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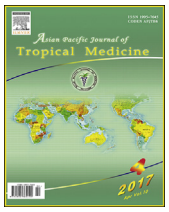

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Acacia karroo Hayne: Ethnomedicinal uses, phytochemistry and pharmacology of an important medicinal plant in southern Africa

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ABSTRACT

Acacia karroo (*A. karroo*) has been used as herbal medicine by the indigenous people of southern Africa for several centuries. The potential of *A. karroo* as herbal medicine, its associated phytochemistry and biological activities are reviewed. The extensive literature survey revealed that *A. karroo* is traditionally used to treat or manage 32 and five human and animal diseases and ailments, respectively. The species is used as herbal medicine for diseases and ailments such as colds, diarrhoea, dysentery, flu, malaria, sexually transmitted infections (STIs), wounds, and also as colic and ethnoveterinary medicine. Multiple classes of phytochemicals such as flavonoids, phenols, phytosterols, proanthocyanidin, tannin, terpenes as well as several minerals have been identified from leaves and roots of *A. karroo*. Scientific studies on *A. karroo* indicate that it has a wide range of pharmacological activities which include antibacterial, antifungal, antigonococcal, antihelmintic, antilisterial, antimalarial, antimycobacterial, antioxidant, HIV-1 reverse transcriptase, anti-inflammatory and analgesic. *A. karroo* has a lot of potential as a possible source of pharmaceutical products for the treatment of a wide range of both human and animal diseases and ailments. Future research should focus on the mechanisms of action of the different plant parts used as herbal medicines, isolated compounds, their efficacy, toxicity and clinical relevance.

1. Introduction

Acacia karroo (*A. karroo*) Hayne is a member of the genus *Acacia* Miller, family Fabaceae and subfamily Mimosoideae. The genus was first described by Philip Miller in 1754, the name was derived from the Greek word 'akis' which means point or barb, referring to the thorns found on African *Acacia* species [1]. The species name 'karroo' is the old spelling for the South African semi-desert natural biome 'karroo', where the species was first described by botanical explorers [2]. The genus contains a large number of species (approximately 1500), making it the largest genus within the Fabaceae family and is widespread, occurring in Australia, Asia, Africa and the Americas [3]. The genus *Acacia* was re-classified recently into five distinct genera, *Vachellia, Senegalia*, *Mariosousa, Acaciella* and *Acacia* which are clearly distinct based on a number of morphological, anatomical and biochemical attributes [4]. *A. karroo* was therefore, renamed *Vachellia karroo* (*V. karroo*, Hayne) Banfi & Galasso when the genus *Acacia* was renamed *Vachellia*. Taxonomically, *Vachellia* is closer to *Senegalia*, the main difference is that *Vachellia* has capitate inflorescences (round, head-like flowers) and spinescent stipules (thorns) while *Senegalia* has spicate inflorescences (flowers in spikes) and the stipules are non-spinescent [3]. But taxonomists worldwide want the name *Acacia* to be conserved as renaming the genus as *Vachellia* will create numerous taxonomic and retypification problems [5]. In literature both names are used, for example *V. karroo* instead of *A. karroo* was used by Taylor and Barker [6] and Idamokoro *et al* [7]. But at the present moment *V. karroo* is regarded as an invalid name by the Royal Botanic Garden and Missouri Botanic Garden plant name database (www.theplantlist.org) and therefore, *A. karroo* has been adopted in this study.

A. karroo has been recorded throughout southern Africa, ranging from the south-western Cape in South Africa, northwards into Lesotho, Swaziland, Namibia, Angola, Botswana, Malawi, Mozambique, Zambia and Zimbabwe [6]. It has been introduced to North Africa, Australia, India, Myanmar and South America

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(Argentina, Bolivia, Chile and Paraguay), where it is often used as live fence around agricultural fields [8,9]. *A. karroo* grows from sea level to 1800 m on soils ranging from pure unconsolidated sand to heavy clays with an annual rainfall from 1500 mm down to less than 200 mm where ground water is available along drainage lines and around pans and dams [8]. The species can grow under different climatic conditions but its limiting factors are water availability and intense cold [8]. *A. karroo* is the most widespread *Acacia* in southern Africa, occupying a diverse range of habitats including dry thornveld, river valley scrub, bushveld, woodland, grassland, river banks and coastal dunes [6]. *A. karroo* shows a huge variety in terms of its growth form, with plants from different areas in the species' geographical range often having a different appearance. In the formal taxonomic revision of the species, Ross [10] detailed the vast range in morphology in this species, describing seven different informal taxonomic entities of the species which were generally correlated to its distribution. Recently, Taylor and Barker [6] evaluated the genetic variability of the species throughout South Africa using the Inter-Simple Sequence Repeat (ISSR) DNA 'fingerprinting' to determine whether there is any genetic structure that correlates to the morphological diversity of the species. The authors concluded that *A. karroo* should be considered as an ochlospecies, as the evolution of the observed morphotypes has been recent and rapid, and therefore the genetic variation observed represents the ancestral gene pool that has not yet undergone lineage sorting as a consequence of isolation.

According to Barnes *et al* [8], *A. karroo* is a multipurpose tree with great potential for increasing productivity in agroforestry and silvopastoral systems over a wide range of sites in the dry zones of the tropics and subtropics. It is also categorized as a species with potential commercial value in Botswana, South Africa and Zimbabwe [8,11,12]. In Botswana, *A. karroo* exudate is used for pharmaceutical purposes and is considered to be of economic importance in this country [11] while the gum is collected and used as a substitute for gum arabic in Zimbabwe [8]. According to van Wyk [12], *A. karroo* bark and leaf have commercial potential as remedies for diarrhoea, its exudates are used as an emollient for conjunctivitis and haemorrhage and also as pharmaceutical aid in solid formulations. The seeds are traditionally roasted and used as a coffee substitute in southern Africa [13,14]. Gum collected from *A. karroo* can be used in the commercial production of sweets and other confectioneries [14]. Over the last three decades, various attempts have been made to investigate chemical constituents, biological activities of *A. karroo* and its ethnomedicinal uses in southern Africa. Unfortunately, no comprehensive review of this important plant species in southern Africa has been published, documenting the species' biology, traditional uses, phytochemistry and pharmacological properties. Therefore, in this study, the advances in traditional utilization, botany, phytochemistry, pharmacology and safety aspects of *A. karroo* are systematically reviewed.

2. Methodology of the review

The literature search was performed from June 2016 to January 2017 using electronic search engines such as Google, Google scholar, publishing sites such as Elsevier, scienceDirect, BioMed Central (BMC) and PubMed. The databases and literature sources were chosen based on the topic covered (*i.e.*, ethnobotany, ethnomedicinal uses, ethnopharmacology, pharmacology, phytochemistry and therapeutic value) and geographical coverage (*i.e.*, southern Africa). The following keywords were used to search literature sources: *A. karroo* and *V. karroo*. Other literature sources included papers published in international journals, reports from international, regional and national organizations, conference papers, books, theses, websites and other grey literature. References were also identified by searching the library collections of the National Herbarium and Botanic Gardens (SRGH), Harare, Zimbabwe and the University of Fort Hare, South Africa.

3. Species description and ethnomedicinal uses

A. karroo varies from a multi-stemmed shrub to a tree of up to 15 m in height [15]. The stem of *A. karroo* is dark brown to almost black characterized by rough and somewhat flaky, revealing reddish underbark [8]. *A. karroo* has pairs of large white spines which occur on the twigs and branches. The leaves comprise about five pairs of leaflets, each divided into ten or more pairs of smaller leaflets of about 5 mm long [16]. The branches bear minute golden-yellow, ball-shaped flowers and the fruit is a long, narrow, spirally twisted pod [8].

A. karroo boasts a large number of recorded ethnomedicinal and traditional uses in southern Africa (Table 1). The roots of *A. karroo* are used as remedy for colic in infants in Lesotho [17,18] and South Africa [19,20] while bark, gum and leaf infusions are used as remedy for diarrhoea and dysentery in South Africa [19–23] and Zimbabwe [24]. *A. karroo* is also widely used as herbal medicine for sexually transmitted infections (STIs) such as gonorrhoea and syphilis in Zimbabwe [25,26], sexually transmitted diseases and venereal diseases in South Africa [20,27]. The bark, gum and leaves are used as emollient and astringent for colds, conjunctivitis and haemorrhage [28]. In Zimbabwe, roots of *A. karroo* are also used as aphrodisiac, for general body pains, convulsions and dizziness [25]. In Mozambique, root bark infusion of *A. karroo* is taken orally as remedy for malaria [29]. Gum of *A. karroo* is used with *Capsicum* spp. fruit and vinegar in a plaster dressing for acute osteomyelitis [28]. The gum from *A. karroo* has been used medicinally as emollient and as pharmaceutical aids such as emulsifiers, stabilisers of suspensions and additives for solid formulations. In South Africa, the gum of *A. karroo* has been applied to mouth ulcers and is diluted with water and used as a mouthwash against oral thrush and sprue [13,30]. Thorns are used to relieve heart pains and for magical purposes [31].

A. karroo is used in ethnoveterinary medicine for diarrhoea, coughs and opthalmia in cattle and dogs [19,32]. Root infusions of *A. karroo* are used in ethnoveterinary medicine as an antidote to poisoning as a result of cattle and goats eating *Moraea* spp. [33]. *A. karroo* is used to treat cattle which have tulp poisoning, that is poisoning caused by consuming parts of *Homeria* spp., a bulbous plant species known to be poisonous to stock [1,13]. *A. karroo* provides shade for livestock such as cattle and goats in southern Africa [8]. The leaves, flowers, pods and its parasitic mistletoes are excellent fodder for livestock and game in southern Africa [8]. The wood is an excellent fuel, the bark can be used for tanning, the inner bark makes good cord and the sawn timber can be used for general purposes. *A. karroo* gum is collected and used as a substitute for gum arabic is Zimbabwe [8]. Seeds of A. karroo have been used as a substitute for coffee [19].

Table 1
Ethnomedicinal and other traditional uses of *Acacia karroo* in southern Africa.

Use	Plant part(s) used	Country practised	Refs
Abscesses	Gum applied externally	South Africa	[28]
Aphrodisiac	Root decoction taken orally	Zimbabwe	[25,26]
Astringent	Bark decoction applied externally	South Africa	[34]
Coagulant	Bark decoction applied externally	South Africa	[28]
Colds	Bark decoction taken orally	South Africa	[19,20]
Colic	Crushed roots mixed with food or root decoction taken orally	Lesotho, South Africa	[17–20]
Convulsions	Root decoction	Zimbabwe	[25,35]
Diarrhoea	Bark, gum and leaf concoctions and infusions taken orally	South Africa; Zimbabwe	[19–24]
Dizziness	Root infusion taken orally	Zimbabwe	[25]
Dysentery	Bark, gum and leaf concoctions and infusions	South Africa; Zimbabwe	[19,20,22,24]
Emetic	Bark decoction taken orally	South Africa	[19,20]
Flu	Bark decoction taken orally	South Africa	[23]
General body pains	Body washed with root infusion	Zimbabwe	[25]
Gonorrhoea	Root decoction taken orally	Zimbabwe	[25,26]
Haemorrhage	Bark, gum and leaf concoctions and infusions taken orally	South Africa	[22]
Headache	Leaf infusion taken orally	South Africa	[36]
Heart pains	Thorn used to relieve pains	South Africa	[31]
Inflammation of eyes	Bark, gum and leaf concoctions and infusions taken orally	South Africa	[20]
Magical purposes	Thorn used for magical purposes	South Africa	[31]
Malaria	Root bark infusion taken orally	Mozambique	[29]
Mouth ulcers	Gum applied to mouth ulcers	South Africa	[13,30]
Oral thrush	Gum diluted with water and taken orally	South Africa	[13]
Osteomyelitis	Gum mixed with *Capsicum* spp. fruit and vinegar applied in a plaster	South Africa	[28]
Purge symptoms of evil and sorcery	Root decoction taken orally	South Africa	[19]
Ringworm	Bark decoction applied on affected body part	South Africa	[37]
Sexually transmitted diseases	Root decoction taken orally	South Africa	[27]
Snake repellent	Root bark decoction sprinkled to repel snakes	South Africa	[38]
Stomach ache	Bark infusions taken orally	South Africa	[28]
Syphilis	Root decoction taken orally	Zimbabwe	[25,26]
Urinary schistosomiasis	Root decoction taken orally	Zimbabwe	[24]
Venereal diseases	Root decoction taken orally	South Africa	[20]
Worms	Bark or leaf decoction	South Africa	[39]
Ethnoveterinary medicine			
Diarrhoea	Bark, leaf and root decoction	Namibia, South Africa	[40–42]
Ectoparasites	Leave root in fowl run	Zimbabwe	[43]
Fractures	Bark decoction applied externally	South Africa	[40]
Tulp poisoning	Bark decoction taken orally	South Africa	[28]
Wounds and myiasis	Leaf decoction applied externally	South Africa	[44]
Other uses			
Coffee substitute		South Africa	[19]
Cord or rope		South Africa	[45]
Dye		Botswana, South Africa, Zimbabwe	[46]
Edible gum		South Africa, Zimbabwe	[8,47]
Fence		Zimbabwe	[48]
Firewood		Botswana, South Africa, Zimbabwe	[31,45,48,49]
Fodder		Botswana, South Africa, Zimbabwe	[8,46]
Shade		Botswana, South Africa, Zimbabwe	[8,46]

4. Phytochemical and nutritional constituents of *A. karroo*

The nutritional composition of *A. karroo* leaves is shown in Table 2. *A. karroo* leaves contain high levels of crude protein and minerals (Table 2) and the crude protein values for the species are within the optimal range of (120–230) g/kg dry matter required for body weight gain, maintenance and production requirements in growing goats [50,51]. *A. karroo* leaves also have moderate levels of detergent fibres which are indication of high feeding values [52,53]. *A. karroo* contains high levels of condensed tannins (Table 2), which have been documented by several other authors such as Mokoboki *et al* [52], Dube *et al* [54], Ngambu *et al* [55], Gxasheka *et al* [56] and Brown *et al* [57]. The inclusion of *A. karroo* leaves as supplementary feed in the diet of goats and other livestock could benefit the smallholder farmers in the communal areas of southern Africa during the critical fodder scarcity.

Phytochemical screenings of various plant parts of *A. karroo* demonstrated the presence of flavonoids, phenols, phytosterols, proanthocyanidin, tannin and terpenes [54,57,61–64]. Nyila *et al* [63] isolated epicatechin **1**, β-sitosterol **2** and epigallocatechin **3** from

Table 2
Nutritional composition of *Acacia karroo* leaves.

Caloric and nutritional composition	Values	Refs
Acid detergent fibre (ADF) (%)	32.4	[57]
Ash (g/kg DM)	51	[58]
Ca	1.73 ± 0.02	[59]
Crude fibre (g/kg DM)	259	[58]
Crude protein (g/kg DM)	148.9	[52]
Cu (ppm)	10.7	[60]
Dry matter (%)	97.0	[59]
Ether extract (%)	2.4	[57]
Fe (ppm)	175 ± 18	[59]
K (%)	0.970 ± 0.001	[59]
Mg (%)	0.320 ± 0.001	[59]
Mn (ppm)	13 ± 3	[59]
Na (%)	0.01 ± 0.00	[59]
Neutral detergent fibre (NDF) (%)	38.0	[57]
Organic matter (%)	92.1	[57]
P (%)	0.13 ± 0.01	[59]
Se (ppm)	0.17	[60]
Tannin (%)	2.220 ± 0.008	[59]
Total phenolics (%)	38.0	[57]
Zn (ppm)	66 ± 2	[59]

ethyl acetate extracts of A. karroo leaves using silica gel column chromatographic (CC) purification technique (Table 3). A chloroform crude extract of *A. karroo* leaves analyzed using the gas chromatography-mass spectrometry (GC-MS) technique [64] yielded three ingredients: cyclohexanone,2-methylene-5-(1-methylethyl) **4**, 4-methyl-2,4-bis(4′-trimethylsilyloxyphenyl)pentene **5** and trimethyl[4-(1,1, 3,3,-tetramethylbutyl)phenoxy]silane **6** (Table 3). The ethyl acetate extract of *A. karroo* leaves contained six chemical compounds [64]: 4-methyl-2,4-bis(4′-trimethy-lsilyloxyphenyl)pentene **5**, cyclotrisiloxane,hexamethyl-trans-decalin **7**, 2-methyl-bicyclo[2.2.1]heptan-2-one,4,7,7-trimethyl **8**, furan, 2-hexyl **9**, cyclohexane,1-methyl-4-(1-methylethenyl) **10** and decalin,2-methyl **11** (Table 3). The ethanol extract of *A. karroo* leaves contained eight chemical compounds [64]: trimethyl[4-(1,1,3,3,-tetramethylbutyl)phenoxy]silane **6**, cyclotrisiloxane, hexamethyl-trans-decalin **7**, cyclodecene,1-methyl **12**, acetamide,*N*-(3-imidazol-1-yl-propyl)-2-methoxy-cyclohexene **13**, cyclohexene,1-pentyl **14**, 2-methyl-bicyclo[2.2.1]heptan-2-one,4,7,7-trimethyl **15**, methyl-2,4-bis(4′-trimethylsilyloxyphenyl)pentene **16** and oxamide,*N*-[3-(1-imidazolyl)propyl]-N′-methyl **17** (Table 3). The chloroform extract of the roots of *A karroo* contained six chemical compounds [64]: decalin,2-methyl **10**, 2-methyl-bicyclo[2.2.1]heptan-2-one,4,7,7-trimethyl **15**, methyl-2,4-bis(4′-trimethylsilyloxyphenyl)pentene **16**, 3-(4,8,12-trimethyltridecyl)furan **18**, bicyclo[4.1.0]heptan-3-one,4,7,7-trimethyl-,1r-(1α,4α,6α) **19**, 1,2-bis(trimethylsilyl)benzene **20**, trimethyl(4-tert.-butylphenoxy)silane **21** (Table 3). The ethyl acetate extract of the roots of *A karroo* contained six chemical compounds [64]: cyclotrisiloxane,hexamethyl-trans-decalin **7**, furan,2-hexyl **9**, decalin,2-methyl **11**, cyclodecene,1-methyl **12**, bicyclo[4.1.0]heptan-3-one,4,7,7-trimethyl-[1r-(1α,4β,6α) **22** and spiro[5.5]undecane **23** (Table 3). The ethanol extract of *A. karroo* roots also contained six chemical compounds [64]: cyclotrisiloxane,hexamethyl-trans-decalin **7**, cyclodecene,1-methyl **12**, bicyclo[4.1.0]heptan-3-one,4,7,7-trimethyl-,[1r-(1α,4α,6α) **19**, trimethyl(4-tert.-butylphenoxy)silane **21**, bicyclo [4.1.0]heptan-3-one,4,7,7-trimethyl-1r-(1α,4β,6α) **22**, 2-cyclohexen-1-one,2-methyl-5-(1-methylethyl),(S) **24** and 1,2-benzisothiazol-3-amine-tbdms **25** (Table 3).

Table 3
Chemical compounds isolated and characterized from *Acacia karroo*.

No.	Compound	Extract	Plant part	Method of characterization	Refs
1	Epicatechin	Ethyl acetate	Leaves	CC	[63]
2	β-sitosterol	Ethyl acetate	Leaves	CC	[63]
3	Epigallocatechin	Ethyl acetate	Leaves	CC	[63]
4	Cyclohexanone,2-methylene-5-(1-methylethyl)	Chloroform	Leaves	GC-MS	[64]
5	4-methyl-2,4-bis(4′-trimethylsilyloxyphenyl)pentene	Chloroform, ethyl acetate, ethanol	Leaves	GC-MS	[64]
6	Trimethyl[4-(1,1,3,3,-tetramethylbutyl)phenoxy]silane	Chloroform, ethanol	Leaves	GC-MS	[64]
7	Cyclotrisiloxane,hexamethyl-trans-decalin	Ethyl acetate, ethanol	Leaves	GC-MS	[64]
8	2-methyl-(bicyclo[2.2.1]heptan-2-one,4,7,7-trimethyl	Ethyl acetate	Leaves	GC-MS	[64]
9	Furan,2-hexyl	Ethyl acetate	Leaves, roots	GC-MS	[64]
10	Cyclohexane,1-methyl-4-(1-methylethenyl)	Ethyl acetate	Leaves	GC-MS	[64]
11	Trans-decalin,2-methyl	Chloroform, ethyl acetate	Leaves, roots	GC-MS	[64]
12	Cyclodecene,1-methyl	Ethanol, ethyl acetate	Leaves, roots	GC-MS	[64]
13	Acetamide,N-(3-imidazol-1-ylpropyl)-2-methoxy	Ethanol	Leaves	GC-MS	[64]
14	Cyclohexene,1-pentyl	Ethanol	Leaves	GC-MS	[64]
15	2-methyl-bicyclo[2.2.1]heptan-2-one,4,7,7-trimethyl	Chloroform, ethanol	Leaves, roots	GC-MS	[64]
16	Methyl-2,4-bis(4′-trimethylsilyloxyphenyl)pentene	Chloroform, ethanol	Leaves, roots	GC-MS	[64]
17	Oxamide,N-[3-(1-imidazolyl)propyl]-N′-methyl	Ethanol	Leaves	GC-MS	[64]
18	3-(4,8,12-trimethyltridecyl) furan	Chloroform	Roots	GC-MS	[64]
19	Bicyclo[4.1.0]heptan-3-one,4,7,7-trimethyl-,[1r-(1α,4α,6α)	Chloroform	Roots	GC-MS	[64]
20	1,2-bis(trimethylsilyl)benzene	Chloroform	Roots	GC-MS	[64]
21	Trimethyl(4-tert.-butylphenoxy)silane	Chloroform, ethanol	Roots	GC-MS	[64]
22	Bicyclo[4.1.0]heptan-3-one,4,7,7-trimethyl-,1r-(1α,4β,6α)	Ethyl acetate, ethanol	Roots	GC-MS	[64]
23	Spiro[5.5]undecane	Ethyl acetate	Roots	GC-MS	[64]
24	2-cyclohexen-1-one,2-methyl-5-(1-methylethyl),(S)	Ethanol	Roots	GC-MS	[64]
25	1,2-benzisothiazol-3-amine tbdms	Ethanol	Roots	GC-MS	[64]

5. Pharmacological activities

A number of pharmacological activities of *A. karroo* have been reported in literature justifying some of its ethnomedicinal uses. These biological activities include antibacterial [14,20,27,62,64–66], antifungal [14,20,27,65,66], antigonococcal [20], antihelmintic [24,58,67–69], anti-inflammatory and analgesic [27,70], antilisterial [63], antimalarial [71], antimycobacterial [62,65], antioxidant [66] and HIV-1 reverse transcriptase [20,27,72].

5.1. Antibacterial

Mulaudzi *et al* [20] investigated the antibacterial effects of aqueous, acetone, dichloromethane, ethanol, methanol and petroleum ether bark extracts of *A. karroo* against *Bacillus subtilis, Escherichia coli, Klebsiella pneumoniae* and *Staphylococcus aureus* using micro-dilution bioassay with neomycin as positive control. The minimal microbicidal concentration (MMC) of the tested bacteria ranged from 0.195 to 3.125 mg/mL, with the best activity with MMC value of 0.195 mg/mL displayed by aqueous extract against *Staphylococcus aureus* [20]. Madureira *et al* [62] evaluated antibacterial activities of hexane, dichloromethane, ethyl acetate and methanol extracts of aerial parts of *A. karroo* against Gram-positive (*Staphylococcus aureus* and *Enterococcus faecalis*) and Gram-negative bacteria (*E. coli*, *Pseudomonas aeruginosa*, *K. pneumoniae*) using the broth microdilution method. The minimal inhibition concentration (MIC) of the tested bacteria ranged from 7.5 to >250 μg/mL, with the best activity with MIC value of 7.5 μg/mL displayed by methanol extract against *Staphylococcus aureus* [62]. Similarly, Nielsen *et al* [65] evaluated antibacterial activities of leaf and stem methanol extracts of *A. karroo* against *Citrobacter, E. coli, K. pneumoniae, P. aeruginosa* and *Staphylococcus aureus* using liquid micro-broth dilution technique with ciprofloxacin as positive control. The minimal inhibition concentration (MIC) of the tested bacteria ranged from 78.12 to 1250.00 μg/mL, with the lowest MIC value of 78.12 μg/mL displayed by stem extracts against *K. pneumoniae* and *Staphylococcus aureus* [65]. The minimal microbicidal concentration (MMC) of the tested bacteria ranged from 156.25 to >2500.00 μg/mL, with the lowest MMC value of 156.25 μg/mL displayed by stem extracts against *Staphylococcus aureus* (Nielsen *et al*., 2012). Cock and van Vuuren [14] evaluated antibacterial activities of methanol and aqueous leaf extracts of *A. karroo* against *Alicaligenes faecalis, Aeromonas hydrophilia, Bacillus cereus, B. subtilis, Citrobacter freundi, E. coli, K. pneumoniae, Proteus mirabilis, Proteus vulgaris, P. aeruginosa, Pseudomonas fluorescens, Salmonella typhimurium, Serratia marcescens, Shigella sonnei, Staphylococcus aureus* and *Staphylococcus epidermidis* using modified disc diffusion method with chloramphenicol, ampliciilin and nystatin as positive controls. The minimal inhibition concentration (MIC) values of the tested microbes ranged from 235 μg/mL to 4836 μg/mL, with lowest MIC value of 235 μg/mL demonstrated by aqueous extracts against *B. subtilis* [14]. Priyanka *et al* [64] evaluated antibacterial activities of leaf and root chloroform, ethanol, ethyl acetate and methanol *A. karroo* extracts using the agar well diffusion method against *Staphylooccus aureus*, *E. coli*, *Salmonella typhi*, *P. aeruginosa*, *K. pneumoniae*, *P. vulgaris* and *B. subtilis* with ampicillin and distilled water as positive and negative controls, respectively. Methanol extracts of *A. karroo* leaves caused the maximum zone of inhibition against *P. vulgaris* (20.33 ± 1.53) mm and the lowest against *S. typhi* (10.33 ± 1.53) mm. An ethyl acetate extract of *A. karroo* root caused the maximum zone of inhibition against *Staphylooccus aureus* (33.30 ± 1.53) mm and the lowest against *E. coli* (8.67 ± 1.53) mm [64]. Mamba *et al* [27] evaluated antibacterial activities of ethanol extracts of *A. karroo* against *Gardnerella vaginalis, Neisseria gonorrhoeae and Oligella ureolytica* using the serial broth micro-dilution assay with ciprofloxacin as the positive control. Good activity was demonstrated by the tested microbes with minimal inhibition concentration (MIC) values of 6.3 mg/mL against *G. vaginalis*, *O. ureolytica* (1.6 mg/mL) and *N. gonorrhoeae* (0.8 mg/mL) [27]. Tshikalange *et al* [66] also evaluated antibacterial activities of ethanol extracts of *A. karroo* roots against *E. coli, Klebsiella oxytoca, K. pneumoniae* subsp. *pneumoniae, N. gonorrhoeae, Staphylococcus aureus* using the serial broth micro-dilution assay with ciprofloxacin as positive control. Lowest minimal inhibition concentration (MIC) value were demonstrated against *K. oxytoca* (0.8 mg/mL), *N. gonorrhoeae* (0.8 mg/mL) and *Staphylococcus aureus* (0.4 mg/mL) [66]. Chattopadhyay *et al* [73] evaluated antibacterial activities of the compound β-sitosterol **1** against *E. coli*, *Enterococcus faecalis*, *P. mirabilis*, *P. aeruginosa*, *Staphylooccus aureus* and *Staphylooccus saprophyticus* using disk diffusion methods with amoxycillin and gentamicin as controls. Weak activity was demonstrated by the tested microbes with minimal inhibition concentration (MIC) values ranging from 512 to 1000 μg/mL [73]. These antibacterial properties displayed by different extracts of *A. karroo* somehow confirm the species' antibacterial potential and its usefulness in the treatment and management of bacterial infections such as diarrhoea, dysentery, gonorrhoea and syphilis, see Table 1.

5.2. Antifungal

Mulaudzi *et al* [20] evaluated the antifungal effects of aqueous, acetone, dichloromethane, ethanol, methanol and petroleum ether bark extracts of *A. karroo* against *Candida albicans* using micro-dilution bioassay with amphotericin as positive control. The minimal inhibition concentration (MIC) of the tested fungus ranged from 3.125 to 6.250 mg/mL, while the minimum fungicidal concentration (MFC) values ranged from 3.125 to >12.500 mg/mL [20]. Nielsen *et al* [65] also evaluated the antifungal activities of leaf and stem methanol extracts of *A. karroo* against *C. albicans* and *Microsporum audouinii* using liquid micro-broth dilution technique. The results of the minimal inhibitory concentration (MIC) indicated the lowest value of 78.12 μg/mL from methanol stem extracts against both species [65]. The results of the minimal microbicidal concentration (MMC) indicated weak activity of 312.50 μg/mL from methanol stem extracts against both species [65]. Cock and van Vuuren [14] evaluated antifungal activities of methanol and aqueous leaf extracts of *A. karroo* against *Aspergillus niger, C. albicans* and *Rhizopus stolonifer* using a modified disc diffusion method with chloramphenicol, ampliciilin and nystatin as positive controls. Antifungal activities were observed in methanol and aqueous leaf extracts against *A. niger* with minimal inhibition concentration (MIC) values of 486 μg/mL and 325 μg/mL, respectively [14]. Recently, Mamba *et al* [27] evaluated antifungal activities of

ethanol extracts of *A. karroo* against *C. albicans* using the serial broth micro-dilution assay. The extract demonstrated good activity with minimal inhibition concentration (MIC) value of 0.8 mg/mL [27]. In a separate study, Tshikalange *et al* [66] evaluated antifungal activities of ethanol extracts of *A. karroo* roots against *C. albicans*. The extract demonstrated some activity with minimal inhibition concentration (MIC) value of 1.6 mg/mL against the fungus [66].

5.3. Antigonococcal

Mulaudzi *et al* [20] evaluated the antigonococcal activities of aqueous, acetone, dichloromethane, ethanol, methanol and petroleum ether bark extracts of *A. karroo* against *N. gonorrhoeae* through determination of clear zones of inhibition with ciprofloxacin and dimethylsulfoxide (DMSO) as positive and negative controls respectively. *A. karroo* showed moderate activity with dichloromethane, ethanol and petroleum ether extracts with %inhibition ranging from 44.0 ± 0.0 to 55.0 ± 2.0 [20]. The good activity observed from the plant extracts tested in this study could lead to the isolation of lead antigonococcal compounds.

5.4. Antihelmintic

Sparg *et al* [67] evaluated the antihelmintic effects of *A. karroo* leaf extracts against schistosomules of the species *Schistosoma haematobium*. *A. karroo* extracts at 50 mg/mL killed 33% of schistosomula worms after 1 h, 66.7% of the worms were killed at 25 mg/mL and *A. karroo* extracts were 100% lethal at 12.5 mg/mL [67]. Mølgaard *et al* [24] evaluated the antihelmintic effects of *A. karroo* leaf and root extracts against schistosomules of the trematode *Schistosoma mansoni* and cysticercoids of the cestode *Hymenolepis diminuta*. The extracts killed the newly excysted cysticercoids within an hour, when incubated in a culture medium. The lethal concentrations of *A. karroo* extracts varied from 0.8 to 17.0 mg/mL after 24 h [24]. The best results against *H. diminuta* were obtained with leaf extracts with lethal concentrations of 3.1 mg/mL and 0.8 mg/mL after 1 h and 24 h, respectively. *A. karroo* extracts showed some activity against *S. mansoni* with lethal concentrations varying from 0.25 to 0.30 mg/mL [24]. *A. karroo* leaf extract was also tested against schistosomules showing weak activity with lethal concentrations of 103.0 mg/mL [24]. These pharmacological evaluations are of importance in the traditional use of *A. karroo* as an antihelmintic [39] and as herbal medicine against urinary schistosomiasis [24] and future research focusing on control and management of schistosomiasis in sub-Saharan Africa.

Kahiya *et al* [68] evaluated the antihelmintic effects of *A. karroo* leaves (200 g/d) on Boer goats orally infected with a single dose of *Haemonchus contortus* third stage larvae. Kahiya *et al* [68] observed a 34% decrease in the faecal egg counts in *A. karroo* fed animals relative to the control group. Similarly, Xhomfulana *et al* [69] evaluated antihelmintic effects of *A. karroo* leaf meal on *H. contortus* and *Oesophagostomum colombianum* in cattle. Faecal samples were collected from the cattle recta every fortnight and examined for nematode egg types using the modified McMaster technique. Xhomfulana *et al* [69] found that the cattle that received the *A. karroo* leaf meal had lower *H. contortus* and *O. colombianum* worm burdens than those that received the control diet. Marume *et al* [58] evaluated antihelmintic effects of *A. karroo* leaf extracts in four month old Xhosa lop-eared goats exposed to a single dose of 6000 freshly cultured L3 *H. contortus* larvae. Marume *et al* [58] observed reduction in faecal larval counts and *H. contortus* worm counts in goats that consumed *A. karroo* leaves (182 g/d). Based on these evaluation reports, *A. karroo* presents an inexpensive, risk-free and eco-friendly approach to controlling worm population in livestock in rural areas and other marginalized communities. According to Brown *et al* [57], the use of *A. karroo* for helminthic control can be used as a feasible alternative to commercially manufactured antihelmintic or as part of an integrated system to reduce future occurrences of antihelmintic resistance to commercial medicines.

5.5. Anti-inflammatory and analgesic

Adedapo *et al* [70] evaluated anti-inflammatory activities of the aqueous extract of the stem bark of *A. karroo* using the carrageenan-induced and histamine-induced rat paw oedema models and analgesic activity was evaluated using acetic acid-induced writhing response in mice. The extract at 100 and 200 mg/kg reduced significantly the formation of oedema induced by carrageenan and histamine [70]. In the acetic acid-induced writhing model, the extract showed a good analgesic effect characterized by a significant reduction in the number of writhes with two doses (100 and 200 mg/kg) used when compared to the untreated control group [70]. In the tail immersion test, the extract at the doses used (100 and 200 mg/kg) increased reaction time to pain after 30 min of oral administration of the extract. Mamba *et al* [27] evaluated anti-inflammatory activities of ethanol extracts of *A. karroo* by determining the inhibitory effect of the extracts on the activities of the pro-inflammatory enzyme, lipoxygenase and inducible nitric oxide synthase with quercetin and dimethyl sulphoxide (DMSO) as positive and negative controls respectively. *A. karroo* showed good 15-LOX inhibition activity with IC_{50} value of 62.24 μg/mL, which is comparable to the IC_{50} value of the positive control quercetin which was 48.86 μg/mL [27].

Chattopadhyay *et al* [73] evaluated anti-inflammatory activities of the methanol extracts of compound β-sitosterol **1** using carrageenan-induced rat paw oedema (acute model), dextran-induced rat paw oedema (sub-acute model) and cotton pellet-induced granuloma (chronic model) with indomethacin as control. The anti-inflammatory activity of β-sitosterol **1** demonstrated maximum inhibition of 64.39% at 25 mg/kg dose in carrageenan-induced rat paw oedema against 67.47% inhibition demonstrated by the standard indomethacin after 3 h of drug treatment. In the dextran-induced rat paw oedema model, β-sitosterol **1** showed inhibition of 60.48% at 25 mg/kg nearly equal to the inhibition of 60.73% produced by indomethacin. The results of the cotton-pellet granuloma model of inflammation that β-sitosterol **1** significantly inhibited the granuloma weight in a dose dependent manner with a maximum inhibition of 51.54% at 25 mg/kg compared to 54.07% for indomethacin [73]. These results gave a scientific basis to the traditional uses of *A. karroo* mainly for wound poultices, eye treatments and cold remedies.

5.6. Antilisterial activity

Nyila *et al* [63] evaluated antilisterial activity of ethyl acetate and chloroform extracts of *A. karroo* against *Listeria monocytogenes* using the disc diffusion method with erythromycin as positive control. The ethyl acetate extract of *A. karroo* showed good antilisterial activity, exhibiting both minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of 3.1 mg/mL, while MIC and MCB for chloroform extract were 6.25 mg/mL [63]. The same authors also evaluated the antilisterial activities of ethyl acetate extracts of three compounds namely epicatechin **1**, β-sitosterol **2** and epigallocatechin **3** isolated from *A. karroo* against *L. monocytogenes* using the disc diffusion method with erythromycin as positive control. The three compounds demonstrated good antilisterial activities with MIC and MCB values ranging from 0.031 to 0.500 mg/mL [63].

5.7. Antimalarial

Ramalhete *et al* [71] evaluated antimalarial activity of *n*-hexane, dichloromethane, ethyl acetate and methanol extracts of aerial parts of *A. karroo* against *Plasmodium falciparum*. *A. karroo* showed moderate to no significant activity with IC_{50} values ranging from (60.00 ± 12.30) μg/mL to > 100 μg/mL [71]. However, it is important to note that *A. karroo* is frequently used to treat fever or malaria in Mozambique [29] and therefore, an explanation for their lack of significant *in vitro* antimalarial inactivity could be that these plants may act as antipyretics or may enhance the immune system, rather than having direct antiparasitic activity [74].

5.8. Antimycobacterial

Madureira *et al* [62] evaluated antimycobacterial activities of hexane, dichloromethane, ethyl acetate and methanol extracts of aerial parts of *A. karroo* against *Mycobacterium smegmatis* using the broth microdilution method. The minimal inhibition concentration (MIC) of the tested bacterium ranged from 31.0 to >250.0 μg/mL, with the best activity with MIC value of 31.0 μg/mL displayed by n-hexane extract [62]. Similarly, Nielsen *et al* [65] evaluated antimycobacterial activities of the stem methanol extract of *A. karroo* against *M. smegmatis* and *Mycobacterium tuberculosis* using the radiometric respiratory techniques with dimethylsulfoxide (DMSO) as control. Both *M. smegmatis* and *M. tuberculosis* demonstrated weak activity with minimal inhibition concentration (MIC) values of 1250 and 2500 μg/mL, respectively [65]. Therefore, these preliminary evaluations done by Madureira *et al* [62] and Nielsen *et al* [65] provide baseline data for future research on the species as a possible source of traditional medicine for treatment of tuberculosis and other respiratory ailments.

5.9. Antioxidant

Tshikalange *et al* [66] evaluated antioxidant activities of ethanol extracts of *A. karroo* roots by assessing the free radical scavenging activity using DPPH (2, 2-diphenyly-1-picrylhydrazyl) with ascorbic acid (vitamin C) as a positive control. The IC_{50} of the extract was 0.83 μg/mL, while vitamin C (positive control) had an IC_{50} value of 1.44 μg/mL [66]. The documented antioxidant activities *A. karroo* root extracts are probably due to flavonoids and phenols that have been isolated from leaves [54,57,61–64]. Flavonoids and phenolic compounds found in plants are known to have antioxidant properties [75].

5.10. HIV-1 reverse transcriptase

Mulaudzi *et al* [20] evaluated anti-HIV activities of aqueous and methanol bark extracts of *A. karroo* using a non-radioactive HIV-1 RT colorimetric ELISA kit. The aqueous and methanol extracts of *A. karroo* bark showed good HIV-1 reverse transcriptase (RT) inhibition percentage (70%) at 1 mg/mL based on COX-assay, with all tested extracts exhibiting dose dependent IC_{50} values of (0.03 ± 0.00) and (0.10 ± 0.01) mg/mL, respectively [20]. Moll *et al* [72] evaluated anti-HIV activities of 50% methanol:dichloromethane (1:1) leaf and twig extracts of *A. karroo* using a reverse transcriptase test kit. *A. karroo* demonstrated some inhibitory activity of reverse transcriptase [72]. Recently, Mamba *et al* [27] evaluated anti-HIV activities of ethanol extracts of *A. karroo* against recombinant HIV-1 enzyme using non-radioactive HIV-RT colorimetric assay with doxorubicin as positive control. *A. karroo* demonstrated moderate inhibition of HIV-1 reverse transcriptase activity with 66.8% inhibition compared to 96.5% inhibitory activity demonstrated by doxorubicin, the positive control. Therefore, the good inhibitory activity on HIV-1 reverse transcriptase demonstrated by *A. karroo* extracts may imply that the species could be a good source of potent compounds for therapeutic strategy against HIV-1 reverse transcriptase.

5.11. Cytotoxicity and toxicity

The aqueous extract from the shoot of *A. karroo* was evaluated for its acute toxicity by the oral route in mice and for the sub-acute effect on haematological, biochemical and histological parameters in Wistar rats [76]. In the acute toxicity test, *A. karroo* extract caused death in animals that received 1600 and 3200 mg/kg doses. Oral treatments in rats with this extract at 800 mg/kg did not cause any significant change in the red blood cell count (RBC), packed cell volume (PCV), haemoglobin concentration (HB), mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC), mean corpuscular haemoglobin (MCH), white blood cells and its differentials. It, however, caused a significance decrease in the levels of platelets [76]. In the biochemical parameters, the extract caused a significant decrease in the levels of total protein, albumin, globulin, aspartate amino transferase (AST), alanine amino transferase (ALT), total and unconjugated bilirubin. Adedapo *et al* [76] noted changes in the body weights of the mice but no significant changes were observed in the levels of some electrolytes (sodium, potassium and chloride). Lung with multiple abscess, kidney and liver with mild congestion were also observed histopathologically [76]. Cock and van Vuuren [14] evaluated toxicity of aqueous and methanol leaf extracts of *A. karroo* using a modified *Artemia franciscana nauplii* lethality assay. *A. karroo* leaf water and methanolic ectracts induced mortalities in the *Artemia nauplii* below 20% following 24 h and 48 h of exposure, indicating that the extracts are of low toxicity.

Nyila *et al* [63] evaluated the cytotoxicity of ethyl acetate and chloroform extracts of *A. karroo* using the XTT method using the cell proliferation kit II (Boehringer-Mannheim) with

zearalenone as positive control. Epicatechin **2** was the least toxic compound with IC_{50} value of >200.0 μg/mL, while β-sitosterol **1** and epigallocatechin **3** were found to be 63.82 and 28.91 μg/mL, respectively [63]. Tshikalange *et al* [66] evaluated cytotoxicity activities of ethanol extracts of *A. karroo* roots on Vero African monkey cells lines with 2, 3-bis[2-methoxy-4-nitro-5-sulfophenyl]-2H-tetrazolium-5-carboxanilide (XTT) reagents with actinomycin D as positive control. The extracts showed toxicity with 50% viability of cells (EC_{50}) at concentrations value of 115 μg/mL against actinomycin D which was used as positive control exhibited an IC_{50} value of 0.009 32 μg/mL [66]. These preliminary cytotoxicity and toxicity evaluations carried out so far [14,63,66,76] study concluded that caution must be exercised in the use of the plant for medicinal purposes.

6. Conclusions

A. karroo has been used in southern Africa as herbal medicine for many centuries. However, chemical profiling and phytochemical research carried out so far on the species is limited. More research is required and future research should focus on more comprehensive chemical characterization of both crude and pure extracts, evaluate potential for commercialization and development of nutraceutical products based on traditional uses of *A. karroo*. Most of the pharmacological research conducted on *A. karroo* so far has focused on the phytochemistry and biological properties of bark, leaves and roots, and little or no phytochemical research and pharmacological evaluations have been done on other plant parts which are traditionally used as herbal medicines. Such plant parts include exudates and gum which are known to have some commercial potential [8,11,12]. Therefore, future research on the species should focus on other plant parts, as well as organ-to-organ, age and seasonal variation evaluations in the phytochemical content and pharmacological activities of the species.

Detailed phytochemical studies of *A. karroo* and its phytochemical properties, especially the mechanisms of action of its bioactive constituents to illustrate the correlation between ethnomedicinal uses and pharmacological activities should be the focus of further research on the species. There is need for extensive *in vivo* experiments to validate the existing pharmacological activities. However, because *A. karroo* contains potentially toxic compounds, its toxicological properties need to be properly established to ensure that potentially toxic components are kept below tolerance levels.

Conflict of interest statement

The author declares that he has no conflict of interest.

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References

[1] Aubrey A. *Acacia karroo* Hayne. Pretoria: South African National Biodiversity Institute (SANBI). Available from: Http://www.plantzafrica.com/plantab/acaciakar.htm.

[2] Palmer E, Pitman P. *Trees for southern Africa covering all known indigenous species in Republic of South Africa, South West Africa, Botswana, Lesotho and Swaziland*. Cape Town: A.A. Balkema; 1972, p. 792.

[3] Dyer C. New names for the African *Acacia* species in *Vachellia* and *Senegalia*. *South For A J For Sci* 2014; **76**(1): 4.

[4] Maslin BR. Generic and subgeneric names in *Acacia* following retypification of the genus. *Muelleria* 2008; **26**(1): 7-9.

[5] Moore G. Action on the proposal to conserve the name *Acacia* at the nomenclature section of the XVII international botanical congress in vienna: did a yes have it? *Linnean* 2008; **24**(1): 16-120.

[6] Taylor CL, Barker NP. Species limits in *Vachellia (Acacia) karroo* (mimosoideae: Leguminoseae): evidence from automated ISSR DNA 'fingerprinting'. *S Afr J Bot* 2012; **83**(1): 36-43.

[7] Idamokoro EM, Masika PJ, Muchenje V. *Vachellia karroo* leaf meal: a promising non-convential feed resource for improving goat production in low-input farming systems of southern Africa. *Afr J Range Forage Sci* 2016; **33**(3): 141-153.

[8] Barnes RD, Filer DL, Milton SJ. *Acacia karroo: monograph and annotated bibliography*. Oxford: Oxford Forestry Institute, University of Oxford; 1996, p. 97. Tropical Forestry Paper No. 32.

[9] Weber J, Surhes S, Zhou Y. *Weed risk assessment: Karroo thorn (Acacia karroo). Queensland: department of employment, economic development and innovation*. Queensland: Department of Employment, Economic Development and Innovation, Queensland Government; 2010, p. 15.

[10] Ross JH. *A conspectus of the African Acacia species*. Pretoria: Botanical Survey of South Africa Memoirs No. 44, National Botanical Institute; 1979, p. 155.

[11] Parratt NT. The potential of non-timber forest products of Botswana. *Botsw Notes Rec* 1996; **28**(1): 203-218.

[12] van Wyk BE. The potential of South African plants in the development of new medicinal products. *S Afr J Bot* 2011; **77**(4): 812-829.

[13] van Wyk BE, Gericke N. *People's plants: a guide to useful plants of southern Africa*. Pretoria: Briza Publications; 2000, p. 352.

[14] Cock IE, van Vuuren SF. South African food and medicinal plant extracts as potential antimicrobial food agents. *J Food Sci Technol* 2015; **52**(11): 6879-6899.

[15] van Wyk BE, van Oudtshoorn B, Gericke N. *Medicinal plants of South Africa*. Pretoria: Briza Publications; 1997, p. 336.

[16] Orwa C, Mutua A, Kindt R, Jamnadass R, Anthony S, Acacia karroo Hayne. *Agroforestry Database: a tree reference and selection guide version 4.0*. Nairobi: World Agroforestry; 2009. Available from: http://www.worldagroforestry.org/sites/treedbs/treedatabases.asp.

[17] Guillarmod AJ. *Flora of Lesotho (Basutoland)*. Lehre: Verlag von J. Cramer; 1971, p. 474.

[18] Moteetee A, van Wyk BE. The medical ethnobotany of Lesotho: a review. *Bothalia* 2011; **41**(1): 209-228.

[19] Watt JM, Breyer-Brandwijk MG. *The medicinal and poisonous plants of Southern and Eastern Africa*. Edinburgh and London: E & S Livingstone Ltd; 1962, p. 1457.

[20] Mulaudzi RB, Ndhlala AR, Kulkarni MG, Finnie JF, van Staden J. Antimicrobial properties and phenolic contents of medicinal plants used by the Venda people for conditions related to venereal diseases. *J Ethnopharmacol* 2011; **135**(2): 330-337.

[21] Appipi JR, Grierson DS, Afolayan AJ. Ethnobotanical study of plants used for the treatment of diarrhoea in the Eastern Cape, South Africa. *Pak J Biol Sci* 2008; **11**(15): 1961-1963.

[22] Olajuyigbe OO, Afolayan AJ. Ethnobotanical survey of medicinal plants used in the treatment of gastrointestinal disorders in the Eastern Cape Province, South Africa. *J Med Pl Res* 2012; **6**(18): 3415-3424.

[23] Mlambo Np. *The screening of medicinal plants traditionally used to treat diarrhoea in Ongoye area, Kwazulu Natal*. Kwadlangezwa: University of Zululand; 2008 [MSc dissertation].

[24] Mølgaard P, Nielsen SB, Rasmussen DE, Drummond RB, Makaza N, Andreassen J. Anthelmintic screening of Zimbabwean plants traditionally used against schistosomiasis. *J Ethnopharmacol* 2001; **74**(3): 257-264.

[25] Gelfand M, Drummond RB, Mavi S, Ndemera B. *The traditional medical practitioner in Zimbabwe: his principles of practice and pharmacopoeia*. Gweru: Mambo Press; 1985, p. 411.

[26] Chigora P, Masocha R, Mutenheri F. The role of indigenous medicinal knowledge (IMK) in the treatment of ailments in rural Zimbabwe: the case of Mutirikwi communal lands. *J Sustain Dev Afr* 2007; **9**(2): 26-43.
[27] Mamba P, Adebayo SA, Tshikalange TE. Anti-microbial, anti-inflammatory and HIV-1 reverse transcriptase activity of selected South African plants used to treat sexually transmitted diseases. *Int J Pharmacogn Phytochem Res* 2016; **8**(11): 1870-1876.
[28] Hutchings A, Scott AH, Lewis G, Cunningham AB. *Zulu medicinal plants. An inventory*. Pietermaritzburg: University of Natal Press; 1996, p. 450.
[29] Bandeira SO, Gaspar F, Pagula F. African ethnobotany and healthcare: emphasis on Mozambique. *Pharm Biol* 2001; **39**(Suppl.): 70-73.
[30] Venter F, Venter JA. *Making the most of indigenous trees*. Pretoria: Briza Publications; 1996, p. 368.
[31] Mabogo DEN. *The ethnobotany of the Vhavenda*. Pretoria: University of Pretoria; 1990 [MSc dissertation].
[32] Roberts M. *Indigenous healing plants*. Pretoria: Southern Book Publishers, Halfway House; 1990, p. 236.
[33] Coates Palgrave K. *Trees of southern Africa*. Cape Town: Struik Publishers; 1977, p. 725.
[34] Gerstner J. A preliminary checklist of Zulu names of plants with short notes. *Bantu Stud* 1941; **15**(2): 277-301.
[35] Maroyi A. Ethnobotanical study of medicinal plants used by people in Nhema communal area, Zimbabwe. *J Ethnopharmacol* 2011; **136**(2): 347-354.
[36] Sewani-Rusike CR, Mammen M. Medicinal plants used as home remedies: a family survey by first year medical students. *Afr J Tradit Complement Altern Med* 2014; **11**(5): 67-72.
[37] Afolayan AJ, Grierson DS, Mbeng WO. Ethnobotanical survey of medicinal plants used in the management of skin disorders among the Xhosa communities of the Amathole District, Eastern Cape, South Africa. *J Ethnopharmacol* 2014; **153**(1): 220-232.
[38] Corrigan BM, van Wyk BE, Geldenhuys CJ, Jardine JM. Ethnobotanical plant uses in the KwaNibela Peninsula, st Lucia, South Africa. *S Afr J Bot* 2011; **77**: 346-359.
[39] Wintola OA, Afolayan AJ. An inventory of indigenous plants used as anthelmintics in Amathole district municipality of the eastern Cape province, South Africa. *Afr J Tradit Complement Altern Med* 2015; **12**(4): 112-121.
[40] van der Merwe D, Swan GE, Botha CJ. Use of ethnoveterinary medicinal plants in cattle by Setswana-speaking people in the Madikwe area of the North West Province. *J South Afr Vet Ass* 2001; **72**(4): 189-196.
[41] McGaw IJ, Eloff JN. Ethnoveterinary use of South African plants and scientific evaluation of their medicinal properties. *J Ethnopharmacol* 2008; **119**(3): 559-574.
[42] Chinsembu KC, Negumbo J, Likando M, Mbangu A. An ethnobotanical study of medicinal plants used to treat livestock diseases in Onayena and Katima Mulilo, Namibia. *S Afr J Bot* 2014; **94**: 101-107.
[43] Nyahangare ET, Mvumi BM, Mutibvu T. Ethnoveterinary plants and practices used for ecto-parasite control in semi-arid smallholder farming areas of Zimbabwe. *J Ethnobiol Ethnomed* 2015; **11**: 30.
[44] Soyelu OT, Masika PJ. Traditional remedies used for the treatment of cattle wounds and myiasis in Amatola Basin, Eastern Cape Province, South Africa. *Onderstepoort J Vet Res* 2009; **76**(4): 393-397.
[45] Liengme CA. Plants used by the Tsonga people of Gazankulu. *Bothalia* 1981; **13**(3–4): 501-518.
[46] Setshogo MP, Venter F. *Trees of Botswana: names and distribution*. Pretoria: Southern African Botanical Diversity Network Report No. 18; 2003, p. 162.
[47] Archer FM. Customary plant use in Namaqualand: Acacia karroo Hayne: a tree with many uses. *Veld Flora* 1988; **74**(2): 111-112.
[48] Maroyi A, Rasethe MT. Comparative use patterns of plant resources in rural areas of South Africa and Zimbabwe. *Phyt Int J Exp Bot* 2015; **84**: 288-297.
[49] Rasethe MT, Semenya SS, Potgieter MJ, Maroyi A. The utilization and management of plant resource in rural areas of the Limpopo province, South Africa. *J Ethnobiol Ethnomed* 2013; **9**: 27.
[50] Meissner HH. Recent research on forage utilization by ruminant livestock in South Africa. *Anim Feed Sci Tech* 1997; **69**(1–3): 103-119.
[51] Negesse T, Rodehutscord M, Pfeffer E. The effect of dietary crude protein level on intake, growth, protein retention and utilization of growing male Saanen kids. *Small Rumin Res* 2001; **39**(3): 243-251.
[52] Mokoboki HK, Ndlovu LR, Ngambi JW, Malatje MW, Nikolova RV. Nutritive value of *Acacia* tree foliages growing in the Limpopo Province of South Africa. *South Afr J Anim Sci* 2005; **35**(4): 221-228.
[53] Mapiye C, Chimonyo M, Marufu MC, Dzama K. Utility of *Acacia karroo* for beef production in Southern African smallholder farming systems: a review. *Anim Feed Sci Tech* 2011; **164**(3–4): 135-146.
[54] Dube JS, Reed JD, Ndlovu LR. Proanthocyanidans and other phenolics in *Acacia* leaves of Southern Africa. *Anim Feed Sci Tech* 2001; **91**(1–2): 59-67.
[55] Ngambu S, Muchenje V, Marume U. The effect of *Acacia karroo* supplementation and thermal preparation on meat sensory characteristics of the indigenous Xhosa lopeared goat genotype. *Afr J Biotechnol* 2012; **11**(65): 12878-12884.
[56] Gxasheka M, Thobela LT, Ning Q, Zhi-Chao L. An overview of tannins rich plants as alternative supplementation on ruminant animals: a Review. *Int J Agric Res Rev* 2015; **3**(6): 343-349.
[57] Brown D, N'gambi JW, Norris D. Feed potential of *Acacia karroo* leaf meal for communal goat production in southern Africa: a review. *J Anim Pl Sci* 2016; **26**(4): 1178-1186.
[58] Marume U, Chimonyo M, Dzama K. Influence of dietary supplementation with *Acacia karroo* on experimental haemonchosis in indigenous Xhosa lop-eared goats of South Africa. *Livest Sci* 2012; **144**(1–2): 132-139.
[59] Aganga AA, Adogla-Bessa T, Omphile UJ, Tshireletso K. Significance of browses in the nutrition of Tswana goats. *Arch Zootec* 2000; **49**(188): 469-480.
[60] Ngwa AT, Nsahlai IV, Bonsi MLK. The rumen digestion of dry matter, nitrogen and cell wall constituents of the pods of *Leucaena leucocephala* and some *Acacia* species. *J Sci Food Agric* 2002; **82**(1): 98-106.
[61] Malan E, Swartz. A comparative study of the phenolic products in the heartwood of *Acacia karroo* from two different localities. *Phytochem* 1995; **39**(4): 791-794.
[62] Madureira AM, Ramalhete C, Mulhovo S, Duarte A, Ferreira MJU. Antibacterial activity of some African medicinal plants used traditionally against infectious diseases. *Pharm Biol* 2012; **50**(4): 481-489.
[63] Nyila MA, Leonard CM, Hussein AA, Lall N. Activity of South African medicinal plants against *Listeria monocytogenes* biofilms, and isolation of active compounds from. *Acacia karroo S Afr J Bot* 2012; **78**: 220-227.
[64] Priyanka C, Kumar P, Bankar SP, Karthik L. *In vitro* antibacterial activity and gas chromatography–mass spectroscopy analysis of *Acacia karroo* and *Ziziphus mauritiana* extracts. *J Taibah Univ Sci* 2015; **9**(1): 13-19.
[65] Nielsen TRH, Kuete V, Jäger AK, Meyer JJM, Lall N. Antimicrobial activity of selected South African medicinal plants. *BMC Compl Altern Med* 2012; **12**: 74.
[66] Tshikalange TE, Mamba P, Adebayo SA. Antimicrobial, antioxidant and cytotoxicity studies of medicinal plants used in the treatment of sexually transmitted diseases. *Int J Pharmacogn Phytochem Res* 2016; **8**(11): 1891-1895.
[67] Sparg SG, van Staden J, Jäger AK. Efficiency of traditionally used South African plants against schistosomiasis. *J Ethnopharmacol* 2000; **73**(1–2): 209-214.
[68] Kahiya C, Mukaratirwa S, Thamsborg SM. Effects of *Acacia nilotica* and *Acacia karroo* diets on *Haemonchus contortus* infection in goats. *Vet Parasitol* 2003; **115**(3): 265-274.
[69] Xhomfulana V, Mapiye C, Chimonyo M, Marufu MC. Supplements containing *Acacia karroo* foliage reduce nematode burdens in Nguni and crossbred cattle. *Anim Prod Sci* 2009; **49**(8): 646-653.

[70] Adedapo AA, Sofidiya MO, Masika PJ, Afolayan AJ. Anti-inflammatory and analgesic activities of the aqueous extract of *Acacia karroo* stem bark in experimental animals. *Basic Clin Pharmacol Toxicol* 2008; **103**(5): 397-400.

[71] Ramalhete C, Lopes D, Mulhovo S, Rosário VE, Ferreira MJU. Antimalarial activity of some plants traditionally used in Mozambique. In: *Workshop Plantas Medicinais e Fitoterapêuticas nos Trópicos, Lisbon*; 2008. Available from: 2.iict.pt/archive/doc/C_Ramalhete_wrkshp_plts_medic.pdf.

[72] Moll A, Heyman HM, Meyer JJM. Plants with activity against the live HIV virus and the enzyme, reverse transcriptase. *S Afr J Bot* 2013; **86**: 148.

[73] Chattopadhyay D, Arunachalam G, Mandal AB, Sur TK, Mandal SC, Bhattcharya SK. Antimicrobial and anti-inflammatory activity of folklore: *Mallotus peltatus* leaf extract. *J Ethnopharmacol* 2002; **82**(2–3): 229-237.

[74] Phillipson JD, Wright CW. Medicinal plants against protozoal diseases. *Trans R Soc Trop Med Hyg* 1991; **85**(1): 155-165.

[75] Miguel MG, Nunes S, Dandlen SA, Cavaco AM, Antunes MD. Phenols, flavonoids and antioxidant activity of aqueous and methanolic extracts of propolis (*Apis mellifera* L.) from Algarve, South Portugal. *Food Sci Tech* 2014; **34**(1): 16-23.

[76] Adedapo AA, Sofidiya MO, Masika PJ, Afolayan AJ. Safety evaluations of the Aqueous extract of *Acacia karroo* stem bark in rats and mice. *Rec Nat Prod* 2008; **2**(4): 128-134.