat-crown albizia, Rough-bark flat-crown albizia,	Bark Leaf Root	Infusion	Skin rashes (purulent), chicken pox, abscess, eczema, scabies, itchy skin complaints, headache, haemorrhoids, bronchitis, cough, sinusitis, respiratory problems, tooth ache, gonorrhoea	Eastern Cape KwaZulu-Natal Limpopo Mpumalanga (Indigenous)	32, 57-58
Allium sativum L.	Alliaceae	Garlic	Leaf Bulb/Rhizome Cloves	Decoction Infusion Pounded Chewed	Throat infection, tuberculosis, asthma, stomach complaints	Eastern Cape (exotic)	59-62
Aloe arborescens Mill.	Asphodelaceae	krantz aloe	Leaf Root	Decoction Powder	Skin problems, wounds, burns, abrasions, ulcers, inflammation, diarrhoea, constipation, tuberculosis, vomiting, urinary problems	Eastern Cape Gauteng KwaZulu-Natal Limpopo Mpumalanga, North West Western Cape (Indigenous	25, 50
Aloe barbadensis Mill.	Asphodelaceae	Aloe vera	Root Leaf	Decoction Topical gel Pulverised	Wounds, burns, oedema, tumour, inflammation, gastric ulcers, HIV/AIDS, stomach complaints, colic	KwaZulu-Natal (indigenous	19, 63-64
Artemisia afra Willd.	Asteraceae	Wild wormwood, African wormwood	Leaf Stem	Decoction Infusion Inhaled	Coughs, colds influenza, fever, and gastrointestinal disorders, earache, intestinal worms, colic, malaria, bladder and kidney problems, gout, mumps, pain	Eastern Cape Free State Gauteng KwaZulu-Natal Limpopo, North West Northern Cape Western Cape	65
Bidens Pilosa L.	Asteraceae	Black jack	Stem Leaf Root	Decoction Infusion	Genital warts, syphilis, abdominal problems, dysentery, diarrhoea, colic, stomach pain, prostate gland tumour, inflammation, wounds or burns	KwaZulu-Natal Limpopo (Exotic	66-67
Boophone distrihca (L.F.) Herb.	Amaryllidaceae	Am Century plant	Bulb	Decoction	Inflammation, wounds, skin rashes, burns, boils, cuts,	Eastern Cape Free State Gauteng	67-68

		Poison bulb, Sore-eye flower aryllidaceae			tuberculosis, gynaecological problems	KwaZulu-Natal Limpopo Mpumalanga Western Cape (Indigenous)	
Caesalpinia decapetala (Roth) Alston.	Fabaceae	Mysore thorn	Stem Root	Decoction	Gonorrhoea Dysmenorrhoea	Limpopo (Indigenous-invasive weed)	27, 69
Cannabis sativa L. var. sativa	Cannabaceae	Marijuana Hemp	Leaf	Maceration	Tuberculosis, headache, pain	Limpopo North-West Gauteng Mpumalanga KwaZulu-Natal Western and Eastern Cape (Exotic)	11, 27
Carica papaya L.	Caricaceae	Papaya Papaw	Leaf Root	Decoction	Gonorrhoea, Stomach problems, venereal infections, STIs	KwaZulu-Natal Limpopo (Maputuland)- (Exotic)	11, 27, 57
Cassia abbreviata Oliv. subsp. beareana (Holmes) Brenan	Fabaceae	Long-tail cassia	Root Bark Twig	Decoction Infusion	All STIs, erectile dysfunction, chest pain, asthma, pneumonia, toothache, stomach problems, AIDS (HIV)	Limpopo Mpumalanga (Indigenous)	5, 28, 61, 67
Citrus limon (L.) Burm.f.	Rutaceae	Lemon tree	Leaf Peel Fruit	Decoction	Coughs, colds, unspecified respiratory symptoms, fever, headache, tuberculosis	KwaZulu-Natal Limpopo (Exotic)	62, 70
Combretum molle R.Br.ex G. Don	Combretaceae	Velvet bush willows	Leaf Root	Decoction Infusion	Gonorrhoea, sores, syphilis, wounds, asthma, stomach complaints	Free State, Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West (Indigenous)	34, 57, 71
Commelina africana L.	Commelinaceae	Yellow commelina, Wandering Jew, Dayflower	Root	Decoction	Venereal diseases, menstrual cramps in women, hypertension, infertility, pelvic pains and bladder complains	Eastern Cape Free State Gauteng, KwaZulu-Natal Limpopo Mpumalanga North West Northern Cape Western Cape (Indigenous)	72-73
Curtisia dentata (Burm.f.) C.A.Sm. (endangered species - legally protected)	Cornaceae	Assegai	Stem bark	Scarce species so only used in special bark mixes called ‘ikhubalo’	Stomach complaints, diarrhoea, STIs, pimples	KwaZulu-Natal Mpumalanga (indigenous)	31,34, 74
Diospyros mespiliformis Hochst. Ex A. DC	Ebenaceae	African ebony	Bark Root (roasted and pulverized) Leaf	Decoction Infusion Powdered	Stomach ailments, ulcers diarrhoea, stop vomiting, treat worms, pneumonia, syphilis, cough, tuberculosis, bronchial diseases, leprosy, wounds	Limpopo (Indigenous)	69, 79
Dombeya	Sterculiaceae	Wild pear	Root	Decoction	diarrhoea and abdominal pains,		27, 73, 75-77

rotundifolia (Hochst.) Planch. var. rotundifolia	(=Malvaceae)		Bark Leaf Wood Whole	Infusion	colic, chest pain, pneumonia, headache, meningitis, fever, abscess, dysentery and other stomach problems, intestinal ulcers	KwaZulu-Natal Limpopo Mpumalanga (Indigenous)	
Euclea divinorum Hiern.	Ebenaceae	Magic guarry	Fruit, root, stem bark twig- used as toothbrush	Decoction Powdered	Diarrhoea, gastrointestinal disorders, wounds, skin diseases, headache, bleeding, noisy stomach, gonorrhoea, sore throat, toothache, oral care (disinfectant), laxative	Limpopo (Indigenous)	79-80
Euclea natalensis A.DC	Ebenaceae	Hairy guarry Large-leaved quarry Natal guarry	Root Bark Leaf sap Twigs-used as chewing sticks or toothbrush	 Infusion Decoction Powdered	Diarrhoea, stomach complaints, urinary tract infections (UTIs), syphilis, gonorrhoea, vaginal discharge, tooth ache, headache, skin infections, toothbrush, mouth rinses, chest pain, tuberculosis, asthma, bronchitis, worms (hookworm, schistosomiasis), burns, sores, wounds, ulcers, headache	Eastern Cape Gauteng KwaZulu-Natal Limpopo Mpumalanga Northern Cape (Indigenous)	10, 28, 34, 38, 80-81
Eucomis autumnalis (Mill.) Chitt	Asparagaceae (Hyacinthaceae)	Pineapple flower	Bulb Root	Decoction	Stomach ache, colic, syphilis, inflammation, fever, low back pain, urinary diseases, pulmonary ailments, fracture healing	Eastern Cape Limpopo (Indigenous)	10, 28, 78
Faurea saligna Harv.	Proteaceae	Red beech, African beech, African red beech, Beechwood	Bark Leaf Root	 Infusion Powdered	Venereal diseases, vagina ulcers, coughs, diarrhoea, schistosomiasis and unspecified purposes	KwaZulu-Natal Limpopo (Indigenous)	38, 41, 82
Ficus carica Linn.	Moraceae	Figs	Fruit Leaf Latex Root Bark	Infusion Decoction	Asthma, coughs, gastrointestinal tract ulcers, vomiting, eye sore, gonorrhoea, scabies, skin infections, sore throat, mouth wash/douche	KwaZulu-Natal Limpopo (Exotic	11, 41, 83
Galenia africana L.	Aizoaceae	Yellow bush Kraalbos	Whole plant	Decoction Lotion Dressing	Coughs, wounds, skin infections, ringworms, tuberculosis, eye inflammation, venereal sores	Eastern Cape Western cape Northern cape	71, 80, 84
Garcinia gerrardii Harv. ex Sim	Clusiaceae	Forest garcinia Forest mangosteen	Root Leaf	Decoction	Chronic coughs, tuberculosis, earache	Eastern Cape, KwaZulu-Natal, Limpopo Mpumalanga (indigenous)	5, 34
Helichrysum caespititium (DC.) Harv.	Asteraceae	Golden everlasting	Whole plant	Decoction Pounded	Cough, asthma, flu, common cold, pneumonia, pains and aches, fatigue, immune booster in HIV positive patients, gonorrhoea,	Limpopo Eastern Cape Free State Gauteng KwaZulu-Natal Limpopo Mpumalanga Northern Cape	61, 67, 85

						North West (Indigenous)	
Helichrysum glomeratum Klatt	Asteraceae	Everlastings	Whole plant	decoction	Coughs, colds, infections, fever, headache, wound dressing, skin blisters, menstrual pains	Eastern Cape Free State KwaZulu-Natal Mpumalanga (Indigenous)	80
Hypoxis colchicifolia Baker	Hypoxidaceae	African potato	Rhizome Tuber	 Decoction Infusion Maceration Pounded	Headache, cancer, gonorrhoea, UTIs, internal tumours, headaches, asthma, tuberculosis, inflammation, burns, HIV/AIDS, diarrhoea	Eastern Cape Free State KwaZulu-Natal Limpopo (indigenous-endemic)	7, 25
Moringa oleifera Lam.	Moringaceae	Horse-radish tree, Drumstick tree	Gum Pod Leaf Root	Decoction Juice	Inflammation, wound healing, asthmatic cough, expectorant, antifungals, antibacterial, fever, heart complaints	Free State Gauteng Kwa-Zulu Natal Limpopo Mpumalanga (Exotic- naturalized)	86-87
Olea europaea subsp. *Africana*	Oleaceae	Wild Olive	Fruit Leaf	Infusion	Bloody stool, immature fruits are consume as astringents against diarrhoea, urinary and bladder infections	Eastern Cape (indigenous	25
Opuntia ficus-indica Mill.	Cactaceae	Indian fig Cactus pear Sweet prickly pear	Root Leaf (cladodes)	Decoction Topical application	Gonorrhoea, hypertension, wound healing, inflammation	Limpopo (Exotic)	27, 71, 75
Parinari curatellifolia Planch. ex Benth	Chrysobalanaceae	Mobola-plum	Leaf Bark Root	Decoction Maceration	Ear and eye infections, pneumonia, inflammation, dysentery	Limpopo Mpumalanga (Indigenous)	80, 88
Pelargonium sidoides DC.	Geraniaceae	Rose-scented Pelargonium, Cape Pelargonium	Root Leaf	Decoction Powdered	Diarrhoea, wounds, gonorrhoea, gastrointestinal tract disorders, ENT infections, respiratory ailments including cough and tuberculosis, stomach ailments in children including dysentery and vomiting	Eastern Cape KwaZulu-Natal Free state (indigenous)	7, 13, 25, 59
Protorhus longifolia (Bernh.) Engl	Anacardiaceae	Red Cape Beech Purple currant	Bark	Infusion	Tooth decay and bad breath, tuberculosis	Eastern Cape KwaZulu-Natal Limpopo Mpumalanga (Exotic)	89
Prunus africana (Hook.f.) kalkman	Rosaceae	African cherry	Bark Root	Infusion	Diarrhoea, abdominal ailments, colds, influenza, prevention and treatment of prostate cancer	Eastern Cape (indigenous)	25
Psiadia punctulata (DC.) Vatke	Asteraceae	Sticky Psiadia	Root	Pounded	Chronic cough, fever, asthma, tuberculosis	Limpopo (Indigenous)	5
Psidium guajava L.	Myrtaceae	Guava	Fruit Leaf Bark Root	Decoction	Diarrhoea, dysentery, coughs, allergies, asthma, pulmonary problems, colds, running nose, unspecified respiratory ailments,	Limpopo (Exotic)	11, 25, 27, 70

					sore throat, inflammation, oral ulcers, gastroenteritis, swollen gum wound, fever, hypertension		
Punica granatum Linn.	Punicaceae	Pomegranate	Root PeelFruit	Decoction	Diarrhoea, diabetes mellitus, asthma, stomach problems	Limpopo (exotic)	27, 61
Salvia aurea L. (= Salvia africana-lutea L.)	Lamiaceae	Golden sage, beach sage, sand sage, dune sage	Whole plant, Aerial parts	Infusion, Decoction	Bronchitis, cough, colds and flu, female problems, diarrhoea	Eastern Cape Northern Cape Western Cape (Indigenous)	90
Salvia disermas L.	Lamiaceae	Wild giant sage	Whole plant	Infusion	Tuberculosis, cough, influenza, bacterial infections, cold	Eastern Cape Free State Gauteng North West Northern Cape (Indigenous)	90
Salvia repens	Lamiaceae	Creeping sage	Root Leave Whole plant	Decoction	stomach problems, diarrhoea	Eastern Cape Northern Cape Western Cape (Indigenous)	90
Sansevieria hyacinthoides (L.) Druce	Dracaenaceae	Mother-in-law's tongue, Piles root, African bowstring hemp	Rhizome Leaf	Decoction	Ear infection, earache, tooth ache, diarrhoea, intestinal worms, stomach complaints, ulcers	KwaZulu-Natal Limpopo Mpumalanga Eastern Cape (Indigenous)	53
Scadoxus puniceus (L.) Friis & Nordal	Amaryllidaceae	Paintbrush lily	Bulb Leaf Root + rhizome	Decoction In mixture (imbiza)	Abdominal pains, stomach complaints, diarrhoea, nausea, kidney and urinary infections, tonsillitis, pneumonia, tuberculosis,	KwaZulu-Natal (Indeginous)	68, 71, 78, 90
Schkuhria pinnata (Lam) Kuntze ex Thell	Asteraceae	Curious weed Dwarf-marigold	Whole plant Leave Root Aerial parts	Decoction Squeezing Chewed (leaf and root)	Stomach problems, oedema, wound infections, prostate inflammation, digestive disorders, yeast infections, , kidney and renal problems, diabetes, hypertension, gonorrhoea, intestinal gas, blood purifier, heart-water, dysmenorrhoea, eye infections, diarrhoea, pneumonia	Limpopo (Exotic)	69, 73, 76
Sclerocarya birrea (A. Rich.) Hochst.	Anacardiaceae	Marula tree	Bark Root Seed	Infusion Decoction Powdered	Eczema, acne, boils, enema for stomach ache, oils, dysentery, diarrhoea, Kidney pain, toothache, fever, UTIs,	KwaZulu-Natal (Indigenous)	32,80
Searsia burchellii (Sond. Ex Engl.) Moffett	Anacardiaceae	Karoo kunibush	Leaf	Decoction	Pulmonary sicknesses, tuberculosis, cough, chest colds, expectorant	Free State Northern Cape Western Cape Lesotho (Indigenous)	52
Solanum lycoperiscum L.	Solanaceae	Tomato	Fruit	Decoction Tincture	Diarrhoea, asthma, cancer	Eastern Cape KwaZulu-Natal	11, 27, 37

				Squeezed juice		Limpopo Mpumalanga Northern Cape Western Cape (Exotic)	
Syzygium cordatum Hochst. ex C. Krauss subsp. cordatum	Myrtaceae	Water berry	Bark Leaf Root Fruit	Decoction Infusion	Stomach complaints, diarrhoea, STIs, respiratory complaints, burns, tuberculosis	KwaZulu-Natal Mpumalanga Western Cape (indigenous)	49
Sutherlandia frutescens (L.) R.Br.	Fabaceae	Cancer bush Balloon pea	Arial parts (leaves, stem, flowers, and pods). Roots Leaves	Infusion Decoction	Stomach, kidney and liver problems, cancers, diabetes, flu rheumatism, fever, wounds and eyes infections, inflammation, HIV/AIDS, improves cachexia (muscle-wasting),gonorrhoea, STIs	Eastern Cape Free State KwaZulu-Natal Mpumalanga Northern Cape Western Cape (Indigenous)	52
Terminalia sericea Burch. ex DC.	Combretaceae	Silver clutter-leaf. Silver terminalia	Root Leaf Stem bark	Decoction Infusion Powder	Diarrhoea, fever, pneumonia, dysentery, diarrhoea, measles, skin infections, leprosy, wounds, tuberculosis, cough, running nose, blocked nose, venereal diseases, gynaecological complaints	Gauteng KwaZulu-Natal Limpopo Mpumalanga North West Northern Cape (Indigenous)	61, 75
Tulbaghia violacea Harv.	Alliaceae	Wild garlic	Leaf Bulb	Decoction-steam inhaled under blanket	Coughs, asthma, colds, fever, sinus headaches, cancer of the oesophagus, tuberculosis, intestinal worms	Eastern Cape KwaZulu-Natal Limpopo (Indigenous)	17, 49, 61
Vernonia amygdalina Del.	Asteraceae	Bitter leaf	Leaf Root	Decoction Crushed Squeezed	Gastrointestinal problems, diarrhoea, schistosomiasis, amoebic dysentery, diabetes, fevers, malaria, cough, hepatitis, venereal diseases	Eastern Cape KwaZulu-Natal Limpopo Northern Cape (Indigenous)	6
Warburgia salutaris (G.Bertol.) Chiov. (Endangered species)	Cancellaceae	Pepper-bark tree	Bark Leaf	Decoction Infusion Powdered	Coughs, chest problems, colds, influenza, diarrhoea, toothache, headache, skin problems, gastric ulcers, venereal diseases	Gauteng KwaZulu-Natal Limpopo Mpumalanga (Exotic)	7, 32, 80
Ximenia americana L. var. americana	Olacaceae	Blue Sour-plum	Bark Root	Decoction Powdered	STIs (clean blood), painful menstruation, venereal diseases, headache due to indigestion, bloody stools, diarrhoea, dysentery in children, coughs, asthma, eye infections	Limpopo (Exotic)	27, 57, 62, 82
Ximenia caffra Sond. var. *caffra*	Olacaceae	Large Sour-plum	Leaf Root Seed	Decoction Pounded Roasted	Venereal diseases, STIs, syphilis, bilharzia, worms, skin and wound infections, eye problems, painful tonsils, diarrhoea, dysentery, severe stomach pains, colic, cough, chest pains,	KwaZulu-Natal, Limpopo-northern and central parts (Indigenous)	28, 57, 61-62

Table 2. South African medicinal plants with promising antimicrobial activity against a variety of susceptible and resistant pathogenic strains

Scientific name of Plant	Common name of plant	Type of extract	Sensitive pathogen	Reported biological ingredients	References
Allium sativum	Garlic	Aqueous, ethanol and chloroform extracts	MDR-TB and XDR-TB, *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus*, *Streptococcus agalactiae*, *Klebsiella pneumoniae* , *Proteus mirabilis*, *Bacillus subtilis*, *Helicobacter pylori*	Allicin which is an alkaloid	133-134
Combretum imberbe	Leadwood	Acetone extract.Crude and organic extracts	*Candida albicans* *Cryptococcus neoformans*, *Schistosoma haematobium*, *Staphylococcus aureus*,	Triterpenoids including glycosidic derivatives of hydroxy-imberbic acid, imberbic acid, glycosides based on imberbic acid	135-137
Combretum molle	Velvet bush willows	Crude and organic extracts	*Bacillus cereus*, *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa*	Flavonoids Steroids Tannins Triterpenoids	135, 138-139
Euclea divinorum	Magic quarry	Root-bark organic and aqueous extract	*Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus, Streptococcus sanguinis,Lactobacillus acidophilu*	Alkaloids Saponins Tannins Amino acids Flavonoids Phenols, Triterpenoids	139-140
Hypericum perforatum L.	St. John's Wort	Organic extract	*Staphylococcus aureus,* Methicillin-resistant *Staphylococcus aureus, Helicobacter pylori*	Hyperforin	141
Punica granatum	Pomegranate	Peel, fruit skin and whole	*Staphylococcus aureus* *Escherichia coli*	Polyphenols including ellagic	142-144

		fruit-hot water and organic extract	*Pseudomonas aeruginosa, Klebsiella pneumoniae, Saccharomyces cerevisiae, Salmonella typhimurium, Bacillus Subtilis, Yersinia enterocolitica.*	tannins, ellagic acid, and gallic acid. Alkaloid,Flavonoid, Glycoside,Phenol, Condensed and hydrolysable tannins	
Pelargonium sidoides DC.	Rose-scented Pelargonium ORCape Pelargonium	Root and leaf ethanolic and methanolic extracts	*Bacillus subtilis, Escherichia coli, Helicobacter pylori, Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus epidermis, Mycobacterium tuberculosis, Mycobacterium smegmatis*	Coumarins, Flavonoids, Gallic acid, Hydroxycinnamic acid, Proanthoc-yanins, Phenolic acids including gallic acid	7, 145
Schrebera alata	Wild Jasmine	Organic extract	MRSA, *Candida albicans*, Multidrug-resistant, *Pseudomonas aeruginosa, Bacillus cereus, Escherichia coli*	Flavonoids, Sterols, Alkaloids, Tannins, Quinones, Terpenoids, Saponins	146-147
Terminalia sericea	Silver clutter-leaf. Silver terminalia	Organic root and leaf extracts	*Helicobacter pylori, Human immunodeficiency virus,Mycobacterium tuberculosis, Mycobacterium smegmatis, Pseudomonas aeruginosa, Staphylococcus aureus*	Alkaloids, Flavonoids, Tannins, Saponins, Phenolic acids, Lignans,Steroids, Glycosides	137, 148
Vernonia amygdalina	Bitter leaf	Organic and aqueous extracts	*Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus*	Vernolide, Vernodalol, Vernodalin, Vernodalinol, Vernomygdin, hydrxyvernolide	132
Ximenia caffra	Sour-plum	Leaf, root- organic and aqueous extract	*Neisseria gonorrhoeae, Escherichia coli Bacillus subtilis Staphylococcus aureus*	Flavonoids Tannins Polyphenols including gallic acid, catechin, quercetin and kaempferol	105, 149-150
Zingiber officinale Roscoe	*Ginger*	Organic and aqueous extracts	*Acinetobacter baumannii, Bacillus subtilis, Bacillus cerus, Escherichia coli,* Methicillin-resistant *Staphylococcus aureus,*	Terpene including zingiberene, Phenols including gingerol, paradols, and shogaol	151-152

Many ethnobotanical surveys in South Africa have reported that most indigents apply a vast number of medicinal plants for the treatment of STIs including but not limited to *Acacia karroo, Bidens pilosa, Carica papaya, Diospyros mespiliformis, Ficus abutilifolia, Rhoicissus tridentata* subsp. *cuneifolia, Ximenia caffra, Vachellia karroo, Trichilia dregeana*, *Terminalia sericea Cambess, Typha capensis Rohrb* and *Ziziphus mucronata* Wild. subsp. *mucronata* [28, 50, 68, 103-104]. According to a research conducted by [104], the root extracts of *Acacia karroo* and *Rhoicissus tridentata* subsp. *cuneifolia* plants were active against *Neisseria gonorrhoeae* with MIC value of 0.8 mg/ml and 0.4 mg/ml respectively.

Similarly, the aqueous extracts of *Bidens Pilosa* leaf (mean MIC 83.2 mg/ml) and *Ximenia caffra* root (mean MIC 62.1 mg/ml) showed inhibitory activity against *Neisseria gonorrhoeae* pathogen [104]. Also, *Trichilia dregeana* produces a mean MIC of 2.0 mg/ml against *Treponema pallidum* [104]. A review by [57, 105], agrees with this and reports on similar findings on the use of medicinal plants to treat STIs in South Africa.

Diarrhoea

According to [106], diarrhoea is a common symptom that is usually related with the disorders of the gastrointestinal tract and is typically characterised by increased in the regularity of bowel movement associated with watery stools. Infectious diarrhoea other gastrointestinal illnesses are frequently triggered by resistant strains of medically important bacteria including *B. cereus*, *E. coli, S. aureus*, *Salmonella typhimurium* (*S. typhimurium*), *Proteus vulgaris* (P. vulgaris), and Shigella spp., [107-108]. Similarly, viral as well as parasitic diarrhoea has been reported [107]. Diarrhoea has been reported as the major cause of death in low and middle income countries with over 6.9% death rate reported [108-109].

In South Africa, the indigents usually apply various medicinal plants to remedy gastrointestinal diseases and conditions associated with diarrhoea [12, 108]. The pomegranate plant (*Punica granatum*), has been widely used to alleviate many health conditions including diarrhoea due to its rich phytochemical constituents such as flavonoids, alkaloids, saponins, tannins, phenols and anthocyanins [109-110]. According to [132], the fruit peel extract of *Punica granatum* inhibits the growth of MRSA with zones of inhibition ranging from 22.0 mm to 11.3 mm. Similar research by [112] agrees with this and adds that the juice of pomegranate fruit shows inhibitory properties against *B. cereus*, *E. coli,* and *S. aureus* and produces 26.0 mm, 20.0 mm and 26.0 mm as diameter of inhibition respectively. Notwithstanding, the bark extract of *Sclerocarya birrea* shows activity against diarrhoeal pathogens with low MIC values including *S. typhimurium* (0.20 mg/ml), *B. cereus* (0.29 mg/ml), *S. aureus* (0.35 mg/ml), *P. vulgaris* (0.75 mg/ml) and *E. coli* (0.95 mg/ml) [108]. On the other hand, the extract from the leaf of *Psidium guajava* (*P. guajava*) shows killing properties against *B. cereus*, *S. typhimurium* and *S. aureus* with MIC values of 0.34, 0.65 and 0.93 mg/ml respectively [108]. Additionally, [25] had similar findings and reports on the MIC values of various medicinal plants in South Africa against diarrhoeal entero-pathogens including *Aloe arborescence* against *S. aureus* (0.018 mg/ml), *Eucomis comosa* against *Enterococcus faecalis* (0.078 mg/ml) and *Acacia mearnsii* against *S. typhimurium* (0.039 mg/ml). This is consistent with the research conducted by [113] on the use of indigenous herbal plants in South Africa to treat diarrhoea caused by enteropathogenic bacterial organisms.

In a majority of instances, reports showed that one plant can be useful in curing multiple conditions and/ diseases (mono-therapy), for example garlic scientifically known as *Allium sativum,* is used to treat throat infections, TB, asthma, stomach diseases [60, 62]. Similarly, the cape aloe (*Aloe ferox*) is used in KwaZulu-Natal to remedy burns, sunburn, acne, insect bites, skin irritation, toothaches, stomach problems, sinusitis [7, 10].

Even though indigenous plants have proven very useful to mankind, however over-exploitation of these plants threatened some species to disappear or near disappear on earth [34]. Due to this, the government of South Africa has introduced regulations and thus label some plants as endangered, and/or protected species including *Curtisia dentata* commonly called "assegai" in Afrikaans, *Warburgia salutaris* known as pepper-bark tree, and *Zanthoxylum capense* – a protected tree [34]. It is interesting to note that, while some of the plants used as medicine are largely distributed in the wild or grown in gardens at home, a majority

are indigenous [37]. Of this, a smaller proportion are exotic and/ endemic in some parts in South Africa including Limpopo, Mpumalanga and KwaZulu Natal provinces [11].

Pathogenic bacterial infections

Infectious diseases are major cause of mortality and disability, and remain the second leading cause of death across the globe [3, 5, 114-115]. This phenomenon is further exacerbated by the emergence of both old familiar and new unrecognised infectious disease pandemics [116-118]. Microbial infectious diseases cause more than 50% of all the deaths that occur in the underdeveloped nations particularly African countries [3, 21, 100].

There is a rising amount of information to indicate that most of the diseases which are problematic to human health are said to be infectious and are mostly caused by pathogenic microorganisms including bacteria, viruses, parasites and fungi [95, 115, 119-120]. It is of importance to note that infectious diseases occurring as a result of bacterial infections are reported to be the number one killer disease than any other category of disease globally [95, 114]. These bacterial infections accounts for 43% mortality rate recorded in the underdeveloped countries whilst only 1% of the mortality rate is recorded in the developed countries [121].

The high level of infectious disease burden in a population with minimal health resources, comes with the associated ramifications including death. According to Stats [95], recorded deaths in South Africa for the period between 2014-2017 caused by infectious and parasitic diseases was 78 562 amounting to 17.2% demises. A substantial amount of health-care costs in South Africa has also been incurred as a result of infectious diseases [25].

Plants as alternative source of antimicrobials

Plants are generally known to be the biggest stores of naturally occurring biochemical compounds and are capable of manufacturing diverse natural chemical constituents including toxins and/ pheromones as a form of defence mechanism against other organisms or for pollination respectively [3, 122-123]. These chemical substances are of course not placebo but are fused with low molecular weight potent bioactive constituents also known as secondary metabolites [124-125].

As early as the 1850s, plants' secondary metabolites have received intense investigation [125-126]. Currently, more than 12,000 bioactive compounds from plants have been isolated and are further classified based either on their chemical composition and structure, their biosynthetic origin or their solubility [124, 127]. Due to this, the compounds were further segregated as alkaloids, terpenoids, phenolics, saponins, lipids and carbohydrates [128-129]. These chemicals have promising therapeutic effects on which human beings rely on [14]. The presence of these phytochemical constituents in plants perhaps explains their countless applications in traditional medicine [129-130].

The inhibitory properties of South African medicinal plants against bacterial pathogens

After unsuccessful attempts to eliminate pathogens with conventional medicines due to drug resistance, some plant secondary metabolites were considered. Numerous scientific studies have revealed significant antibacterial activities of some plants against multidrug-resistant pathogens of bacterial origin [128, 130-131] (Table 2).

According to [132]; organic and aqueous extracts of *Vernonia amygdalina* shows antibacterial effect against *Pseudomonas aeruginosa*, *Klebsiella* spp., *Streptococcus* spp., *Bacillus cereus*, *Bacillus pumilus*, *Bacillus subtilis*, *Enterobacter cloacaem*, *E. coli* and *Staphylococcus aureus*. In a research conducted by [25], plant extracts from *Psidium guajava, Eucomis autumnalis* and *Cyathula uncinulata* showed promising antibacterial effect against *S. aureus* with minimum inhibitory concentration (MIC) values ranging from 0.018 mg/ml to 2.5 mg/ml. Correspondingly, [101] reported that the extracts from the leaves of *Eucomis autumnalis* was active against *Bacillus pumilus, Escherichia coli* and *Staphylococcus aureus* at a minimum inhibitory concentration (MIC) of 0.098 mg/ml, 0.130 mg/ml and 0.098 mg/ml respectively. This is in consistence with the research conducted by [105], in which the *Bolusanthus speciosus* bark used by the Veda indigents to treat venereal diseases showed good inhibitory activity against *E. coli* and *S. aureus* with ranges of MIC values between 0.012 mg/ml and 0.098 mg/ml. This validates the idea that plants could be used as alternative source of antibiotics.

CONCLUSION

The reviewed publications are focussed on biological activities, antioxidant and antimicrobial activities of South African plants used to treat human bacterial infections. Yet additional data and published clinical trials are still needed to confirm therapeutic properties of the researched medicinal plants. The practice of traditional medicine through the application of plant natural product still plays a vital role in fulfilling the rudimentary health care needs of the people of South Africa. *Acacia karroo, Bidens pilosa, Diospyros mespiliformis* and *Ximenia caffra* were the commonly applied herbs for the treatment of venereal diseases. On the other hand, diarrhoea and other stomach related ailments caused by pathogenic bacteria were remedied with *Allium sativum, Eucomis comosa, Psidium guajava, Punica granatum* and *Aloe* spp. Moreover, *Aloe barbadensis, Cassia abbreviata, Helichrysum caespititium, Hypoxis colchicifolia and Sutherlandia frutescens* were mostly used by HIV positive patients to alleviate opportunistic infections including TB, diarrhoea and skin infections. The leaves, bark and root were frequently used plant parts while the preferred methods of preparation were decoction and infusion. This study demonstrates the usefulness of plant natural product as medicine to prevent and treat human pathogenic infections caused by resistant bacteria in South Africa.

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Conflict of interest

The authors declare no conflict of interest.

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