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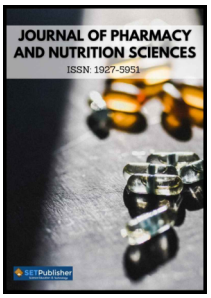

Family Araliaceae in Southern Africa: A Review of Ethnobotanical Uses, Phytochemistry, Pharmacology, and Toxicology

Alfred Maroyi*

Department of Botany, University of Fort Hare, Private Bag X1314, Alice 5700, South Africa

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Abstract:

There is widespread use of species belonging to the family Araliaceae in traditional medicine in southern Africa. This review aimed to assess the medicinal uses, phytochemistry, pharmacology, and toxicological properties of indigenous species belonging to the family Araliaceae in south Africa. Relevant articles, books, theses, dissertations, patents, and other English-only reports on the therapeutic uses, chemical, biological and toxicological activities of species belonging to the family Araliaceae in southern Africa (Angola, Botswana, Eswatini, Lesotho, Malawi, Mozambique, Namibia, South Africa, Zambia, and Zimbabwe) were reviewed. Databases such as PubMed, Web of Science, Elsevier, Google Scholar, Scopus, Springer, Science Direct, Taylor and Francis between January and July 2022. Eleven species, namely *Cussonia Arborea, C. arenicola, C. natalensis, C. nicholsonii, C. paniculata, C. sphaerocephala, C. spicata, C. transvaalensis, C. thyrsiflora, C. zuluensis*, and *Neocussonia umbellifer*s are used as traditional medicines against 48 human and animal diseases. This study showed alkaloids, anthocyanins, anthracene glycosides, botulin, flavonoids, free gallic acid, iridoids, phenolics, saponins, steroids, tannins, triterpenoids, and volatile oils have been identified from these species. Pharmacological research revealed that the crude extracts and compounds isolated from these species are characterized by Aβ42 protein reduction, acetylcholinesterase, analgesic, antibacterial, antifungal, antiviral, anticancer, antihyperglycemic, anti-inflammatory, antileishmanial, antioxidant, antiplasmodial, antiprotozoal, anti-ulcer, immunomodulatory, larvicidal, molluscicidal, spermicidal, cytotoxicity and toxicity activities. Reports of medicinal uses, phytochemistry, pharmacology and toxicological properties of species belonging to the family Araliaceae in southern Africa could only be found for 11 species, suggesting that further investigation of largely unexplored family members is necessary.

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*Corresponding Author
Tel/Fax: +27406022322;
E-mail: amaroyi@ufh.ac.za

INTRODUCTION

The family Araliaceae is reported to have 55 genera and over 1500 species and infraspecific taxa [1] distributed in tropical, subtropical, and temperate regions. The members of the family Araliaceae are known to have various classes of secondary metabolites, which are characterized by several phytochemical properties [2-9]. Research by Kinghorn and Balandrin [10] showed that natural products and their phytochemical compounds represent more than 50% of all pharmaceutical drugs in clinical use worldwide. Similarly, an estimated 25% of the pharmaceutical drugs and 11% of pharmaceutical drugs considered essential by the World Health Organization (WHO) are derived from plants, and many synthetic drugs are also obtained from precursor phytochemical compounds originating from plants [11]. The worldwide burden of diseases and ailments has forced scientists to explore medicinal plants as alternative therapies based on their traditional uses as herbal medicines. Medicinal plants have been used since ancient times to treat and manage various human and animal diseases and ailments. In some communities, medicinal plants are an important aspect of their daily lives and a crucial part of their cultural heritage [12,13]. In the last 70 years, documentation of medicinal uses of species belonging to the family Araliaceae has expanded in southern Africa [14-18]. However, these studies have yet to be compiled and analyzed. It is, therefore, within this context that this study was undertaken aimed at critically assessing the medicinal uses, phytochemistry, pharmacology, and toxicological properties of indigenous species belonging to the family Araliaceae in southern Africa (Angola, Botswana, Eswatini, Lesotho, Malawi, Mozambique, Namibia, South Africa, Zambia, and Zimbabwe). This review sought to collate and synthesize information about the ethnopharmacology of the family Araliaceae in southern Africa into a scientific report that is easy to use as a quick reference. This is important as some of the species belonging to the family Araliaceae are widely used as traditional medicines in the region, and information about their ethnopharmacology is currently scattered in several reports, some of which are not readily accessible. There is a need to characterize the phytochemical compounds of these plants used as traditional medicines to understand their mechanisms of action and therapeutic effects.

MATERIALS AND METHODS

Relevant original articles, books, theses, dissertations, and other grey literature written in English on medicinal uses, phytochemistry, pharmacology, and toxicological properties of indigenous species belonging to the family Araliaceae in southern Africa (Angola, Botswana, Eswatini, Lesotho, Malawi, Mozambique, Namibia, South Africa, Zambia, and Zimbabwe) were searched in PubMed, Web of Science, Elsevier, Google Scholar, Scopus, Springer, Science Direct, Taylor and Francis between January and July 2022. The literature search from different scientific databases provided 426 articles (Figure **1**). After removing the duplicates and adding 11 articles identified from dissertations, theses, book chapters, and books retrieved from the University of Fort Hare library, 225 articles were retained. Of these, 106 reports were discarded mainly due to lack of information on medicinal uses, phytochemistry, pharmacology, and toxicological properties of indigenous species belonging to the family Araliaceae in southern Africa, bias, limited raw data, and 119 articles contributed to the generated inventory in this review (Figure **1**). Scientific names of the plant species were verified using Plants of the World Online (POWO, http://powo.science.kew.org/).

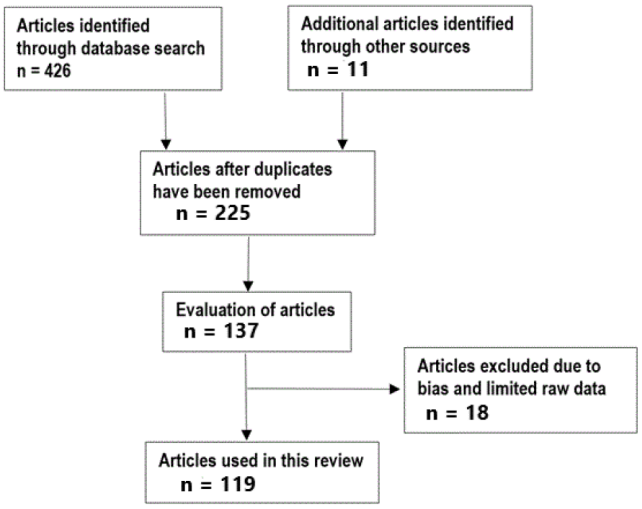

Figure 1: Flow chart showing the number of research publications used in this study.

RESULTS AND DISCUSSION

Medicinal Uses

Table **1** shows 11 species belonging to the family Araliaceae that are used as sources of traditional medicines in southern Africa. Such species included *Cussonia Arborea* Hochst. ex A. Rich., *C. arenicola*

Table 1: Medicinal Uses of Indigenous Species of the Araliaceae Family in Southern Africa

Medicinal uses	Parts used	Country	References
C. arborea			
Convulsions	Leaf infusion sprinkled on the face	Zimbabwe	[16]
Heart pains	Heartwood root infusion is taken orally	Zimbabwe	[16]
Menstrual problems	Root decoction is taken orally and mixed with the root of *Steganotaenia araliacea* Hochst. and fruits of *Vigna unguiculata* (L.) Walp.	Zimbabwe	[16]
Mental problems	A leaf infusion is orally mixed with *Ipomoea batatas* (L.) Lam. and *Musa* spp.	Malawi	[16]
Painful legs	Leaf infusion applied topically	Malawi	[16]
Painful uterus	Root infusion mixed with those of *Pappea capensis* Eckl. & Zeyh. inserted into vagina	Zimbabwe	[16]
Postpartum	Heartwood infusion is taken orally	Zimbabwe	[16]
Pregnancy	Not specified	Zimbabwe	[20]
Sexually transmitted diseases	Bark and root bark decoction is taken orally	Zambia	[21]
Ethnoveterinary medicine (blood in dung and urine of cattle)	Cattle drenched with bark infusion	Zimbabwe	[16]
C. arenicola			
Venereal diseases	A root infusion is taken orally	Mozambique	[22]
C. natalensis			
Emetic	Root decoction is taken orally	Eswatini	[7,18,23]
Gastro-intestinal problems	Stem bark decoction is orally mixed with *Gardenia volkensii* K. Schum. subsp. *spatulifolia* (Stapf. & Hutch.) Verdc.	Eswatini	[7,24]
Gastro-intestinal problems (diarrhea and stomach ache)	Bark and root decoction are taken orally	Eswatini and Zimbabwe	[7,23-25]
Protective charm	Bark, fruits, and roots used	Eswatini	[7,18]
Purgative	Bark decoction is taken orally	Eswatini	[7,23]
C. nicholsonii			
Emetic	Not specified	Eswatini	[18]
Gastro-intestinal (biliousness)	Not specified	South Africa	[26]
Musculoskeletal (inflammation)	Not specified	South Africa	[26]
Tonic	Not specified	South Africa	[26]
C. paniculata			
Anemia	Bark decoction is taken orally	Lesotho	[4,27]
Biliousness	Not specified	Lesotho and South Africa	[28]
Bladder problems	Bark decoction is taken orally	Lesotho	[4,15,28-31]
Boils, shingles, and skin diseases	Bark and leaf decoction is taken orally	Lesotho and South Africa	[4,15,28-35]
Breast and cervical cancer	A leaf infusion is taken orally	Lesotho	[4,31,36]
Cardiovascular problems	Bark decoction is taken orally	Lesotho	[4,27]
Cleanses blood	Bark decoction is taken orally	Lesotho	[4,27]
Colic	Bark and leaf decoction is taken orally	South Africa	[2,4,37-39]

(Table 1). Continued.

Medicinal uses	Parts used	Country	References
Colic, menstrual problems, mental disease, and nervous system problems	Bark and leaf decoction is taken orally and mixed with *Searsia divaricata* (Eckl. and Zeyh.) Moffett, *S. zeyheri* (Sond.) Moffett and *Scabiosa columbaria* L.	Lesotho and South Africa	[28,36,40]
Emetic	Bark and leaf decoction is taken orally	Eswatini and Lesotho	[4,15,18,28-31]
Gastro-intestinal problems (indigestion and stomach complaints)	Leaf and root decoction are taken orally	Lesotho and South Africa	[4,15,28-33,41-43]
Heartburn	Bark decoction is taken orally	Lesotho	[4,15,27-30,42]
Human immunodeficiency virus (HIV) opportunistic infections	Bark and leaf decoction is taken orally	South Africa	[4,32-34]
Immune booster	Bark, leaf, and root decoction are taken orally	Lesotho and South Africa	[4,32-35,42]
Intestinal ulcers	Leaf decoction is taken orally	Lesotho	[4,15,28-31,42]
Intestinal parasites and worms	Bark, fruit, root, and stem decoction are taken orally	Lesotho and South Africa	[4,14,27,44]
Kidney problems	A leaf infusion is taken orally	Lesotho	[4,15,28-31]
Loss of appetite	A root infusion is taken orally	Lesotho	[4,42]
Malaria	Root decoction is taken orally	South Africa	[4,32,33,43,45,46]
Menstrual problem	Leaf decoction is taken orally	South Africa	[2,4,37,39]
Mental disease	Leaf decoction is taken orally	Eswatini and South Africa	[2,4,14,18,37,38,47-50]
Nervous system problem	Leaf decoction is taken orally	South Africa	[2,4,14,37-39,47]
Phlegm	Bark decoction is taken orally	Lesotho	[4,27]
Pellagra	Bark decoction is taken orally	Lesotho	[4,27]
Purgative	Leaf decoction is taken orally	South Africa	[4,32,33]
Rheumatism and swollen limbs	A leaf infusion is taken orally	South Africa	[4,38,39,51]
Sores and wounds	Leaf decoction applied topically	South Africa	[4,14,15,27,29-31,51,52]
Tonic	Bark and leaf decoction is taken orally	South Africa	[4,32,33,34]
Tuberculosis	Not specified	Lesotho and South Africa	[28]
Ethnoveterinary medicine (biliousness in livestock)	Not specified	Lesotho and South Africa	[28]
C. sphaerocephala			
Emetic	Not specified	Eswatini	[18]
C. spicata			
Abdominal pain	Bark and root decoction are taken orally	South Africa	[5,53]
Antifebrile and fever	Leaf, root bark, and root decoction are taken orally	South Africa	[5,17,53-57]
Appetite stimulant	Root decoction is taken orally	South Africa	[5,41]
Cardiovascular	Not specified	Zimbabwe	[5,16]
Convulsions and epilepsy	Leaf infusion sprinkled on the face and taken orally	Zimbabwe	[5,16,35,39]
Diabetes mellitus	Root decoction is taken orally	South Africa	[5,58]
Diuretic	A root infusion is taken orally	South Africa	[5,17,55,59,60]
Emetic, nausea, and vomiting	Fruit, root, and stem infusion taken orally	Eswatini and South Africa	[2,5,14,17,53-57,61]

(Table 1). Continued.

Medicinal uses	Parts used	Country	References
Fever	A leaf infusion is taken orally	South Africa	[59]
Gastro-intestinal problems (biliousness, constipation, indigestion, and stomach complaints)	Flower, flower stalk, and root powder decoction is taken orally	South Africa	[2,5,17,26,32-35,55,60,62-64]
Gonorrhea and venereal diseases	Bark, flower, fruits, root, and stem decoction are taken orally	Lesotho and South Africa	[2,5,17,18,32,33,53,55,62,63]
HIV	Flower, fruit, root, and stem decoction are taken orally	South Africa	[5,32,33]
Immune booster	Flower, fruit, leaf, root, and stem decoction are taken orally	South Africa	[5,32-35]
Inflammation	Root infusion applied topically	South Africa	[5,26]
Laxative and purgative	Flower, fruit, root, and stem decoction are taken orally	South Africa	[5,17,32,33,55,59,60]
Magical purposes	Bark used	South Africa	[5,17,47,65]
Malaria	Bark, flower, fruit, root, and stem infusion taken orally	Eswatini, South Africa, and Zimbabwe	[2,5,17,18,37,60,62,63]
Menstrual problems	Root and stem decoction is taken orally	South Africa and Zimbabwe	[2,5,16,37]
Mental illness	Bark and root bark decoction is taken orally	South Africa and Zimbabwe	[5,16,17,47,49]
Muscular spasms, camps, and painful legs	Bark decoction applied topically	South Africa and Zimbabwe	[2,5,16,66-68]
Nausea	A leaf infusion is taken orally	South Africa	[60]
Skin diseases (measles, pimples, shingles, and skin irritation)	Flower, fruit, leaf, root, and stem decoction are taken orally	South Africa	[5,17,32-34]
Stomach ulcers	Bark infusion is taken orally	South Africa	[2,5,17,55,65]
Tonic	Flower, fruit, root, and stem decoction are taken orally	South Africa	[5,26,32-34]
Uterine pain	Root decoction is taken orally	South Africa and Zimbabwe	[5,16,17,53,55]
Venereal diseases	A leaf infusion is taken orally	South Africa	[60]
Vomiting	Not specified	Eswatini	[18]
Wounds	Bark, leaf, and root decoction applied topically	South Africa	[5,69]
Ethnoveterinary medicine			
Anthelmintics	Animals drenched with bark decoction	South Africa	[5,70-72]
Bloody urine after calving, endometriosis, and vaginitis	Leaves mixed with those of *Olea europaea* L. subsp. *Africana* (Mill.) P.S. Green	South Africa	[5,73,74]
Gallsickness	Animals drenched with bark and leaf decoction	South Africa	[5,73-77]
Heartwater	Animals drenched with bark decoction	South Africa	[5,78,79]
Paralyzed goats	Animals drenched with leaf decoction	South Africa	[5,17,62,74]
Redwater	Animals drenched with bark and leaf decoction	South Africa	[5,77,78]
Retained placenta	Animals drenched with bark decoction	South Africa	[5,73,74,80]
C. thyrsiflora			
Diuretic	Root decoction is taken orally	South Africa	[81]
Laxative	Root decoction is taken orally	South Africa	[81]

(Table 1). Continued.

Medicinal uses	Parts used	Country	References
C. transvaalensis			
Malaria	Root decoction is taken orally	South Africa	[81]
C. zuluensis			
Emetic	Root infusion is taken orally	Eswatini	[7,18,82]
Fever	Root decoction is taken orally	Eswatini	[7,82]
Purgative	Root infusion is taken orally	South Africa	[7,83]
Swellings	Root infusion applied topically	South Africa	[7,83]
N. umbellifera			
Colic	Leaf decoction is taken orally	South Africa	[2,9,14,17]
Diuretic	Root infusion is taken orally	South Africa	[83,85]
Gastro-intestinal problems (stomachache)	Leaf decoction is taken orally	South Africa	[61,86]
Inflammation	Bark, leaf, and root decoction applied topically	South Africa	[87,88]
Inflammation of navel	Root decoction applied topically	Zimbabwe	[16,17]
Insanity	Leaf decoction is taken orally	South Africa	[2,9,14,17,48,62]
Laxative	Root infusion is taken orally	South Africa	[84,90]
Malaria	Bark and leaf decoction is taken orally	Eswatini, South Africa, and Zimbabwe	[2,9,16,17,89]
Nausea	Root infusion is taken orally	South Africa	[84,89]
Protective charm (good luck and magical)	Bark used	Eswatini and South Africa	[14,18]
Rheumatism	Leaf decoction is taken orally	Eswatini and South Africa	[2,9,18,88]
Stomach ulcers	Bark decoction is taken orally	South Africa	[14,89]
Venereal diseases	Root decoction is taken orally	South Africa	[84,89]
Weaning infants	Root infusion is taken orally	South Africa	[85,89]

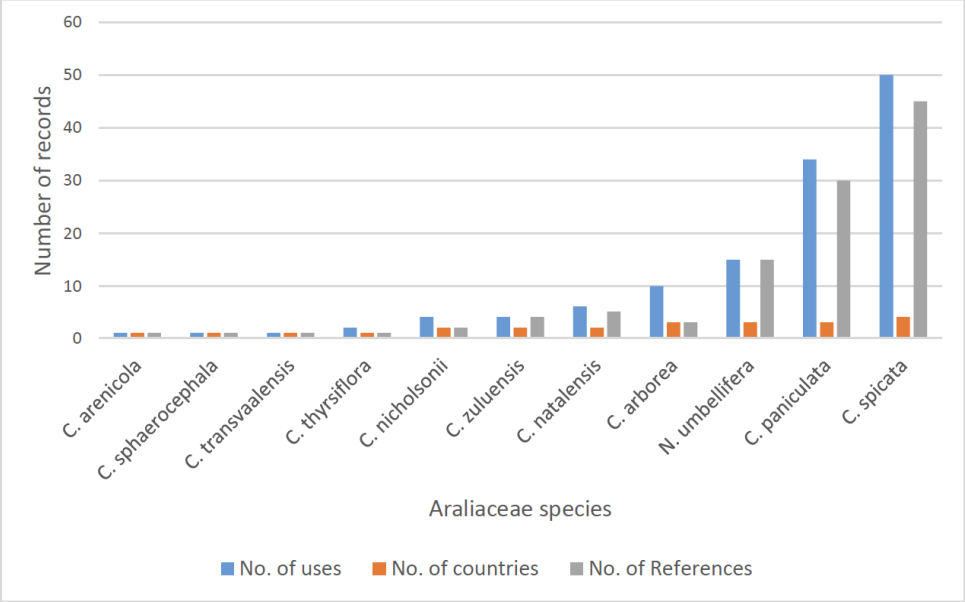

Figure 2: Species belonging to the family Araliaceae used as sources of traditional medicines in southern Africa.

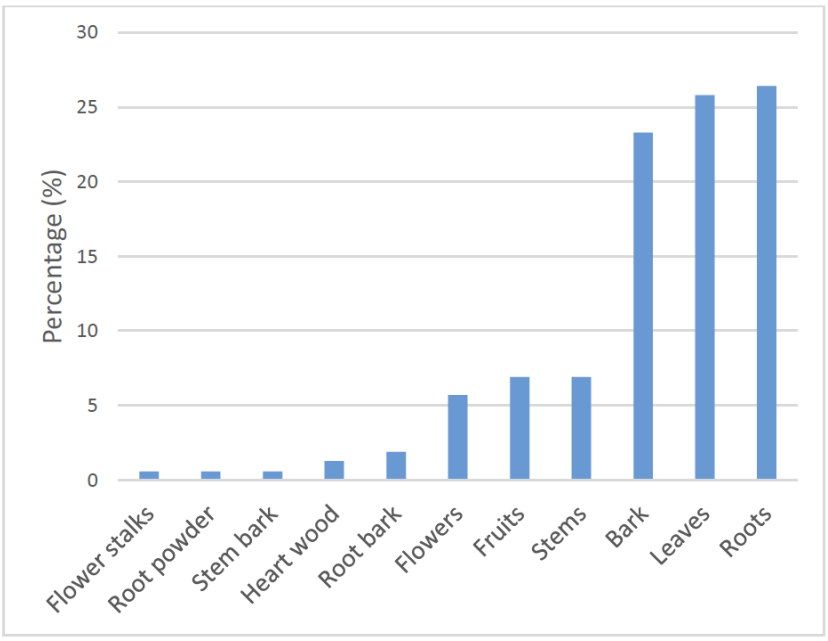

Figure 3: Plant parts of species belonging to the family Araliaceae used as sources of traditional medicines in southern Africa.

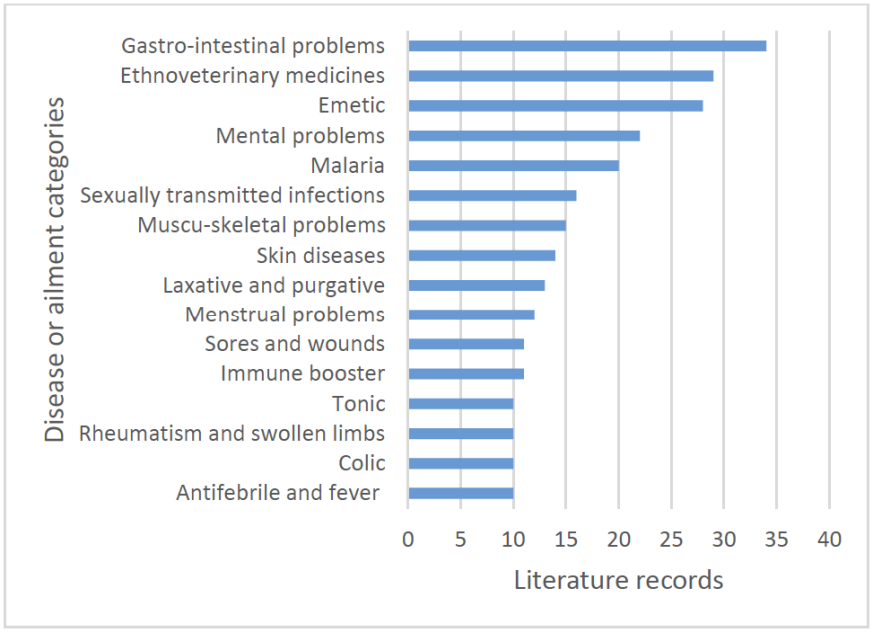

Figure 4: Medicinal uses of species of the Araliaceae family in southern Africa.

Strey, *C. natalensis* Sond., *C. nicholsonii* Strey, *C. paniculata* Eckl. & Zeyh., *C. sphaerocephala* Strey, *C. spicata* Thunb., *C. transvaalensis* Reyneke, *C. thyrsiflora* Thunb., *C. zuluensis* Thunb. and *Neocussonia umbellifera* (Sond.) Hutch (Figure **2**). The widely used species is *C. spicata*, used in countries such as Eswatini, Lesotho, South Africa, and Zimbabwe, followed by *C. paniculata* (Eswatini, Lesotho, and South Africa), *N. umbellifera* (Eswatini, South Africa and Zimbabwe) and *C. Arborea* used in Mozambique, Zambia and Zimbabwe (Table **1**; Figure **2**). The bark, flowers, flower stalks, fruits, heartwood, leaves, roots, root bark, root powder, stem and stem bark of *C. arborea, C. arenicola, C. natalensis, C. nicholsonii, C. paniculata, C. sphaerocephala, C. spicata, C. zuluensis* and *N. umbellifera* (Figure **3**) are used against 48 human and animal ailments or diseases, mainly as antifebrile, colic, emetic, immune booster, laxative, purgative, tonic and ethnoveterinary medicines as well as traditional medicines against fever, rheumatism, swollen limbs, sores, wounds, menstrual problems, skin diseases, muscu-skeletal

problems, sexually transmitted infections, malaria, mental problems and gastro-intestinal problems (Table **1**; Figure **4**).

Species such as *C. arborea, C. arenicola, C. natalensis, C. paniculata, C. spicata, C. zuluensis*, and *N. umbellifera* are important components of traditional pharmacopeia in southern Africa [2-8]. Hence, the bark, leaves, roots, and stems of *C. arenicola* and *S. spicata* are sold in informal herbal medicine markets as a source of traditional medicines in Kenya, Mozambique, and South Africa [5,19]. The thick tuberous roots of *C. paniculata, C. spicata*, and *C. thyrsiflora* Thunb. They are peeled and eaten raw as emergency food or as a source of water in South Africa [4,5]. Such socio-cultural indigenous knowledge base about species belonging to the family Araliaceae is still relatively underdeveloped in the region.

This study showed that alkaloids, anthocyanins, anthracene glycosides, botulin, flavonoids, free gallic acid, iridoids, phenolics, saponins, steroids, tannins, triterpenoids, and volatile oils have been identified from the leaves, roots, root bark, stems, stem bark and twigs of *C. arborea, C. natalensis, C. paniculata, C. spicata, C. zuluensis* and *N. umbellifera* (Table **2**). The documented species of the Araliaceae family appear to be important sources of triterpenes, triterpene glycosides, and triterpenoid saponins (Table **2**). This diversity of phytochemical compounds associated with species belonging to the Araliaceae family emphasizes the importance of evaluating the toxicological properties of the species used as traditional medicines. Pharmacological research revealed that *C. arborea, C. natalensis, C. paniculata, C. spicata, C. zuluensis*, and *N. umbellifera* crude extracts and compounds demonstrated Aβ42 protein reduction, acetylcholinesterase, analgesic, antibacterial, antifungal, antiviral, anticancer, antihyperglycemic, anti-inflammatory, antileishmanial, antioxidant, antiplasmodial, antiprotozoal, anti-ulcer, immunomodulatory, larvicidal, molluscicidal, spermicidal, cytotoxicity and toxicity activities.

Summary of the Pharmacological Activities of Araliaceae Species

Extracts and isolated compounds from *C. arborea, C. natalensis, C. paniculata, C. spicata, C. zuluensis*, and *N. umbellifera* have been reported to possess Aβ42 protein reduction, acetylcholinesterase, analgesic, antibacterial, antifungal, antiviral, anticancer, antihyperglycemic, anti-inflammatory, antileishmanial, antioxidant, antiplasmodial, antiprotozoal, anti-ulcer, immunomodulatory, larvicidal, molluscicidal, spermicidal, cytotoxicity and toxicity activities.

Aβ42 Protein Reduction Activities

Thakur *et al*. [39]) evaluated the Aβ42 protein reduction activities of dichloromethane: methanol (1:1) extracts of *C. paniculata* leaves and stems using ELISA – sAPPα, sAPPβ, and Aβ peptide assays. The extracts reduced the secreted level of Aβ42 by 57.5% in a dose-dependent manner compared to the control. The extract also decreased the levels of Aβ40, sAPPβ-sw, and sAPPα in a dose-dependent way [39].

Acetylcholinesterase Inhibitory

Amoo *et al*. [103] evaluated acetylcholinesterase inhibitory properties of aqueous extract of *C. spicata* leaves using a colorimetric assay with galanthamine at 20.0 μM as a positive control. The extract exhibited acetylcholinesterase inhibitory activities of 72.1%–86.5% at 1.0 mg/ml.

Analgesic Activities

Adedapo *et al*. [105] evaluated the analgesic activities of the aqueous extract of *C. paniculata* stem bark using the formalin test by treating male Wistar rats with the extract; 10 mg/kg of indomethacin; and 2 ml/kg of normal saline and the licking time and frequency of the injected paw were recorded for 30 min. In the acetic acid-induced writhing model, the extract showed a good analgesic effect characterized by a reduction in the number of writhes when compared to the control, and the extract also caused a dose-dependent decrease of licking time and licking frequency in rats injected with 2.5% formalin, signifying its analgesic effect [105].

Antibacterial Activities

McGaw *et al*. [61] evaluated the antibacterial activities of aqueous, ethanol, and hexane extracts of *C. spicata* leave against *Bacillus subtilis, Escherichia coli, Klebsiella pneumoniae,* and *Staphylococcus aureus* using the disc diffusion assay with neomycin (5 μg) as the positive control. The ethanol and water extracts were active against all tested pathogens exhibiting minimum inhibitory concentration (MIC) values ranging from 3.1 mg/ml to 12.5 mg/ml [61]. Tetyana [37] and Tetyana *et al*. [2] evaluated the antibacterial activities of ethanolic, ethyl acetate, and water extracts of *C. spicata* and N. *umbellifera* bark and roots against *Bacillus subtilis, Escherichia coli, Klebsiella*

Table 2: Phytochemical Composition of Species Belonging to the Family Araliaceae

Phytochemical compound	Plant part	Reference
C. arborea		
2,3-dihydroxyolean-12-en-28-oic acid	Root bark and stem bark	[91,92]
3*β*-hydroxylolean-12-en-28-oic	Root bark and stem bark	[91,92]
3β-hdroxylolean-12-en-28-oic acid	Root bark	[93]
3-O-*α*-L-arabinopyranosylolean-12-en-28-oic acid	Stem bark	[92]
3-O-*β*-D-glucopyranosyl stigmasterol	Root bark and stem bark	[91-93]
3-O-*β*-D-xylopyranosylolean-12-en-28-oic acid	Stem bark	[92]
3-O-*β*-D-glucopyranosyl-23-hydroxyurs-12-en-28-oic acid	Stem bark	[92]
3-O-*β*-D-glucopyranosyl-(1→2)-*α*-L-arabinopyranosyl-3*β*-hydroxyolean-12-en-28-oic acid	Stem bark	[92]
3,23-dihydroxyo lean-12-en-28-oic acid	Root bark and stem bark	[91,92]
3,23-dihydroxyurs-12-en-28-oic acid	Stem bark	[92]
3,23-dihydroxy-12-oleanen-28-oic acid	Root bark	[93]
23-hydroxy-3-oxours-12-en-28-oic acid	Root bark and stem bark	[91-93]
28-O-α-L-rhamnopyranosyl-(1→4)-*β*-D-glucopyranosyl-(1→6)-*β*-D-glucopyranosyl-23-hydroxyursolic acid	Root bark and stem bark	[91,92]
β-resorcylic acid (5), mixture of 3-O-*β*-D-glucopyranosyl-23-hydroxyolean-12-en-28-oic acid	Stem bark	[92]
Alkaloids	Root bark	[94,95]
Anthocyanins	Root bark	[95]
Cardiac glycosides	Root bark	[94-96]
Ciwujianoside C3	Root bark and stem bark	[91,92]
Flavonoids	Root bark	[94,95]
Polyphenols	Root bark	[95]
Protocatechuic acid	Stem bark	[92]
Quinones	Root bark	[95]
Saponins	Root bark	[94-96]
Saponinsarboreasides A-E	Root bark and stem bark	[91,92]
Steroids	Root bark	[95]
Stigmasterol	Root bark and stem bark	[91-93]
Tannins	Root bark	[94-96]
Triterpenes	Root bark	[94,95]
C. natalensis		
23-hydroxy3-oxo-urs-12-en-28-oic acid	Leaves and twigs	[97]
Oleanolic acid	Leaves and twigs	[97]
C. paniculata		
3-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of 23-hydroxybetulinic acid	Leaves	[98]
28-O-(2-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of 23-hydroxybetulinic acid	Leaves	[98]
28-O-(2-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of hederagenin	Leaves	[98]
3-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of hederagenin	Leaves	[98]

(Table 2). Continued.

Phytochemical compound	Plant part	Reference
3-O-α-L-arabinopyranosyl-28-O-(2-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-Dglucopyranosyl-(1→6)-O-β-D-glycopyranosides of oleanic acid	Leaves	[98]
3-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-Dglucopyranosyl-(1→6)-O-β-D-glycopyranosides of oleanic acid	Leaves	[98]
3-O-α-L-arabinopyranosyl-28-O-(2-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-Dglucopyranosyl-(1→6)-O-β-D-glycopyranosides of ursolic acid	Leaves	[98]
3-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-Dglucopyranosyl-(1→6)-O-β-D-glycopyranosides of ursolic acid	Leaves	[98]
3-O-α-L-arabinopyranosyl-28-O-(4-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-Oβ-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of hederagenin	Leaves	[98]
2-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-Oβ-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of hederagenin	Leaves	[98]
3-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-Oβ-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of hederagenin	Leaves	[98]
3-O-β-D-glucopyranosyl-(1→2)-O-α-L-arabinopyranosyl-28-O-(2-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of oleanic acid	Leaves	[98]
3-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of oleanic acid	Leaves	[98]
28-O-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranoside of 23-hydroxyursolic acid	Leaves	[99]
3-O-β-D-glucopyranoside of β-sitosterol	Leaves	[99]
3-O-α-L-arabinopyranosides of oleanolic acid	Leaves	[99]
3-O-α-L-arabinopyranosides of ursolic acid	Leaves	[99]
3-O-α-L-arabinopyranosides of hederagenin	Leaves	[99]
3-O-β-D-glucopyranosyl-(1→2)-α-L-arabinopyranoside of oleanolic acid	Leaves	[99]
3-O-α-L-arabinopyranosyl-28-O-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of oleanolic acid	Leaves	[99]
3-O-α-L-arabinopyranosyl-28-O-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of ursolic acid	Leaves	[99]
Clethroidoside B	Leaves	[39]
Pseudoprostodioscin	Leaves	[39]
Rutin	Leaves	[39]
Spinasaponin A	Leaves	[39]
C. spicata		
α- and β-amyrin	Leaves and stems	[100]
[α-L-arabinofuranosyl-(1→4)-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid	Stem bark	[101]
[α-L-arabinofuranosyl-(1→4)-β-D-galactopyranosyl-(1→2))-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid	Stem bark	[101]
Alkaloids	Root bark	[102]
Anthocyanins	Root bark	[102]
Anthracene glycosides	Root bark	[102]
Botulin	Leaves and stems	[100]
Flavonoids	Leaves	[103]
Free gallic acid	Leaves	[103]
Gallotannins	Leaves	[103]
Iridoids	Leaves	[103]

(Table 2). Continued.

Phytochemical compound	Plant part	Reference
Lupeol	Leaves and stems	[100]
Phenolics	Leaves	[103]
Saponins		[5]
Steroids		[5]
Tannins	Leaves	[103]
Triterpenoids	Root bark	[102]
Volatile oils	Root bark	[102]
C. zuluensis		
Cardiac glycosides	Roots	[82]
Flavonoids	Roots	[82]
Polyphenols	Roots	[82]
Saponins	Roots	[82,85,104]
Steroids	Roots	[82]
Tannins	Roots	[85,104]
N. umbellifera		
Betulin	Not specified	[9,89]
Ent-Kaur-16-en-19-oic-acid	Not specified	[9,89]
7-Hydroxy-6-methoxycoumarin	Not specified	[9,89]

pneumoniae, Micrococcus luteus, Pseudomonas aeruginosa, Staphylococcus aureus, and *Staphylococcus epidermidis* using the disc diffusion assay with neomycin as a positive control. The extracts exhibited activities against *Staphylococcus aureus* (2,37]. McGaw *et al*. [106] evaluated the antibacterial activities of aqueous, methanol, and hexane extracts of *C. spicata* roots against *Enterococcus faecalis, Escherichia coli, Pseudomonas aeruginosa* and *Staphylococcus aureus* using the serial microplate dilution method with neomycin as the positive control. The extracts exhibited activities with MIC values ranging from 6.3 mg/ml to >12.5 mg/ml [106]. Shai [85] and Shai *et al*. [68] evaluated the antibacterial activities of acetone, dichloromethane, and n-hexane extracts of *C. zuluensis* leaves against *Enterococcus faecalis, Pseudomonas aeruginosa, Escherichia coli* and *Staphylococcus aureus* using the microdilution method with gentamicin as a positive control. The extracts exhibited activities against the tested pathogens with MIC values ranging from 0.3 mg/ml to 2.5 mg/ml and total activity ranging from 8.0 ml to 267.0 ml [68,85]. De Villiers *et al*. [3] evaluated the antibacterial activities of methanol and water extracts of *C. arborea, C. arenicola, C. natalensis, C. nicholsonii, and C. paniculata* subsp. *paniculata, C. paniculata* subsp. *sinuata, C. sphaerocephala, C. spicata, C. thyrsiflora, C. zuluensis* and *N. umbellifera* leaves against *Pseudomonas aeruginosa, Neisseria gonorrhoeae, Enterococcus faecalis, Staphylococcus aureus* and *Escherichia coli* using the microdilution method with ciprofloxacin (0.01 mg/ml) as a positive control. Both extracts exhibited activities against tested pathogens, with the MIC values ranging from 0.02 mg/mL to 16.0 mg/ml [3]. Amoo *et al*. [60] evaluated the antibacterial activities of aqueous extract of *C. spicata* leaves using the microdilution bioassay against *Pseudomonas aeruginosa* and *Staphylococcus aureus* with neomycin as a positive control. The extract exhibited activities against tested pathogens with MIC and minimum microbicidal concentration (MMC) values ranging from 1.6 mg/ml to >6.3 mg/ml [60]. Moungang *et al*. [95] evaluated the antibacterial activities of ethanol and hydro-ethanolic extracts of *C. arborea* root bark against *Proteus mirabilis, Salmonella* spp., *Shigella* spp., and *Staphylococcus aureus* using the microdilution technique. The extracts exhibited activities against the tested pathogens with the minimum inhibitory concentrations (MIC) and the minimum bactericidal concentrations (MBC) values ranging from 25.0 mg/mL to 200.0 mg/ml [95].

Antifungal Activities

Shai [85] and Shai *et al*. [68] evaluated the antifungal activities of acetone, dichloromethane, and n-hexane extracts of *C. zuluensis* leaves against *Cryptococcus neoformans, Aspergillus fumigatus, Candida albicans, Micrococcus canis* and *Sporothrix schenckii* using the microdilution method with amphotericin B as a positive control. The extracts exhibited activities against tested pathogens with MIC values ranging from 0.06 mg/ml to 2.5 mg/ml and total activity ranging from 8.0 ml to 133.0 ml [68,85]. Mokoka [107] and Mokoka *et al*. [108] evaluated the antifungal activities of hexane, dichloromethane, acetone, and methanol extracts of *C. zuluensis* leaves against *Cryptococcus neoformans* using the two-fold serial dilution microplate and microdilution methods. The extracts exhibited activities against the tested pathogen with MIC values ranging from 0.02 mg/ml to 0.6 mg/ml and total activity ranging from 9.0 ml/g to 496.0 ml/g [107,108]. Mangoyi and Mukanganyama [109] evaluated the antifungal activities of ethanol extracts of *C. natalensis* leaves against *Candida krusei* and *Candida albicans* using the agar disc diffusion and broth dilution methods with miconazole as a positive control. The extract exhibited activities against *Candida albicans* with a zone of inhibition value of 16.0 mm, MIC and minimum fungicidal concentration (MFC) values of 0.3 mg/ml and 1.3 mg/ml, respectively [109]. Amoo *et al*. [60] evaluated the antifungal activities of aqueous extract of *C. spicata* leaves using the microdilution bioassay against *Candida albicans* with amphotericin B as a positive control. The extract exhibited activities against tested pathogens with MIC and MMC values of 6.3 mg/ml [60].

Antiviral Activities

McGaw *et al*. [106,110] evaluated the antiviral activities of acetone extracts of *C. spicata* leaves using an antiviral assay against the sensitive feline herpesvirus type 1, and the extract exhibited activities. Nthambeleni *et al*. [111] evaluated the anti-HIV activities of aqueous extract of *N. umbellifera* leaves using EMF and InPheno bioassay screening against the cellular co-receptor types for HIV, CCR5, and CXCR4 viruses and the extract exhibited moderate activities [111].

Anticancer Activities

Fouché *et al*. [112] evaluated the anticancer activities of dichloromethane extracts of *C. paniculata* leaves against sixty human cancer cell lines organized into subpanels representing leukemia, melanoma, and cancer of the lung, colon, kidney, ovary, and central nervous system. The extracts exhibited moderate growth inhibition of above 50% for two or more of the cell lines (GI_{50}), with values ranging from >0 µg/ml to 1.1 µg/ml [112]. Similarly, Fouché *et al*. [113] evaluated the anticancer activities of dichloromethane: methanol (1:1) extracts of *C. paniculata* leaves against sixty human cancer cell lines organized into subpanels representing leukemia, melanoma, and cancer of the lung, colon, kidney, ovary, and central nervous system. The extracts exhibited activities against leukemia RPMI-8226, colon HCT-116, and colon KM12 with total growth inhibition (TGI) values of 1.0 µg/ml, 1.5 µg/ml, and 2.7 µg/ml, respectively [113].

Antihyperglycemic Activities

Triterpenoids content fraction of methanol extract of *C. arborea* root bark and stem bark have been reported to have antihyperglycemic activities by reducing fasting blood sugar (FBS) from 310.0 to 74.0 mg/dl) [91]. Aba *et al*. [96] and Aba and Asuzu [94,114-116] reported that administration of 125 mg/kg bw of the extract to the diabetic rats significantly increased red blood cell, packed cell volume, haemoglobin, mean corpuscular volume, and conjugated bilirubin levels. It also considerably decreased total bilirubin and unconjugated bilirubin values compared to the untreated diabetic group.

Anti-Inflammatory Activities

Tetyana [37] and Tetyana *et al*. [2] evaluated the anti-inflammatory activities of ethanolic, ethyl acetate, and water extracts of *C. paniculata, C. spicata*, and *N. umbellifera* bark, leaves, roots, and stems using the cyclooxygenase-1 (COX-1) assay. The extracts inhibited COX in the COX-1 assay. Adedapo *et al*. [105] evaluated the anti-inflammatory activities of aqueous extract of *C. paniculata* stem bark using the carrageenan-induced rat paw edema and histamine-induced rat paw edema assays with indomethacin and cyproheptadine as positive controls. The extract reduced the formation of edema induced by carrageenan and histamine [105].

Antileishmanial Activities

Mokoka [117] and Mokoka *et al*. [118] evaluated the antileishmanial activities of dichloromethane and dichloromethane: methanol (1:1) extracts of *N. umbellifera* roots against *Leishmania donovani*. The

extracts exhibited activities. Bapela *et al*. [119] evaluated antileishmanial activities of dichloromethane and 50% methanol extracts of *C. spicata* root bark against *Leishmania donovani.* The dichloromethane extracts displayed inhibitory effects on the growth of amastigote forms of *Leishmania donovani* with half-maximal inhibitory concentration (IC_{50}) values of 8.2 µg/ml [119].

Antioxidant Activities

Amoo *et al*. [103] evaluated the antioxidant activities of the aqueous extract of *C. spicata* leaves using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging and β-carotene linoleic acid model assays. The DPPH results showed half-maximal effective concentration (EC_{50}) values of 14.3 µg/ml to 43.6 µg/ml, while the antioxidant activity of 41.8% to 55.7% at 200.0 µg/ml was exhibited using the β-carotene linoleic acid model assay [103]. Aba *et al*. [96] evaluated the antioxidant activities of the methanolic extract of *C. arborea* stem bark using the DPPH and ferric reducing antioxidant power (FRAP) assays with 2.0 µm ascobic acid as a positive control. The results of both the DPPH and FRAP assays showed that the extract exhibited activities [96].

Antiplasmodial Activities

Tetyana [37] and Tetyana and Van Staden [2] evaluated antiplasmodial activities of the ethanolic, ethyl acetate, and water extracts of *C. paniculata*, *C. spicata,* and *N. umbellifera* bark against *Plasmodium falciparum* in an *in vitro* assay, a slightly modified version of the parasite lactate dehydrogenase assay with chloroquine as a positive control. The extracts exhibited weak inhibitory activities. Kraft *et al*. [120] evaluated the *in vitro* antiplasmodial activities of petrol ether: ethylacetate (1:1) extracts of *C. spicata* bark and leaves using the [G-^{3}H] hypoxanthine incorporation assay using the chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium falciparum*. The leaf extract exhibited weak activities with IC_{50} values of 45.1 µg/ml and 47.5 µg/ml against chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium falciparum*, respectively [120]. Clarkson *et al*. [121] evaluated antiplasmodial activities of *C. spicata* and *N. umbellifera* aqueous, dichloromethane, dichloromethane-methanol (1:1) extracts against *Plasmodium falciparum* using the parasite lactate dehydrogenase assay. The extracts exhibited weak activities. De Villiers *et al*. [3] evaluated the antiplasmodial activities of methanol and water extracts of *C. arborea, C. natalensis, C. paniculata* subsp. *paniculata, C. paniculata* subsp. *sinuata, C. sphaerocephala, C. spicata, C. zuluensis,* and *N. umbellifera* leaves using the [G-^{3}H] hypoxanthine incorporation assay using chloroquine-sensitive (3D7) strain of *Plasmodium falciparum* as the test organism. The extracts exhibited activities. Similarly, Bapela *et al*. [56], Bapela [57], and Bapela *et al*. [122] evaluated antiplasmodial activities of dichloromethane and 50% methanol root bark extract of *C. spicata* using the [G-^{3}H]-hypoxanthine incorporation assay using chloroquine-sensitive (NF54) strain of *Plasmodium falciparum* as the test organism with chloroquine as a positive control. The dichloromethane extract exhibited pronounced activities with an IC_{50} value of 3.3 µg/ml [56,57,122]. Mthembu [84] and Mthembu *et al*. [89] evaluated the antiplasmodial activities of dichloromethane and dichloromethane: methanol (1:1) extracts of N. *umbellifera* leaves and the compounds 7-hydroxy-6-methoxycoumarin, botulin and entkaur16-en-19-oic acid isolated from the species against the chloroquine-susceptible *Plasmodium falciparum* D10 using a parasite lactate dehydrogenase (pLDH) assay with chloroquine used as a reference drug. The dichloromethane and dichloromethane: methanol (1:1) extracts and the compound betulin exhibited activities with IC_{50} values ranging from 3.2 µg/ml to 5.0 µg/ml compared to IC_{50} value of 27.2 ng/ml exhibited by the reference compound [84,89]. Mokoka [117] and Mokoka *et al*. [118] evaluated the antimalarial activities of dichloromethane and dichloromethane: methanol (1:1) extracts of *N. umbellifera* roots against *Plasmodium falciparum* with benznidazole chloroquine (IC_{50} = 0.05 µM) as a positive control using the [G-^{3}H]-hypoxanthine incorporation assay. The dichloromethane and dichloromethane: methanol (1:1) extracts exhibited weak activities with IC_{50} values of 2.7 µg/ml and 7.7 µg/ml, respectively [117,118].

Antiprotozoal Activities

De Villiers et al. [3] evaluated the antiprotozoal activities of methanol and water extracts of C. arborea, C. natalensis, C. nicholsonii, C. paniculata subsp. paniculata, C. paniculata subsp. sinuata, C. sphaerocephala, C. spicata, C. thyrsiflora, C. zuluensis, and N. umbellifera leaves against the protozoan pathogen associated with urogenital or sexually transmitted infections, Trichomonas vaginalis using the microdilution method with ciprofloxacin (0.01 mg/ml) as a positive control. The methanol extract exhibited activities against the tested pathogen. Mokoka [117]

and Mokoka et al. [118] evaluated the antiprotozoal activities of dichloromethane and dichloromethane: methanol (1:1) extracts of N. umbellifera roots against Trypanosoma cruzi and Trypanosoma brucei rhodesiense. The extracts exhibited antiprotozoal activities.

Anti-Ulcer Activities

Preliminary research by Fourie *et al*. [97] showed that the triterpene acid, 23-hydroxy-3-oxo-urs-12-en-28-oic acid isolated from the leaves and twigs of *C. natalensis* exhibited anti-ulcer activities.

Immunomodulatory Activities

Oladimeji *et al*. [93] evaluated the immunomodulatory activities of the compounds 3,23-dihydroxy-12-oleanen-28-oic acid, 3β-hdroxylolean-12-en-28-oic acid, stigmasterol and 3-O-β-D-glucopyranosyl stigmasterol isolated from the root-bark of *C. arborea* by assessing the effect on production of intracellular reactive oxygen species (ROS) from zymosan activated whole blood phagocytes and on proliferation of phytoheamagglutinin (PHA) activated T-lymphocytes. The compounds 3,23-dihydroxy-12-oleanen-28-oic acid and 3β-hdroxylolean-12-en-28-oic acid moderately inhibited the production of ROS with IC_{50} values of 24.4 and 37.5 µg/ml, respectively whereas compound 3β-hdroxylolean-12-en-28-oic acid exhibited the highest inhibitory effect with IC_{50} value of 12.6 µg/ml on PHA [93].

Larvicidal Activities

Maharaj *et al*. [123,124] evaluated the larvicidal activities of aqueous, dichloromethane, dichloromethane: methanol (1:1), and methanol extracts of *C. spicata* and *N. umbellifera* fruits against the 3rd instar larvae of *Anopheles arabiensis* using Temephos (Mostop; Agrivo) as a positive control. The extract exhibited activities.

Molluscicidal Activities

Marston and Hostettmann [125] and Msonthi *et al*. [126] evaluated the molluscicidal activities of the water extract of *C. spicata* stem bark using bioassays made with *Biomphalaria glabrata* snails, the intermediate host of *Schistosoma mansoni*. The extract showed activities of 400 ppm within 24 h against *Biomphalaria glabrata* snails [125,126]. Similarly, Gunzinger *et al*. [101] evaluated the molluscicidal activities of the compounds [α-L-arabinofuranosyl-(1→4)-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid and [α-L-arabinofuranosyl-(1→4)-β-D-galactopyranosyl-(1→2))-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid isolated from *C. spicata* stem bark using bioassays that were made with *Biomphalaria glabrata* snails. The compound [α-L-arabinofuranosyl-(1→4)-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid was active at 12.5 mg/l while [α-L-arabinofuranosyl-(1→4)-β-D-galactopyranosyl-(1→2))-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid was active at 100 mg/l [101].

Spermicidal Activities

Hostettmann *et al*. [127] evaluated the spermicidal activities of the compounds [α-L-arabinofuranosyl-(1→4)-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid and [α-L-arabinofuranosyl-(1→4)-β-D-galactopyranosyl-(1→2)-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid against human spermatozoids. The compound [α-L-arabinofuranosyl-(1→4)-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid was active at 1 mg/l and compound [α-L-arabinofuranosyl-(1→4)-β-D-galactopyranosyl-(1→2))-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid was active at 3 mg/l, within 3 min [127].

Cytotoxicity Activities

De Villiers *et al*. [3] evaluated the cytotoxicity activities of methanol and water extracts of *C. arborea, C. natalensis, C. paniculata* subsp. *paniculata, C. paniculata* subsp. *sinuata, C. spicata* and *N. umbellifera* against the human T-cell leukemia (Jurkat) cell line using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) calorimetric assay with (S)-(+)- camptothecin as a positive control. Mokoka [117] and Mokoka *et al*. [118] evaluated the cytotoxicity activities of dichloromethane and dichloromethane: methanol (1:1) extracts of *N. umbellifera* roots against the rat myoblast L6 cells with podophyllotoxin (IC_{50} = 0.05 µM) as a reference drug. The dichloromethane and dichloromethane: methanol (1:1) extracts exhibited activities with IC_{50} values of 13.9 µg/mL and 48.3 µg/mL, respectively [117,118]. Bapela [57] and Bapela *et al*. [56,119,122] evaluated cytotoxicity activities of dichloromethane and 50% methanol root bark extracts of *C. spicata* against mammalian L-6 rat skeletal myoblast cells with podophyllotoxin as a control. The dichloromethane extract demonstrated IC_{50} value of 47.8 µg/ml and selectivity index value of 15 and 50% methanol extract exhibited IC_{50} value of 69.1 µg/ml which was considered

to be non-toxic to rat skeletal myoblast L6 cells [56,57,119,122].

Toxicity Activities

McGaw *et al*. [106] evaluated toxicity activities of aqueous, methanol, and hexane extracts of *C. spicata* roots using the brine shrimp lethality mortality assay against the larvae of *Artemia salina* with podophyllotoxin as a positive control. Only the aqueous extract showed activities with a median lethal concentration (LC_{50}) value of 2.6 µg/mL, comparable to the LC_{50} value of 7.0 µg/ml exhibited by the control [106]. Adedapo *et al*. [105] evaluated acute toxicity activities of the aqueous extract of *C. paniculata* stem bark by oral administration of graded doses of the extract of 200 mg/kg, 400 mg/kg, 800 mg/kg, 1600 mg/kg, and 3200 mg/kg body weight in Wistar male rats. All the rats were allowed free access to food and water and observed throughout 48 h for signs of acute toxicity and death within this period. Acute toxicity tests showed that the extract caused 80% mortality in rats; hence, *C. paniculata* can be considered toxic [105].

CONCLUSION

Despite several species belonging to the family Araliaceae in southern Africa, only 11 species have been documented as used in traditional medicine or investigated for their chemical composition or biological activities. Such results highlight that this family is highly understudied despite its promising medicinal value. This study explored the correlation between the documented species' medicinal uses, phytochemistry, and pharmacological properties. Therefore, this review helps to identify medicinal plants with clinical potential for further *in vitro* or *in vivo* pharmacological investigation.

LIST OF ABBREVIATIONS

Aβ = amyloid β-protein

COX-1 = cyclooxygenase-1

DPPH = 2,2-diphenyl-1-picrylhydrazyl

EC_{50} = half maximal effective concentration

ELISA = Enzyme-linked immunosorbent assay

FBS = fasting blood sugar

FRAP = ferric reducing antioxidant power

GI_{50} = half maximal growth inhibition

HIV = Human immunodeficiency virus

IC_{50} = half maximal inhibitory concentration

LC_{50} = half maximal lethal concentration

MBC = minimum bactericidal concentrations

MFC = minimum fungicidal concentration

MIC = minimum inhibitory concentration

MMC = minimum microbicidal concentration

MTT = 3-(4,5-dimethylthiazol-2-yl)-2,5- diphenyl tetrazolium bromide

PHA = phytoheamagglutinin

pLDH = parasite lactate dehydrogenase

POWO = Plants of the World Online

ROS = reactive oxygen species

sAPPα = soluble amyloid precursor protein (APPα)

sAPPβ = soluble amyloid precursor protein (APPβ)

TGI = total growth inhibition

µM = micrometre

WHO = World Heath Organization

AUTHOR'S CONTRIBUTIONS

The author declares that this work was done by the author named in this article.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest regarding the publication of this paper.

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