A Review Of Medicinal Uses, Phytochemistry And Pharmacological Activities Of Alepidea Species

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Abstract—Alepidea species are widely used as traditional medicines in southern Africa. This study aims at providing comprehensive information on the medicinal uses, phytochemical and pharmacological properties of Alepidia species. Electronic databases, including Web of Science, Science Direct, Google Scholar, Scopus, PubMed, and Springer Link were used as information sources. Additional information was obtained pre-electronic sources such as books, book chapters, scientific journals and other grey literature obtained from the University library. The diterpenoids, particularly kaurene derivatives, alkaloids, flavonols, flavonoids, phenols, proanthocyanidin, saponins and tannins were the main phytochemical classes identified in the extracts of Alepidea species. Some species of Alepidea exhibited various pharmacological activities, including antibacterial, antifungal, anti-HIV, anti-inflammatory, anti-hypertensive, antioxidant, antiplasmodial, antiprotozoal, cardiovascular, diuretic and cytotoxicity activities. The genus Alepidea is a valuable source of bioactive phytochemical compounds with therapeutic potential in different diseases. More in vitro and in vivo animal studies are required to confirm the efficacy, safety and the mechanisms of actions before future clinical studies involving Alepidea species.

Keywords— Alepidea, Apiaceae, herbal medicine, indigenous knowledge, southern Africa, Umbelliferae

1 INTRODUCTION

The genus Alepidea F. Delaroche belongs to the Apiaceae, Umbelliferae, celery, carrot or parsley family. The Apiaceae family is one of the largest and widely distributed plant families with approximately 3750 species and 434 genera [1], and these species have played an important role in human nutrition, medicine and religion in various cultures in throughout the world [2-5]. The genus Alepidea comprises 32 species with its centre of diversity in southern Africa, and one or two species extending to East and North-east Africa [6-8]. The genus name *Alepidea* means "without a scale", based on the Greek prefix "***a***" meaning without, and the word "*lepis*" meaning "a scale". Some species belonging to the genus Alepidia have been used as traditional medicines in southern Africa [6, 9-11]. Such medicinal plants have played an important role as primary sources of traditional medicines for centuries and still continue to provide humankind with new pharmaceutical drugs and health products. The genus Alepidea is also known for having several species with food, medicinal and other traditional uses. The roots of A. amatymbica Eckl. & Zeyh. are used as food flavourant, seasoning and preservative agent in the Eastern Cape province in South Africa [12,13]. In Eswatini and South Africa, the leaves of A. longifolia (E. Mey.) Dümmer and A. natalensis J.M. Wood & M.S. Evans are edible as leafy vegetables when young [14-17]. The young leaves of A. peduncularis A. Rich. are collected from the wild and used as cooked leafy vegetables, particularly in southern Africa [13-15,18]. Van Wyk [19] and Van Wyk [20] argued that the roots of Alepidea species such as A. amatymbica and A. cordifolia B.-E. Van Wyk have potential in the development of new commercial medicinal products which can be used against chest ailments, colds and influenza.

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2 MATERIALS AND METHODS

Several electronic databases were searched which included Web of Science, Elsevier, Pubmed, Google scholar, Springer, Science Direct, Scopus, Taylor and Francis. Additional information was obtained from pre-electronic sources such as books, book chapters, scientific journals and other grey literature obtained from the University library. The relevant terms included ethnobotany, medicinal uses, traditional uses, phytochemistry, pharmacology and toxicity of the extracts, and phytochemical compounds isolated from the genus Alepidea. The Alepidea species names were authenticated using The Plant List managed by the Royal Botanic Gardens, Kew and the Missouri Botanical Garden (http://www.theplantlist.org/). Plant authorities were also authenticated through this process. The ultimate goal of this search was to explore articles that investigated the medicinal uses, phytochemical and pharmacological properties of Alepidea species. A total of 99 articles published between 1938 and 2020 matched the inclusion criteria and were included in this review (Fig. 1).

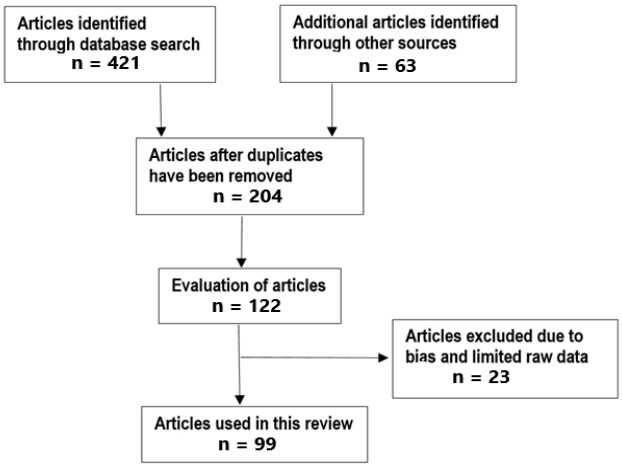

Fig. 1. Flow diagram with the number of selected articles

3 RESULTS AND DISCUSSION

3.1 Medicinal uses of Alepidea species

Plants of the genus Alepidea are widely used in ethnomedicine and ethnoveterinary medicine. A total of 10 species of Alepidea (31.3%) have been identified to be used in folk medicine as herbal medicines, insecticides, tonics, and other uses. These species include A. amatymbica, A. capensis, A. cordifolia, A. longifolia, A. natalensis, A. peduncularis, A. pilifera, A. serrata, A. setifera and A. thodei (Table 2). These species are mainly used as charm and ritual purposes, and traditional medicine for snake bites, venereal diseases, rheumatism, gastro-intestinal problems, headache, fever and respiratory infections (Table 2, Fig. 2). The following section presents a review of ethnomedicinal uses of Alepidea species and more details on this aspect and the associated references are indicated in Table 2. Generally, rhizomes and roots are the widely used plant parts against a large variety of diseases. The herbal preparations mentioned include crushing, decoction, infusion, maceration, inhalation and poultice. Most of the Alepidea species are reported to be used in South Africa, Lesotho, Eswatini and Zimbabwe (Table 2). Alepidea species are used against a wide range of diseases, and treatments of inflammatory conditions, body pain, wounds and skin infections. The species are also used for non-medicinal purposes such as charm and magical rituals, when species are used for good luck, protection purposes or as incense to communicate with the ancestors (Table 2). In most ethnobotanical studies, Alepidea species are used alone, but often mixed with other species. For example, in South Africa, the rhizomes of A. amatymbica are mixed with those of Gunnera perpensa L. as traditional medicine against stomach ache [10,17,21]. In Lesotho and South Africa, the rhizomes and roots of either A. amatymbica or A. cordifolia or A. pilifera or A. setifera are mixed with Cannabis sativa L. are used against asthma [17,22,23]. In South Africa, the roots of A. amatymbica are mixed with bark of Pterocelastrus echinatus N.E.Br., Pterocelastrus rostratus (Thunb.) Walp. and Pterocelastrus tricuspidatus (Lam.) Walp. as traditional medicine against respiratory infection [10,24].

Alepidea amatymbica is an ingredient of a multipurpose herbal concoction called “sejeso” which is sold in informal street herbal medicine markets, herbal medicine shops, supermarkets and pharmacies in South Africa. herbal concoction called “sejeso”. Ndhlala et al. [25] and Madikizela et al. [26] reported the use of “sejeso” for heartburn, stomachache, stomach cramps, indigestion, constipation, vomiting and loss of appetite. This herbal concoction “sajeso” is prepared from five plant species which include Elephantorrhiza burkei Benth. (family Fabaceae), Senegalia caffra (Thunb.) P.J.H. Hurter and Mabb. (Fabaceae), Peltophorum africanum Sond. (Fabaceae), Alepidea amatymbica Eckl. & Zeyh. (Apiaceae) and Hypoxis obtusa Burch. ex Ker Gawl. (Hypoxidaceae) [26]. In South Africa, the rhizomes, roots and whole plant parts of A. amatymbica are traded in informal herbal medicine markets throughout the country in the Eastern Cape [27-29], Gauteng [30,31], KwaZulu Natal [32,33], Limpopo [34,35], Mpumalanga [27], Northern Cape [36] and Western Cape [28] provinces of South Africa and Lesotho [17,29]. Since A. amatymba is widely used as traditional medicine and also sold in informal herbal medicine markets, Gerstner [37] and Wiersum et al. [38] argued that cultivation of the species can serve as a tool for combined biodiversity conservation and poverty alleviation in South Africa. The roots of A. delicatula are traded as herbal medicine in informal herbal medicine markets in the Eastern Cape [28] and Western Cape [28] provinces of South Africa. In Cape Town in South Africa, the roots of A. longifolia are sold as herbal medicine in combination with Cissampelos capensis L.f., Glycyrrhiza glabra L., Stoebe fusca (L.) Thunb. and Tulbaghia violacea Harv. [39,40]. Similarly, the roots of A. longifolia are traded in informal herbal medicine markets in the Gauteng province [30] of South Africa. The roots of A. pilifera and A. setifera are traded in informal herbal medicine markets in the Gauteng province [30] of South Africa. Similarly, the rhizomes and roots of A. cordifolia and A. macowanii are traded as herbal medicines in informal herbal medicine markets in South Africa [31].

TABLE 1
MEDICINAL USES OF ALEPIDEA SPECIES

Scientific name	Plant part	Country /region	Reference
A. amatymbica			
Appetite booster	Roots	South Africa	41
Belching	Rhizomes and roots	South Africa	42
Charm and ritual (good luck and protection)	Rhizome, roots and whole plant	South Africa	17,18,23,35,43,44]
Cleansing blood	Roots	South Africa	41
Cryptococcal meningitis	Rhizomes and roots	South Africa	45
Diabetes mellitus	Roots and whole plant	South Africa	35
Fever	Rhizomes	South Africa	26,46-50
Fungal infections	Rhizomes and roots	South Africa	45
Gastro-intestinal problems (abdominal cramps, abdominal pains, constipation, diarrhoea, dysentery, stomach ache and stomach pains)	Rhizomes and roots	South Africa	6,9,10,17, 22,26,31,42,47,51-66
Stomach ache	Rhizomes mixed with those of Gunnera perpensa L.	South Africa	10,17,21
Headache	Rhizomes and roots	South Africa	18,26,58
Inflammation	Rhizomes and roots	South Africa	67
Oesopharyngeal candidiasis	Rhizomes and roots	South Africa	41
Pain	Rhizomes and roots	South Africa	67
Poison antidote	Roots	South Africa	52
Purgative	Rhizomes and roots	South Africa	6,9
Respiratory infections (asthma, chest complaints, chest pains, chronic cough, colds, cough, influenza, pneumonia, sore throat and tuberculosis)	Rhizomes, rhizomes and whole plant	South Africa	6,9,10,12, 17,18,20,22,23,26,31,35,42-44,49,51,52,54-56,58,59,61,63-74
Asthma	Rhizome and roots mixed with	South Africa	17,22,23

	Cannabis sativa L.		
Respiratory infections	Roots mixed with bark of Pterocelastrus echinatus N.E.Br., P. rostratus (Thunb.) Walp. and P. tricuspidatus (Lam.) Walp.	South Africa	10,24
Rheumatism	Rhizomes and roots	South Africa	6,9,10,12, 17,23,26,48,51,61,64,65
Skin infections (pimples and skin disorders)	Rhizomes and roots	South Africa	47,75
Ulcers	Rhizomes and stems	South Africa	59,76
Weight loss	Roots	South Africa	57
Wounds	Rhizomes and roots	South Africa	10,12,22,26,47,57,58,64
A. capensis			
Charm and ritual (incense to communicate with the ancestors)	Roots and stems	South Africa	77
Human immunodeficiency virus (HIV) opportunistic infections	Roots and stems	South Africa	77
Respiratory problems (asthma, bronchitis, chest pain, cough and tuberculosis)	Roots and stems	South Africa	77,78
A. cordifolia			
Charm and ritual (good luck and protection)	Rhizomes and roots	Eswatini, Lesotho and Zimbabwe	10,16,17,23,79-81
Fever	Roots	Lesotho	79,81
Gastro-intestinal problems (abdominal pains and diarrhoea)	Rhizomes	Zimbabwe	10,17,80,82
Headache	Rhizome and roots	Eswatini, Lesotho, South Africa and Zimbabwe	10,16,17,23,80,83
Malaria	Roots	Mozambique	84,85
Painful joints	Roots	Lesotho	79,81
Repel bees	Rhizome	Zimbabwe	10,17,80
Respiratory infections (asthma, chest pains, colds, cough and influenza)	Rhizomes and roots	Eswatini, Lesotho, South Africa and Zimbabwe	16,20,23,79,81
Asthma	Rhizome and roots mixed with C. sativa L.	Lesotho and South Africa	23
Rheumatism	Roots	Eswatini	16
A. longifolia			
Fever (febrile)	Rhizomes and roots	South Africa	17,86
Gastro-intestinal problems	Rhizomes and roots	South Africa	17,86
Respiratory infections (chest pains and cough)	Rhizomes and roots	South Africa	6,9,10,17,86
Snake bite	Rhizomes and roots	South Africa	17,86
Venereal diseases	Rhizomes and roots	South Africa	17,86
A. natalensis			
Fever (febrile)	Rhizomes and roots	South Africa	17,86
Gastro-intestinal problems (abdominal cramps and diarrhoea)	Rhizomes and roots	South Africa	17,54,55,86
Respiratory infections (asthma, colds, cough and influenza)	Rhizomes and roots	South Africa	17,54,55,86
Snake bite	Rhizomes and roots	South Africa	17,86
Venereal diseases	Rhizomes and roots	South Africa	17,86
A. peduncularis			
Fever	Roots	Eastern Africa	15
Respiratory infections (cough)	Roots	Southern Africa	15
A. pilifera			
Charm and ritual	Rhizomes and roots	Lesotho	23
Fever	Roots	Lesotho	79,81
Headache	Rhizomes and roots	Lesotho and South Africa	23,87
Respiratory infections (asthma, chest pains, colds and cough)	Rhizomes and roots	Lesotho and South Africa	6,9,23,79,81
Asthma	Rhizome and roots mixed with C. sativa L.	Lesotho and South Africa	23
A. serrata			
Charm and ritual	Roots	South Africa	88,89
Fever	Roots	Lesotho	79,81
Headache	Roots	Lesotho	87
Respiratory infections (chest pains, colds, cough and influenza)	Roots	Lesotho and South Africa	47,79,81,89
Toothache	Roots	South Africa	89
A. setifera			
Charm and ritual	Rhizomes and roots	Lesotho	23
Headache	Rhizomes and roots	Lesotho	23
Respiratory infections (chest pains, colds, cough	Rhizomes and roots	Lesotho	6,9,23
Asthma	Rhizome and roots mixed with C. sativa L.	Lesotho and South Africa	23
A. thodei			
Respiratory infections	Roots	Lesotho	90

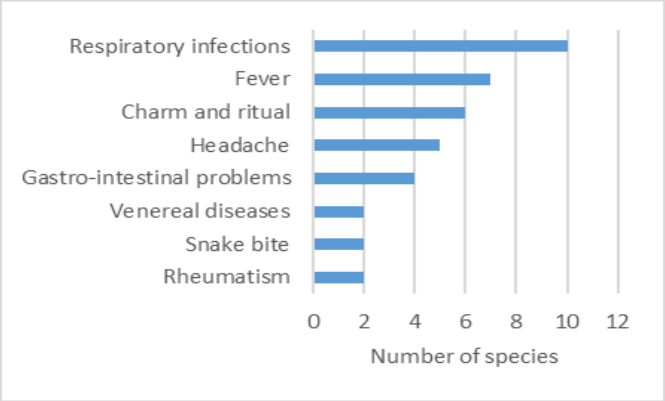

Figure 2. Medicinal uses of Alepidea species

3.2 Phytochemistry

Alepidea chemistry is considerably diverse (Table 2). The diterpenoids appear to be the predominant phytochemical constituents in the genus, chiefly kaurene derivatives. Kaurene derivatives have been identified from more than a third (34.4%) of Alepidea species and these include A. amatymbica, A. capensis, A. comosa, A. galpinii, A. insculpta, A. longifolia, A. natalensis, A. serrata, A. setifera, A. thodei and A. woodii [51,65,70,91]. These phytochemical compounds identified from several Alepidea species enhances the importance of the genus from the medicinal point of view. Similarly, Okem et al. [63] and Mangoale and Afolayan [92] identified alkaloids, flavonols, flavonoids, phenols, proanthocyanidin, saponins and tannins from the rhizomes and roots of A. amatymbica.

TABLE 2
PHYTOCHEMICAL COMPOUNDS ISOLATED FROM ALEPIDEA SPECIES

Phytochemical compound	Value	Plant part	Reference
14-acetoxy ent-kaur-16-en-19-oic acid	-	Root	65
14-acetoxo-12-oxokaur-16-en-19-oic acid	-	Root	65
14-oxokaur-16-en-19-oic acid	-	Root	65
16-hydroxy-kaur-6-en-19-oic acid	-	Root	65
3β-acetoxywedelia-seco-kaurenolide	-	Aerial parts	70,91
11α-acetoxy-ent-kaur-16-en-19-oic acid	-	Rhizome	51
16α-methoxy-ent-kaur-11-en-19-oic acid	-	Rhizome	51
Alkaloids (%)	12.0 – 17.8	Rhizomes	92
Caffeic acid	-	Roots	93
Dehydrokaurenoic acid	-	Roots	70
ent-9,(11)-dehydro-16-kauren-19-oic acid	-	Rhizomes	70
ent-12-oxo-9(11),16-kauradien-19-oic acid	-	Aerial parts	91
ent-13-hydroxy-16-kauren-19-oic acid	-	Root	65
ent-16-kauren-12-on-19-oic acid	-	Roots	91
ent-16-kauren-19-oic acid	-	Aerial parts, rhizomes and roots	70,91
ent-kaur-16-en-19-oic acid	-	Rhizome	51
ent-kaura-9(11),16-dien-19-oic acid	-	Rhizome	51
Flavonoids (mg CTE/g)[1]	0.04	Roots	63
Hydroxykaurenoic acid	-	Roots	70
Kaempferol	-	Leaves	94
Kaurene hydrate	-	Roots	70
Kaurenoic acid	-	Roots	70
Lactone	-	Roots	70
Quercetin	-	Leaves	94
(R)-3'-O-β-D-glucopyranosylrosmarinic acid	-	Roots	93
Rosmarinic acid	-	Aerial parts and roots	61,93
Saponin (%)	10.8 – 34.5	Rhizomes	92
Tannin (mg/g)	9.8 – 62.4	Rhizomes	92
Total flavonols (mg QE/mg)[2]	10.6 – 68.8	Rhizomes	92
Total phenolics (mg GAE/g)[3]	0.2 – 117.8	Rhizomes and roots	63,92
Total proanthocyanidin (mg CTE/g)[1]	144.7 – 325.7	Rhizomes	92
Trachyloban-19-oic acid	-	Rhizome	51
Wedelia seco-kaurenolide	-	Rhizome	51,70, 91
A. capensis			
Dehydrokaurenoic acid	-	Roots	70
Kaurenoic acid	-	Roots	70
Lactone	-	Roots	70
A. comosa			
Caffeic acid	-	Roots	93
Dehydrokaurenoic acid	-	Roots	70
Hydroxykaurenoic acid	-	Roots	70
Kaurenoic acid	-	Roots	70
(R)-3'-O-β-D-glucopyranosylrosmarinic acid	-	Roots	93
Rosmarinic acid	-	Roots	93
A. galpinii			
Dehydrokaurenoic acid	-	Roots	70
Kaurene hydrate	-	Roots	70
Kaurenoic acid	-	Roots	70
A. insculpta			
Dehydrokaurenoic acid	-	Roots	70
Kaurene hydrate	-	Roots	70
Kaurenoic acid	-	Roots	70
A. longifolia			
Caffeic acid	-	Roots	93
Dehydrokaurenoic acid	-	Roots	70
Hydroxykaurenoic acid	-	Roots	70
Kaurenoic acid	-	Roots	70
Lactone	-	Roots	70
(R)-3'-O-β-D-glucopyranosylrosmarinic acid	-	Roots	93
Rosmarinic acid	-	Roots	93
A. natalensis			
Dehydrokaurenoic acid	-	Roots	70
Kaurene hydrate	-	Roots	70
Kaurenoic acid	-	Roots	70
Lactone	-	Roots	70
Wedelia seco-kaurenolide	-	Rhizomes	70
A. serrata			
Dehydrokaurenoic acid	-	Roots	70
Kaurenoic acid	-	Roots	70
Lactone	-	Roots	70
A. setifera			
Dehydrokaurenoic acid	-	Roots	70
Kaurenoic acid	-	Roots	70
A. thodei			
Kaurenoic acid	-	Roots	70
A. woodii			
Kaurenoic acid	-	Roots	70

[1]Values expressed as catechin equivalents (CTE) per gram of plant extracts
[2]Values expressed as quercetin equivalent (QE) per gram plant extracts
[3]Values expressed as gallic acid equivalent (GAE) per gram of plant extracts

3.3 Pharmacological activities

The medicinal uses and phytochemical compounds of some species from the genus Alepidea have led researchers to study their pharmacological activities aimed at correlating their medicinal uses with their ethnopharmacological properties. The plant extracts and phytochemical compounds of some Alepidea species such as A. amatymbica and A. natalensis possess a wide range of pharmacological properties such as antibacterial, antifungal, anti-HIV, anti-inflammatory, anti-hypertensive, antioxidant, antiplasmodial, antiprotozoal, cardiovascular, diuretic and cytotoxicity activities.

3.3.1 Antibacterial activities

Stafford et al. [95] evaluated the antibacterial activities of ethanol extract of A. amatymbica leaves and rhizomes against Bacillus subtilis, Staphylococcus aureus, Escherichia coli and Klebsiella pneumoniae using the micro plate method. The extract exhibited activities against the tested pathogens with minimum inhibitory concentration (MIC) values ranging from 1.6 mg/ml to 3.1 mg/ml [95]. Afolayan and Lewu [22] evaluated the antibacterial activities of methanol and acetone extracts of A. amatymbica roots, stems, leaves and rhizomes against Serratia marcescens, Staphylococcus epidermidis, Klebsiella pneumonae, Micrococcus kristinae, Bacillus aereus, Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Streptococcus pyrogenes and Salmonella pooni using the agar dilution method. The extracts exhibited activities against Staphylococcus epidermidis, Bacillus aereus, Staphylococcus aureus and Streptococcus pyrogenes with MIC values ranging from 5.0 mg/mL to 10.0 mg/mL [22]. Mulaudzi [17] and Mulaudzi et al. [56] evaluated the antibacterial activities of aqueous, 80.0% ethanol, dichloromethane and petroleum ether of A. amatymbica rhizomes against Bacillus subtilis, Staphylococcus aureus, Escherichia coli and Klebsiella pneumoniae using micro-dilution bioassay with neomycin (0.1 mg/ml) as a positive control. The extracts exhibited activities against tested pathogens with MIC values ranging from 0.4 mg/ml to 3.1 mg/ml [17,56]. Njume et al. [96] evaluated the antibacterial activities of aqueous, ethyl acetate, methanol, ethanol and acetone extracts of A. amatymbica against Helicobacter pylori using the agar well diffusion method with metronidazole and amoxicillin as positive controls. The extracts exhibited activities against tested pathogens with zone of inhibition ranging from 6.1 mm to 8.5 mm [96]. Okem et al. [63] evaluated the antibacterial activities of ethanol extracts of A. amatymbica roots against Escherichia coli and Staphylococcus aureus using the microdilution assay with neomycin as the positive control. The extracts exhibited activities against Escherichia coli and Staphylococcus aureus with MIC values of 0.2 mg/mL and 0.4 mg/mL, respectively [63]. Muleya et al. [64] evaluated the antibacterial activities of hexane, crude, methanol, dichloromethane, acetone and ethyl acetate extracts of A. amatymbica roots against Staphylococcus aureus, Enterococcus faecalis, Escherichia coli and Pseudomonas aeruginosa using serial dilution microplate assay with gentamycin as a positive control. The extracts exhibited activities against the tested pathogens with MIC values ranging from 150.0 µg/ml to 650.0 µg/ml [64]. Madikizela et al. [26] evaluated the antibacterial activities of aqueous and 70% acetone extracts of A. amatymbica whole plant parts against Shigella flexneri, Campylobacter jejuni, Staphylococcus aureus and Escherichia coli using the microtitre plate method with streptomycin and neomycin as positive controls. The extracts exhibited activities against tested pathogens with MIC values ranging from 0.8 mg/ml to 12.5 mg/ml [26]. Muleya et al. [65] evaluated the antibacterial activities of the compounds ent-13-hydroxy-16-kauren-19-oic acid, 16-hydroxy-kaur-6-en-19-oic acid, 14-acetoxy ent-kaur-16-en-19-oic acid, 14-oxokaur-16-en-19-oic acid and 14-acetoxo-12-oxokaur-16-en-19-oic acid isolated from A. amatymbica roots against Staphylococcus aureus, Pseudomonas aeruginosa, Enterococcus faecalis and Escherichia coli using microtitre plate method. The compounds exhibited activities against the tested pathogens with MIC values ranging from 50.0 µg/ml to 1250.0 µg/ml [65].

Mulaudzi [17] and Mulaudzi et al. [56] evaluated the antibacterial activities of aqueous, 80.0% ethanol, dichloromethane and petroleum ether of A. natalensis leaves and rhizomes against Bacillus subtilis, Staphylococcus aureus, Escherichia coli and Klebsiella pneumoniae using micro-dilution bioassay with neomycin (0.1 mg/ml) as a positive control. The extracts exhibited activities against the tested pathogens with MIC values ranging from 0.8 mg/ml to 12.5 mg/ml [17,56].

3.3.2 Antifungal activities

Afolayan and Lewu [22] evaluated the antifungal activities of methanol and acetone extracts of A. amatymbica roots, stems, leaves and rhizomes against Aspergillus niger, Aspergillus flavus and Penicillium notatum using the agar dilution method. The extracts exhibited activities against the tested pathogens with extracts showing more than 50.0% inhibition at 5.0 mg/mL [22]. Mulaudzi [17] and Mulaudzi et al. [56] evaluated the antifungal activities of aqueous, 80.0% ethanol, dichloromethane and petroleum ether of A. amatymbica rhizomes against Candida albicans using the micro-dilution bioassay with amphotericin B as a positive control. The extracts exhibited activities against tested pathogen with the MIC and minimum fungicidal concentration (MFC) values ranging from 0.2 mg/ml to 6.3 mg/ml [17,56]. Muleya et al. [64] evaluated the antifungal activities of hexane, crude, methanol, dichloromethane, acetone and ethyl acetate extracts of A. amatymbica roots against Aspergillus fumigatus and Candida albicans using the serial dilution microplate assay with amphotericin B as a positive control. The extracts exhibited activities against the tested pathogens with MIC values ranging from 150.0 µg/ml to 650.0 µg/ml [64].

Mulaudzi [17] and Mulaudzi et al. [56] evaluated the antifungal activities of aqueous, 80.0% ethanol, dichloromethane and petroleum ether of A. natalensis leaves and rhizomes against Candida albicans using the micro-dilution bioassay with amphotericin B as a positive control. The extracts exhibited activities against the tested pathogen with MIC and MFC values ranging from 0.2 mg/ml to 6.3 mg/ml [17,56].

3.3.3 Anti-HIV activities

Louvel et al. [61] evaluated the anti-HIV activities of aqueous extracts of A. amatymbica aerial parts and roots as well as the phytochemical compound rosmarinic acid isolated from the species against CXCR4-tropic (NL4-3) and CCR5-tropic (NL-AD87) wild-type viruses using the cell-based replicative assay. The extract exhibited moderate activities against the tested viruses with the half maximal effective concentration (EC50)

value of 22.0 µg/mL against the HIV-1 strain NL4-3 and 85.0 µg/mL against NL-AD87. The phytochemical compound rosmarinic acid exhibited EC50 value of 30.0 µM and 47.0 µM against NL4-3 and NL-AD87, respectively [61].

3.3.4 Anti-inflammatory activities

Stafford et al. [95] evaluated the anti-inflammatory activities of ethanol extracts of A. amatymbica leaves and rhizomes using the cyclooxygenase (COX-1) inhibition assay. The COX-1 inhibition exhibited by the leaf and rhizome extracts ranged from 77.0% to 96.0% [95]. Mulaudzi [17] and Mulaudzi et al. [56] evaluated the anti-inflammatory activities of aqueous, 80.0% ethanol, dichloromethane and petroleum ether of A. amatymbica rhizomes using the enzyme-based cyclooxygenase assays COX-1 and COX-2 with indomethacin as a positive control. The COX-1 and COX-2 inhibition exhibited by the dichloromethane and petroleum ether extracts were higher than 90.0% [17,56]. Muleya et al. [64] evaluated the anti-inflammatory activities of acetone extracts of A. amatymbica roots against 15-soybean lipoxygenase enzyme. The inhibition activity of 15-soybean lipoxygenase enzyme by the crude extracts of A. amatymbica at concentration of 25.0 µg/ml was 55.0% [64]. Muleya et al. [65] evaluated the anti-inflammatory activities of the phytochemical compounds ent-13-hydroxy-16-kauren-19-oic acid, 16-hydroxy-kaur-6-en-19-oic acid, 14-acetoxy ent-kaur-16-en-19-oic acid, 14-oxokaur-16-en-19-oic acid and 14-acetoxo-12-oxokaur-16-en-19-oic acid isolated from A. amatymbica roots using 15-soybean lipoxygenase inhibition assay. The inhibition activities of 15-soybean lipoxygenase enzyme exhibited by the phytochemical compounds ranged from 40.0% to 80.0% and EC50 values ranging from 19.1 µg/ml to 81.2 µg/ml [65].

Mulaudzi [17] and Mulaudzi et al. [56] evaluated the anti-inflammatory activities of aqueous, 80.0% ethanol, dichloromethane and petroleum ether of A. natalensis leaves and rhizomes using the enzyme-based cyclooxygenase assays COX-1 and COX-2 with indomethacin as a positive control. The COX-1 and COX-2 inhibition exhibited by the dichloromethane and petroleum ether extracts were higher than 75.0% [17,56].

3.3.5 Anti-hypertensive activities

Somova et al. [51] evaluated the anti-hypertensive activities of the phytochemical compounds diterpene kaurenoids ent-kaur-16-en-19-oic acid, ent-kaura-9(11),16-dien-19-oic acid, trachyloban-19-oic acid, 16α-methoxy-ent-kaur-11-en-19-oic acid, 11α-acetoxy-ent-kaur-16-en-19-oic acid and wedelia seco-kaurenolide isolated from A. amatymbica by measuring the blood pressure in conscious rats using the tail cuff method. The phytochemical compounds exhibited the anti-hypertensive activities [51].

3.3.6 Antioxidant activities

Muleya et al. [64] evaluated the antioxidant activities of hexane, crude, methanol, dichloromethane, acetone and ethyl acetate extracts of A. amatymbica roots using the 2,2′-azino-bis(3-ethylbenzothiazoline)-6-sulfonic acid (ABTS) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assays with trolox and ascorbic acid as positive controls. The extracts exhibited activities with EC50 values ranging from 1.3 µg/ml to 152.0 µg/ml in ABTS and EC50 values ranging from 4.2 µg/ml to 36.3 µg/ml in DPPH [64]. Mangoale and Afolayan [92] evaluated the antioxidant activities of aqueous, methanol and acetone extracts of A. amatymbica rhizomes using ABTS, DPPH, ferric reducing antioxidant power (FRAP), hydrogen peroxide (H2O2) and nitric oxide (NO) assays with vitamin C and butylated hydroxytoluene (BHT) as positive controls. The extracts exhibited concentration-dependent increase in inhibition which were comparable to activities exhibited by the positive controls with half maximal inhibitory concentration (IC50) values ranging from 0.0004 mg/mL to 2.7 mg/mL [92].

3.3.7 Antiplasmodial activities

Clarkson et al. [97] evaluated the antiplasmodial activities of aqueous, dichloromethane and dichloromethane : methanol (1:1) extracts of A. amatymbica whole plant parts against Plasmodium falciparum strain D10 using the parasite lactate dehydrogenase (pLDH) assay. The dichloromethane : methanol (1:1) extract exhibited moderate activities with IC50 value of 12.5 µg/ml [97]. Mokoka [98] and Mokoka et al. [99] evaluated the antiplasmodial activities of dichloromethane and dichloromethane: methanol (1:1) extracts of A. amatymbica whole plant parts against Plasmodium falciparum with benznidazole chloroquine (IC50 = 0.05 µM) as a positive control using the [G-3H]-hypoxanthine incorporation assay. The dichloromethane and dichloromethane : methanol (1:1) extracts exhibited activities with IC50 values of 2.7 µg/mL and 3.7 µg/mL, respectively [98,99].

3.3.8 Antiprotozoal activities

Mokoka [98] and Mokoka et al. [99] evaluated the antiprotozoal activities of dichloromethane and dichloromethane : methanol (1:1) extracts of A. amatymbica whole plant parts against Trypanosoma cruzi, Trypanosoma brucei rhodesiense and Leishmania donovani with benznidazole (IC50 = 0.5 µg/mL), melarsoprol (IC50 = 0.03 µM) and miltfosine (IC50 = 0.2 µg/mL) as reference drugs. The determination of the activities of the extracts against these pathogens was done using Almar Blue and resazurin assays. The extracts exhibited activities with IC50 values ranging from 5.0 µg/mL to 99.5 µg/mL [99].

3.3.9 Cardiovascular activities

Somova et al. [51] evaluated the cardiovascular activities of the phytochemical compounds diterpene kaurenoids ent-kaur-16-en-19-oic acid, ent-kaura-9(11),16-dien-19-oic acid, trachyloban-19-oic acid, 16α-methoxy-ent-kaur-11-en-19-oic acid, 11α-acetoxy-ent-kaur-16-en-19-oic acid and wedelia seco-kaurenolide isolated from A. amatymbica by assessing the coronary flow on isolated rat heart and by testing the potential coronary vasodilating effects. The phytochemical compounds exhibited the cardiovascular activities [51].

3.3.10 Diuretic activities

Somova et al. [51] evaluated the diuretic activities of the phytochemical compounds diterpene kaurenoids ent-kaur-16-en-19-oic acid, ent-kaura-9(11),16-dien-19-oic acid, trachyloban-19-oic acid, 16α-methoxy-ent-kaur-11-en-19-oic acid, 11α-acetoxy-ent-kaur-16-en-19-oic acid and wedelia seco-kaurenolide isolated from A. amatymbica by using the Lipschitz test in rats. The phytochemical compounds exhibited the diuretic activities [51].

3.3.11 Cytotoxicity activities

Muleya et al. [65] evaluated the cytotoxicity activities of the phytochemical compounds ent-13-hydroxy-16-kauren-19-oic acid, 16-hydroxy-kaur-6-en-19-oic acid, 14-acetoxy ent-kaur-16-en-19-oic acid, 14-oxokaur-16-en-19-oic acid and 14-acetoxo-12-oxokaur-16-en-19-oic acid isolated from A. amatymbica roots against the dermal mesenchymal stem cells line and monkey Vero cells. The phytochemical compounds exhibited activities against both the dermal mesenchymal stem cells line and monkey Vero cells with IC50 values ranging from 20.0 µg/mL to 55.0 µg/mL [65].

4 CONCLUSION

This review provides a summary of the current knowledge of the medicinal uses, phytochemistry and pharmacological activities of Alepidea species. Several species are known to have medicinal uses and also used as charm and for ritual purposes. Extracts of Alepidea were found to be rich in diterpenoids, particularly kaurene derivatives. Many biological activities have been investigated, in particular antibacterial, antifungal, anti-HIV, anti-inflammatory, anti-hypertensive, antioxidant, antiplasmodial, antiprotozoal, cardiovascular, diuretic and cytotoxicity activities. Most of the studies focused on crude extracts, and only a few on phytochemical compounds isolated from the Alepidea species. Although several studies have been conducted into the phytochemistry and pharmacological properties of A. amatymbica and A. natalensis, there are still gaps on the correlation of medicinal application of the Alepidea species, their ethnopharmacological properties and toxicity. Therefore, detailed studies focusing on the phytochemical, pharmacological and toxicological properties of Alepidea species are recommended.

CONFLICTS OF INTEREST

No conflict of interest is associated with this work.

REFERENCES

[1] Duran A, Doğan B, Duman H, Martin E, Öztürk M and Çetin Ö. Taxonomic studies on the genus Rhabdosciadium (Apiaceae) with particular reference to Turkish species and their relationships with some closely related genera. Biologia. 2010; 65: 45-62.

[2] Olle M and Bender I. The content of oils in umbelliferous crops and its formation. Agronomy Reasearch. 2010; 8: 687–696.

[3] Heywood VH. The socio-economic importance of the Apiales. Journal of the Faculty of Pharmacy of Istanbul University. 2014; 44: 113-130.

[4] Aćimović MG. Nutraceutical potential of Apiaceae. In: Mérillon JM and Ramawat K (Eds.), Bioactive molecules in food: Reference series in phytochemistry. Springer, Cham; 2017, pp. 1-31.

[5] Sayed-Ahmad B, Talou T, Saad Z, Hijazi A and Merah O. The Apiaceae: Ethnomedicinal family as source for industrial uses. Industrial Crops and Products. 2017; 109: 661–671.

[6] De Castro A and Van Wyk B-E. Diagnostic characters and geographic distribution of Alepidea species used in traditional medicine. South African Journal of Botany. 1994; 60: 345-350.

[7] Van Wyk B-E, Tilney PM and Magee AR. African Apiaceae: A synopsis of the Apiaceae/Umbelliferae of sub-Saharan Africa and Madagascar. Briza Academic Books, Pretoria; 2013.

[8] Hutchinson S-L, Van Wyk B-E and Magee AR. A taxonomic revision of the Alepidea setifera group (Apiaceae, Apioideae), the description of a new species, A. inflexa, and the reinstatement of A. jenkinsii. South African Journal of Botany. 2017; 111: 1–11.

[9] Watt JM and Breyer-Brandwijk MG. The medicinal and poisonous plants of southern and eastern Africa. 2nd ed. Livingstone, London; 1962.

[10] Hutchings A, Scott AH, Lewis G and Cunningham A. Zulu medicinal plants: An inventory. University of Natal Press, Pietermaritzburg; 1996.

[11] Van Wyk B-E, Van Oudtshoorn B and Gericke N. Medicinal plants of South Africa. Briza Publications, Pretoria; 2013.

[12] Asowata-Ayodele AM, Afolayan AJ and Otunola GA. Ethnobotanical survey of culinary herbs and spices used in the traditional medicinal system of Nkonkobe Municipality, Eastern Cape, South Africa. South African Journal of Botany. 2016; 104: 69–75.

[13] Welcome AK and Van Wyk B-E. An inventory and analysis of the food plants of southern Africa. South African Journal of Botany. 2019; 122: 136–179.

[14] Fox FW and Norwood Young ME. Food from the Veld. Delta Books, Johannesburg; 1982.

[15] Jansen PCM. *Alepidea peduncularis* Steud. ex A.Rich. In: Grubben GJH and Denton OA (Eds.), Plant resources of tropical Africa 2: Vegetables. Backyhuys Publishers, Leiden; 2004, pp. 40-41.

[16] Long C. Swaziland's Flora: siSwati names and uses. Swaziland National Trust Commission; 2005. Available at: http://www.sntc.org.sz/index.asp, accessed on 15 February 2021.

[17] Mulaudzi RB. Seed germination and medicinal properties of Alepidea species. MSc Dissertation. University of KwaZulu-Natal, Pietermaritzburg; 2009.

[18] Van Wyk B-E and Gericke N. People's plants: A guide to useful plants of southern Africa. Briza Publications, Pretoria, South Africa; 2018.

[19] Van Wyk B-E. The potential of South African plants in the development of new food and beverage products. South African Journal of Botany. 2011; 77: 857–868.

[20] Van Wyk B-E. A review of African medicinal and aromatic plants. In: Neffati M, Najjaa H and Mathé A (Eds.), Medicinal and aromatic plants of the world: Africa volume 3. Springer, Leiden; 2017, pp. 19-60.

[21] Maroyi A. From traditional usage to pharmacological evidence: Systematic review of Gunnera perpensa L. Evidence-Based Complementary and Alternative Medicine. 2016, volume 2016, article ID 1720123.

[22] Afolayan AJ and Lewu FB. Antimicrobial activity of Alepidea amatymbica. Pharmaceutical Biology. 2009; 47: 436-439.

[23] Moffett R. Sesotho plant and animal names and plants used by the Basotho. Sun Press, Bloemfontein; 2010.

[24] Pujol J. Nature Africa: The herbalist handbook. Jean Pujol Natural Healers' Foundation, Durban; 1990.

[25] Ndhlala AR, Anthonissen R, Stafford GI, Finnie JF, Verschaeve L and Van Staden J. In vitro cytotoxic and mutagenic evaluation of thirteen commercial herbal mixtures sold in KwaZulu-Natal South Africa. South African Journal of Botany. 2010; 76: 132–138.

[26] Madikizela B, Ndhlala AR, Rengasamy KRR, McGaw LJ and Van Staden J. Pharmacological evaluation of two South African commercial herbal remedies and their plant constituents. South African Journal of Botany. 2017; 111: 291–298.
[27] Dold AP and Cocks ML. The trade in medicinal plants in the Eastern Cape province, South Africa. South African Journal of Science. 2002; 98: 589-597.
[28] Loundou PM. Medicinal plant trade and opportunities for sustainable management in the Cape Peninsula, South Africa. MSc Dissertation. University of Stellenbosch, Stellenbosch; 2008.
[29] Van Wyk B-E, De Castro A, Tilney PM, Winter PJD and Magee AR. A new species of Alepidea (Apiaceae, subfam Saniculoideae). South Africa Journal of Botany. 2008; 74: 740–745.
[30] Williams VL, Balkwill K and Witkowski ETF. A lexicon of plants traded in the Witwatersrand umuthi shops, South Africa. Bothalia. 2001; 31: 71-98.
[31] Hutchinson S-L, Sandasi M, Viljoen AM, Van Wyk B-E and Magee AR. Chemical and DNA fingerprinting of ikhathazo (Alepidea, Apiaceae): Applications for conservation and monitoring of trade. South African Journal of Botany. 2016; 103: 3018.
[32] Cunningham AB. African medicinal plants: setting priorities at the interface between conservation and primary health care. People and Plants working paper 1, UNESCO, Paris; 1993.
[33] Mander M. Marketing of indigenous medicinal plants in South Africa: A case study in KwaZulu-Natal. Food and Agriculture Organization, Rome; 1998.
[34] Moeng ET and Potgieter MJ. The trade of medicinal plants by muthi shops and street vendors in the Limpopo Province, South Africa. Journal of Medicinal Plants Research. 2011; 5: 558-564.
[35] Rasethe MT, Semenya SS and Maroyi A. Medicinal plants traded in informal herbal medicine markets of the Limpopo province, South Africa. Evidence-Based Complementary and Alternative Medicine. 2019, volume 2019, article ID 2609532.
[36] Monakisi CM. Knowledge and use of traditional medicinal plants by the Setswana-speaking community of Kimberley, Northern Cape of South Africa. MSc Dissertation. University of Stellenbosch, Stellenbosch; 2007.
[37] Gerstner J. A preliminary checklist of Zulu names of plants. Bantu Studies. 1938; 12: 215-236.
[38] Wiersum KF, Husselman M, Dold AP and Cocks ML. Cultivation of medicinal plants as a tool for biodiversity conservation and poverty alleviation in the Amatola region, South Africa. In: Bogers RJ, Craker LE and Lange D (Eds.), Medicinal and aromatic plants: Agricultural, commercial, ecological, legal, pharmacological and social aspects. Springer, Dordrecht; 2006, pp. 43–57.
[39] Zonyane S, Vuuren SFV and Makunga NP. Antimicrobial interactions of Khoi-San poly-herbal remedies with emphasis on the combination; Agathosma crenulata, Dodonaea viscosa and Eucalyptus globulus. Journal of Ethnopharmacology. 2013; 148: 144–151
[40] Maroyi A. Cissampelos capensis L.f. (Menispermaceae): Review of its medicinal uses, phytochemical and pharmacological properties. International Journal of Research in Pharmaceutical Sciences. 2020; 11: 5948-5955.
[41] Omoruyi BE, Bradley G and Afolayan AJ. Ethnomedicinal survey of medicinal plants used for the management of HIV/AIDS infection among local communities of Nkonkobe Municipality, Eastern Cape, South Africa. Journal of Medicinal Plants Research. 2012; 6: 3603-3608.
[42] Njume C, Afolayan AJ and Ndip RN. Diversity of plants used in the treatment of Helicobacter pylori associated morbidities in the Nkonkobe municipality of the Eastern Cape province of South Africa. Journal of Medicinal Plants Research. 2011; 5: 3146-3151.
[43] Sewani-Rusike CR and Mammen M. Medicinal plants used as home remedies: A family survey by first year medical students. African Journal of Traditional Complementary and Alternative Medicine. 2014; 11: 67-72.
[44] Masafa MM, Mbajiorgu CA, Nemadodzi LE and Kabine ES. A study of natural habitats and uses of medicinal plants in Thulamela and JS Moroko Municipalities, South Africa. Indian Journal of Traditional Knowledge. 2016; 15: 363–369.
[45] Otang WM, Grierson DS and Ndip RN. Ethnobotanical survey of medicinal plants used in the management of opportunistic fungal infections in HIV/AIDS patients in the Amathole District of the Eastern Cape province, South Africa. Journal of Medicinal Plants Research. 2012; 6: 2071-2080.
[46] Bhat RB. Medicinal plants and practices of Xhosa people in Transkei region of Eastern Cape, South Africa. Indian Journal of Traditional Knowledge. 2014; 13: 292–298.
[47] Maroyi A. Diversity of use and local knowledge of wild and cultivated plants in the Eastern Cape province, South Africa. Journal of Ethnobiology and Ethnomedicine. 2017; 13: 43.
[48] Semenya SS and Maroyi A. Therapeutic plants used by traditional health practitioners to treat pneumonia in the Limpopo province, South Africa. Latin American and Caribbean Bulletin of Medicinal and Aromatic Plants. 2018; 17: 583-603.
[49] Semenya SS and Maroyi A. **DATA ON MEDICINAL PLANTS USED TO TREAT RESPIRATORY INFECTIONS AND RELATED SYMPTOMS IN SOUTH AFRICA. DATA IN BRIEF. 2018; 21: 419-423.**
[50] Semenya SS and Maroyi A. Source, harvesting, conservation status, threats and management of indigenous plant used for respiratory infections and related symptoms in the Limpopo Province, South Africa. Biodiversitas. 2019; 20: 790-811.
[51] Somova LI, Shode FO, Moodley K and Govender Y. Cardiovascular and diuretic activity of kaurene derivatives of Xylopia aethiopica and Alepidea amatymbica. Journal of Ethnopharmacology. 2001; 77: 165–174.
[52] Cocks ML and Dold AP. Cultural significance of biodiversity: The role of medicinal plants in urban African cultural practices in the Eastern Cape, South Africa. Journal of Ethnobiology. 2006; 26: 60–81.
[53] Appidi JR, Grierson DS and Afolayan AJ. Ethnobotanical study of plants used for the treatment of

diarrhoea in the Eastern Cape, South Africa. Pakistan Journal of Biological Sciences. 2008; 11: 1961–1963.
[54] Mulaudzi RB, Kulkarni MG, Finnie JF and Van Staden J. Optimizing seed germuination and seedling vigour of Alepidea amatymbica and Alepidea natalensis. Seed Science and Technology. 2009; 37: 527-533.
[55] Mulaudzi R, Kulkarni M, Finnie J and Van Staden J. Seed germination of Alepidea species: Heavily traded and threatened medicinal plants in South Africa. African Journal of Traditional Complementary and Alternative Medicines. 2009; 6: 345-346.
[56] Mulaudzi RB, Ndhlala AR, Finnie JF and Van Staden J. Antimicrobial, anti-inflammatory and genotoxicity activity of Alepidea amatymbica and Alepidea natalensis (Apiaceae). South African Journal of Botany. 2009; 75: 584–587.
[57] Afolayan AJ and Mbaebie BO. Ethnobotanical study of medicinal plants used as anti-obesity remedies in Nkonkobe Municipality of South Africa. Pharmacognosy Journal. 2010; 2: 368-373.
[58] Wintola OA and Afolayan AJ. Ethnobotanical survey of plants used for the treatment of constipation within Nkonkobe Municipality of South Africa. African Journal of Biotechnology. 2010; 9: 7767-7770.
[59] Philander LA. An ethnobotany of Western Cape Rasta bush medicine. Journal of Ethnopharmacology. 2011; 138: 578–594.
[60] Olajuyigbe OO and Afolayan AJ. Ethnobotanical survey of medicinal plants used in the treatment of gastrointestinal disorders in the Eastern Cape province, South Africa. Journal of Medicinal Plants Research. 2012; 6: 3415-3424.
[61] Louvel S, Moodley N, Seibert I, Steenkamp P, Nthambeleni R, Vidal V, Maharaj V and Klimkait T. Identification of compounds from the plant species Alepidea amatymbica active against HIV. South African Journal of Botany. 2013; 86: 9–14.
[62] Afolayan AJ and Wintola OA. A survey of medicinal plants used in the treatment of dysentery in Amathole District Municipality, South Africa. Pakistan Journal of Botany. 2014; 46: 1685-1692.
[63] Okem A, Southway C, Stirk WA, Street RA, Finnie JF and Van Staden J. Heavy metal contamination in South African medicinal plants: A cause for concern. South African Journal of Botany. 2014; 93: 125–130.
[64] Muleya E, Ahmed AS, Sipamla AM, Mtunzi FM and Mutatu W. Pharmacological properties of Pomaria sandersonii, Pentanisia prunelloides and Alepidea amatymbica extracts using in vitro assays. Journal of Pharmacognosy and Phytotherapy. 2015; 7: 1-8.
[65] Muleya E, Okoli BJ, Mtunzi FM and Sekomeng MJ. 2017. Diterpenoids of Alepidea amatymbica Eckl. & Zeyh: Studies of their cytotoxic, antimicrobial and lipoxygenase inhibitory activities. MOJ Biorganic and Organic Chemistry. 2017; 1: 103–111.
[66] Wintola OA, Otang WM and Afolayan AJ. The prevalence and perceived efficacy of medicinal plants used for stomach ailments in the Amathole District Municipality, Eastern Cape, South Africa. South African Journal of Botany. 2017; 108: 144–148.
[67] Komoreng L, Thekisoe O, Lehasa S, Tiwani T, Mzizi N, Mokoena N, Khambule N, Ndebele S and Mdletshe N. An ethnobotanical survey of traditional medicinal plants used against lymphatic filariasis in South Africa. South African Journal of Botany. 2017; 111: 12–16.
[68] Gerstner J. 1939. A preliminary checklist of Zulu names of plants with short notes. Bantu Studies. 1939; 13: 307-326.
[69] Hutchings A. Observations on plant usage in Xhosa and Zulu medicine. Bothalia. 1989; 19: 225–235.
[70] Holzapfel CW, Van Wyk B-E, De Castro A, Marais W and Herbst M. A chemotaxonomic survey of kaurene derivatives in the genus Alepidea (Apiaceae). Biochemical Systematics and Ecology. 1996; 23: 799–803.
[71] Madikizela B, Kambizi L and McGaw LJ. An ethnobotanical survey of plants used traditionally to treat tuberculosis in the eastern region of O.R. Tambo district, South Africa. South African Journal of Botany. 2017; 109: 231–236.
[72] Semenya SS and Maroyi A. Plants used by Bapedi traditional healers to treat asthma and related symptoms in Limpopo province, South Africa. Evidence-Based Complementary and Alternative Medicine. 2018; volume 2018, article ID 2183705.
[73] Semenya SS and Maroyi A. Ethnobotanical survey of plants used by Bapedi traditional healers to treat tuberculosis and its opportunistic infections in the Limpopo province, South Africa. South African Journal of Botany. 2019; 122: 401–421.
[74] Semenya SS and Maroyi A. Ethnobotanical survey of plants used to treat respiratory infections and related symptoms in the Limpopo Province, South Africa. Journal of Herbal Medicine. 2020; 24: 100390.
[75] Afolayan AJ, Grierson DS and 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. Journal of Ethnopharmacology. 2014; 153: 220–232.
[76] Bhat RB. Plants of Xhosa people in the Transkei region of Eastern Cape (South Africa) with major pharmacological and therapeutic properties. Journal of Medicinal Plants Research. 2013; 7: 1474-1480.
[77] Hughes G, Blouws T, Aboyade O, Davids D, Mbamalu O, Van't Klooster C, De Jong J and Gibson D. An ethnobotanical survey of medicinal plants used by traditional health practitioners to manage HIV and its related opportunistic infections in Mpoza, Eastern Cape province, South Africa. Journal of Ethnopharmacology. 2015; 171: 109–115.
[78] Semenya SS and Maroyi A. Source of plants, used by Bapedi traditional healers for respiratory infections and related symptoms in the Limpopo Province, South Africa. Journal of Biological Sciences. 2019; 19: 101-121.
[79] Jacot Guillarmod A. Flora of Lesotho. Cramer, Lehre; 1971.
[80] Gelfand M, Mavi S, Drummond RB and Ndemera B. The traditional medical practitioner in Zimbabwe: His principles of practice and pharmacopoeia. Mambo Press, Gweru, Zimbabwe; 1985.
[81] Moteetee A and Van Wyk B-E. The medical ethnobotany of Lesotho: A review. Bothalia. 2011; 41: 209–228.

[82] Mavi S. Medicinal plants and their uses in Zimbabwe. In: Norman H, Snyman I and Cohen M (Eds.), Indigenous knowledge and its uses in southern Africa. Human Sciences Research Council, Pretoria; 1996, pp. 67-73.
[83] Chinemana F, Drummond RB, Mavi S and De Zoysa I. Indigenous plant remedies in Zimbabwe. Journal of Ethnopharmacology. 1985; 14: 159-172.
[84] Bandeira SO, Gaspar F and Pagula FP. African ethnobotany and healthcare: Emphasis on Mozambique. Pharmaceutical Biology. 2001; 39: 70–73.
[85] Fowler DG. Traditional fever remedies: A list of Zambian plants. Royal Botanic Gardens, Kew, Richmond; 2006.
[86] Hutchings A. A survey and analysis of traditional medicinal plants as used by the Zulu, Xhosa and Sotho. Bothalia. 1989; 19: 111–123.
[87] Watt JM and Brandwijk MG. Suto (Basuto) medicines. Bantu Studies. 1927; 3: 154–178.
[88] Moeng ET. Analysis of Muthi shops and street vendors on medicinal plants of the Limpopo Province. MSc Dissertation. University of Limpopo, Mankweng; 2010.
[89] Mogale MMP, Raimondo DC and Van Wyk B-E. The ethnobotany of central Sekhukhuneland, South Africa. South African Journal of Botany. 2019; 122: 90–119.
[90] Moteetee A, Moffett RO and Seleteng-Kose L. A review of the ethnobotany of the Basotho of Lesotho and the Free State province of South Africa (South Sotho). South African Journal of Botany. 2019; 122: 21–56.
[91] Rustaiyan A and Sadjadi AS. Kaurene derivatives from Alepidea amatynsia. Phytochemistry. 1987; 26: 2106-2107.
[92] Mangoale RM and Afolayan AJ. Comparative phytochemical constituents and antioxidant activity of wild and cultivated Alepidea amatymbica Eckl & Zeyh. BioMed Research International. 2010; volume 2020, article ID 5808624.
[93] Olivier D, Van Wyk B-E and Van Heerden F. The chemotaxonomic and medicinal significance of phenolic acids in Arctopus and Alepidea (Apiaceae subfamily Saniculoideae). Biochemical Systematics and Ecology. 2008;36:724–729.
[94] Crowden RK, Harborne JB and Heywood VH. Chemosystematics of the Umbelliferae: A general survey. Phytochemistry. 1969; 8: 1963-1984.
[95] Stafford GI, Jäger AK and Van Staden J. Effect of storage on the chemical composition and biological activity of several popular South African medicinal plants. Journal of Ethnopharmacology. 2005; 97: 107–115.
[96] Njume C, Afolayan AJ and Ndip RN. Aqueous and organic solvent-extracts of selected South African medicinal plants possess antimicrobial activity against drug-resistant strains of Helicobacter pylori: Inhibitory and bactericidal potential. International Journal of Molecular Sciences. 2011; 12: 5652-5665.
[97] Clarkson C, Maharaj VJ, Crouch NR, Grace OM, Pillay P, Matsabisa MG, Bhagwandin N, Smith PJ and Folb PI. In vitro antiplasmodial activity of medicinal plants native to or naturalised in South Africa. Journal of Ethnopharmacology. 2004; 92: 177-191.
[98] Mokoka TA. The discovery and characterization of antiprotozoal compounds from South African medicinal plants by a HPLC-based activity profiling technique. MSc Dissertation. University of KwaZulu-Natal, Pietermaritzburg; 2013.
[99] Mokoka TA, Zimmermann S, Julianti T, Hata Y, Moodley N, Cal M, Adams M, Kaiser M, Brun R, Koorbanally N and Hamburger M. In vitro screening of traditional South African malaria remedies against Trypanosoma brucei rhodesiense, Trypanosoma cruzi, Leishmania donovani, and Plasmodium falciparum. Planta Medica. 2011; 77: 1663–1667.