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Review Article

HETEROMORPHA ARBORESCENS: A REVIEW OF ITS BOTANY, MEDICINAL USES, AND PHARMACOLOGICAL PROPERTIES

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ABSTRACT

Heteromorpha arborescens is an important medicinal plant species throughout its distributional range in tropical Africa. This study evaluated the botany, medicinal uses, and pharmacological activities of *H. arborescens*. Literature focusing on the botany, phytochemical, pharmacological, and toxicological properties of *H. arborescens* were obtained from scientific databases such as SCOPUS, Science Direct, PubMed, SciFinder, Medline, and Google Scholar. Pre-electronic literature sources such as book chapters, books, journal articles, conference papers, and other scientific documents were obtained from the University library. Literature search revealed that *H. arborescens* is used as an aphrodisiac, as herbal medicine for shortness of breath, intestinal worms, inflammation, pain, respiratory problems, skin infections, headache, fever, and malaria. Pharmacological studies of compounds and *H. arborescens* extracts revealed anthelmintic, antiarthritic, antibacterial, antifungal, anti-inflammatory, antimycobacterial, antinociceptive, antioxidant, antipeptic ulcer, anti-scabies, antispasmodic, antiviral, cytotoxicity, genotoxicity, and uterotonic activities. More detailed research is needed aimed at assessing phytochemical, pharmacological, and toxicological properties of different plant parts and phytochemical compounds isolated from the species.

Keywords: Apiaceae, *Heteromorpha arborescens,* Traditional medicine, Tropical Africa.

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INTRODUCTION

Heteromorpha arborescens (Spreng.) Cham. and Schltdl. is a large shrub, small or medium deciduous tree which belongs to the carrot and parsley or Apiaceae family. Van Wyk [1] listed the stems of *H. arborescens* as commercially relevant medicinal and aromatic component of herbal medicines in east and southern Africa as aphrodisiac, for hypertension and headache. In a previous study, Van Wyk [2] argued that the essential oil of *H. arborescens* is important in the development of new pharmaceutical and health products in southern Africa for headache, inhalant, and aromatherapy. In Southern Africa, the leaves, roots, and bark of the species are used to treat abdominal pains, asthma, colic, cough, dysentery, fever, headaches, infertility, intestinal worms, mental problems, nervous disorders, shortness of breath, and tuberculosis [3-5]. Based on its popularity as traditional medicine in tropical Africa, *H. arborescens* is included in the monographic treatment of "medicinal plants of South Africa" [6], providing an overview of important medicinal plants in the country. The leaves and roots of *H. arborescens* are sold in informal herbal medicine markets in Botswana [7], Malawi [8], and South Africa [9]. Leaves of *H. arborescens* are eaten as vegetables in Kenya [10] while the roots of the species are fed to malnourished children in Botswana [7] and Swaziland [11]. It is within this context that the current study was carried out aimed at reviewing the botany, medicinal uses, phytochemical, and pharmacological properties of *H. arborescens* so as to provide baseline data required for assessing the therapeutic potential of the species.

BOTANICAL DESCRIPTION OF *H. ARBORESCENS*

H. arborescens is a member of the *Heteromorpha* Charm. and Schltdl. genus consisting of predominantly woody trees, shrubs, or suffrutices. The genus consists of seven species restricted to temperate and subtropical Africa and southern Yemen [12]. Calviño *et al*. [13] argued that the genus is monophyletic taxon based on analyses of ITS only or when using combined ITS and cpDNA data sets and the African species share the woody habit with the related genus *Polemannia* Eckl. and Zeyh. as well as fruit characters with the genus *Polemanniopsis* B. L. Burtt which are regarded as sister genera to *Heteromorpha* [12]. *H. arborescens* is a straggling, open-branched shrub, or small- to medium-sized deciduous tree, up to 15 m in height [12,14]. The species has been recorded in several areas including fringing evergreen forest, where it reaches its greatest size, wooded ravines, hillsides, rocky outcrops, wooded grassland, bushveld, and forest margins [14,15]. The bark is satiny smooth, glossy, coppery brown, somewhat waxy in appearance, and peels off horizontally in papery flakes [14,15]. Leaves are simple to variously compound, varying even on the same branch and thinly textured. The flowers of the species are small, greenish-white, or yellowish in color, occurring in dense round heads or compound umbels [14,15]. The fruits are small, dry, pale brown, and slightly winged capsules held in round clusters [16].

H. arborescens is very variable over its distributional range and has been split into five infraspecific taxa based on leaf and fruit morphology and also whether the taxa is a shrub which is rarely taller than 2 m or typically a tree with height ranging from 2 to 15 m [12,15]. The infraspecific taxa are var. *abyssinica* (A. Rich.) H. Wolff, var. *arborescens*, var. *collina* (Eckl. and Zeyh.) Sond., var. *frutescens* Winter and Van Wyk, and var. *montana* Winter [12,15]. The majority of literature sources do not separate *H. arborescens* into infraspecific taxa, but *H. arborescens sensu lato* is widely used, and this is the name that has been adopted in this study. Synonyms of *H. arborescens* are *Bupleurum collinum* (Eckl. and Zeyh.) D. Dietr., *Buprestis arborescens* Spreng., *Franchetella arborescens* (Spreng.) Kuntze, *H. arborescens* var. *collina* (Eckl. and Zeyh.) Sond., *H. collina* Eckl. and Zeyh., *H. trifoliate sensu* Cufod., *H. trifoliata* (H.L. Wendl.) Eckl. and Zeyh., and *Tenoria arborescens* (Spreng.) Spreng. [12,15,17-28].

MEDICINAL USES OF *H. ARBORESCENS*

The different plant parts of *H. arborescens* including the bark, charcoal, leaves, milky exudate, roots, and root bark are used as herbal medicines in tropical Africa (Table 1). The major medicinal uses of *H. arborescens* recorded in at least three countries (in descending order of importance)

Table 1: Medicinal uses of *Heteromorpha arborescens* in tropical Africa

Medicinal use	Parts of the plant used	Country	References
Inflammation and pain (painful joints, rheumatism, abdominal, general body, and back pains)	Bark, leaves, and roots	Malawi, South Africa, Swaziland, and Zimbabwe	[3-6,11,29-32]
Aphrodisiac	Roots and root bark	Botswana, Malawi, Mozambique, South Africa, and Zimbabwe	[3,4,33]
Aphrodisiac	Roots took by mouth mixed with those of *Carissa spinarum* L. and *Xylopia parviflora* (A. Rich.) Benth	South Africa	[29]
Respiratory problems (asthma, chest pains, coughs, and tuberculosis)	Bark, charcoal, leaves, and roots	Kenya, Lesotho, South Africa, and Zimbabwe	[3-6,16,30,32,34-37]
Blood purifier	Leaves and roots	South Africa	[3,16]
Purifying blood	Leaves and roots	South Africa	[6]
Skin infections (boils, measles, ringworm, and scabies)	Bark, leaves, and roots	Kenya, Rwanda, South Africa, and Tanzania	[33,38-40]
Cancer	Roots	Zimbabwe	[4]
Colic	Bark and leaves	South Africa	[3,6,32]
Contraceptive	Roots	Zimbabwe	[41]
Depressed fontanelles	Bark and roots	South Africa	[3]
Diabetes	Leaves and roots	South Africa and Tanzania	[42,43]
Shortness of breath	Leaves and roots	Botswana, Eritrea, and South Africa	[3,6,44,45]
Dysentery and stomach problems	Bark, leaves, and roots	South Africa	[3,6,16,32,36,46]
Dysmenorrhea	Roots	South Africa	[47]
Fever and malaria	Bark and leaves and roots	Malawi, South Africa, Uganda, Tanzania, and Zimbabwe	[4,6,16,32,36,48-50]
Fungal infections	Roots	Tanzania	[42]
Gonorrhea	Milky exudate	Ethiopia	[51]
Headache	Bark, charcoal, leaves, and roots	Eritrea, Kenya, Lesotho, South Africa, Swaziland, and Zimbabwe	[3-6,11,16,29,31,32,34-36,45,46,52,53]
Heart problems	Roots	Botswana	[44]
Induce appetite	Roots	South Africa	[33]
Infertility	Roots, bark, and leaves	Zimbabwe and South Africa	[4,6,32,36,46,54]
Intestinal worms	Leaves and roots	Lesotho, South Africa, and Swaziland	[3,6,11,16,30,35,36]
Jaundice	Leaves and roots	Ethiopia	[55]
Kidney problems	Leaves and roots	South Africa	[6,16,56]
Mental disorder	Bark, leaves, and roots	South Africa and Swaziland	[3,5,6,11,33]
Nervous disorder	Roots and leaves	South Africa	[3,6,16,36]
Peptic ulcers	Roots and root bark	Kenya and Zimbabwe	[56,57]
Rabies	Leaves and roots	Ethiopia	[55]
Snakebite	Roots	Ethiopia	[58]
Ethnoveterinary medicine (colic, gall sickness, Redwater, threadworms, tuberculosis, and vermifuge)	Bark	South Africa	[3,59,60]

include shortness of breath, intestinal worms, inflammation and pain, respiratory problems, aphrodisiac, skin infections, fever and malaria, and headache (Fig. 1). In multitherapeutic applications, the roots of *H. arborescens* are taken by mouth mixed with roots of *Carissa spinarum* L. and *Xylopia parviflora* (A. Rich.) Benth. as an aphrodisiac [29].

PHYTOCHEMISTRY AND PHARMACOLOGICAL PROPERTIES

Villegas *et al*. [61] isolated falcarindiol and sarisan from the leaves of *H. arborescens*. These two compounds exhibited antifungal activities and falcarindiol has analgesic effects which may account for the treatment of abdominal pain and headaches [6]. Recio *et al*. [62] identified 16β,23-dihydroxy-13,28-epoxyolean-11-en-3β-yl-[β-D-glucopyranosyl (1→2)]-[β-D-glucopyranosyl (1→3)]-β-D-fucopyranoside and 16β,23,28-trihydroxy-11α-methoxyolean-12-en-3β-yl-[β-D-glucopyranosyl (1→2)]-[β-D-glucopyranosyl (1→3)]-β-D-fucopyranoside which exhibited anti-inflammatory activities from the leaves of *H. arborescens*. Makungo and van Ree [63] isolated an anti-inflammatory compound 6,7-dimethoxy-2H-chromen-2-one from the leaves and branches of *H. arborescens*. The volatile oil of *H. arborescens* is known to contain sabinene, δ-3-carene, myrcene, germacrene-D, limonene, (Z)-β-ocimene, β-phellandrene, and α-pinene as major constituents [64,65] (Table 2). The volatile oil of *H. arborescens* exhibited antibacterial and antifungal activities against several microbes [66].

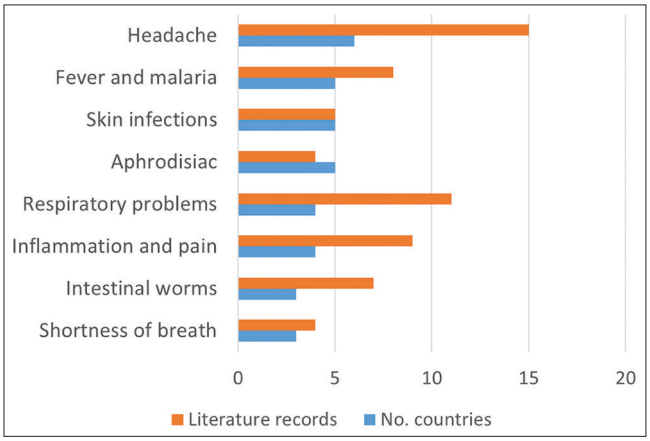

Fig. 1: Main medicinal uses of *Heteromorpha arborescens* in tropical Africa

Anthelmintic activities

McGaw *et al*. [68] evaluated anthelmintic activities of hexane, ethanol, and waterleaf extracts of *H. arborescens* on the mortality and reproductive ability of the free-living nematode *Caenorhabditis elegans*

Table 2: Essential oil, total flavonoids, and phenolics content of *Heteromorpha arborescens*

Phytochemical composition	Values	Plant parts	References
Essential oils			
Acetic acid (%)	0.1	Leaves and flowering parts	[64]
Alloaromadendrene (%)	0.1–0.2	Leaves	[65]
Apiole (%)	0.3–2.9	Leaves	[65]
Bicyclogermacrene (%)	0.6–1.0	Leaves and flowering parts	[64,65]
α-bisabolol (%)	0.05–0.7	Leaves and flowering parts	[64,65]
β-bourbonene (%)	0.2	Leaves and flowering parts	[64]
Borneol (%)	0.05	Leaves and flowering parts	[64]
Bornyl acetate (%)	0.05	Leaves and flowering parts	[64]
α-cadinol + elemicin (%)	0.4	Leaves and flowering parts	[64]
T-cadinol (%)	0.2	Leaves and flowering parts	[64]
Camphene (%)	0.3–2.7	Leaves and flowering parts	[64,65]
δ-cadinene (%)	0.05–1.8	Leaves and flowering parts	[64,65]
γ-cadinene (%)	1.0	Leaves and flowering parts	[64]
δ-3-carene (%)	0.4–10.1	Leaves and flowering parts	[64,65]
β-caryophyllene (%)	0.6–1.1	Leaves and flowering parts	[64,65]
β-caryophyllene oxide (%)	0.2	Leaves and flowering plants	[64]
Caryophyllene oxide (%)	0.05–0.1	Leaves	[65]
trans-carveol (%)	0.05	Leaves and flowering plants	[64]
α-copaene (%)	0.4–2.9	Leaves and flowering plants	[64,65]
α-cubebene (%)	0.4	Leaves and flowering plants	[64]
β-cubebene (%)	0.1–0.6	Leaves	[65]
p-cymen-8-ol (%)	0.05–0.7	Leaves	[65]
p-cymene (%)	0.5–2.9	Leaves and flowering parts	[64,65]
trans-dec-2-enal (%)	0.05	Leaves and flowering parts	[64]
Dill apiole (%)	0.6–3.8	Leaves	[65]
trans-β-farnesene (%)	0.05	Leaves and flowering parts	[64]
Geranial (%)	0.2–1.2	Leaves	[65]
Geraniol (%)	0.1–0.2	Leaves	[65]
Geranyl acetate (%)	0.05–0.5	Leaves	[65]
Germacrene-B (%)	0.2	Leaves and flowering parts	[64]
Germacrene-D (%)	0.05–17.9	Leaves and flowering parts	[64,65]
Heptanal (%)	0.05	Leaves and flowering parts	[64]
trans-hex-2-enal (%)	0.05	Leaves and flowering parts	[64]
3-hexenol (%)	0.05–2.2	Leaves	[65]
α-humulene (%)	0.05–1.6	Leaves and flowering parts	[64,65]
α-humulene-1,2-epoxide (%)	0.05	Leaves and flowering plants	[64]
Isoamyl isovalerate (%)	0.05–0.2	Leaves	[65]
Limonene (%)	2.4–15.7	Leaves and flowering parts	[64,65]
Linalool (%)	0.05–0.9	Leaves and flowering parts	[64,65]
Linalyl acetate (%)	0.05	Leaves and flowering parts	[64]
p-menth-2-en-1-ol (%)	0.05	Leaves	[65]
trans-p-menth-2-en-1-ol (%)	0.05	Leaves and flowering parts	[64]
2-methylpent-2-enoic acid (%)	0.05	Leaves and flowering plants	[64]
3-methylbutyl 2-methylbutyrate (%)	0.05	Leaves and flowering plants	[64]
T-muurolol (%)	0.6	Leaves and flowering parts	[64]
Myrcene (%)	3.6–16.4	Leaves and flowering plants	[64,65]
Myristicin (%)	4.5	Leaves and flowering plants	[64]
Neral (%)	0.05–1.1	Leaves	[65]
trans-nerolidol (%)	0.8	Leaves and flowering plants	[64]
Nonan-2-one (%)	0.05	Leaves and flowering plants	[64]
cis-β-ocimene (%)	2.0	Leaves and flowering plants	[64,65]
(E)-β-ocimene (%)	1.0–6.3	Leaves	[65]
trans-β-ocimene (%)	4.0	Leaves and flowering plants	[64,65]
(Z)-β-ocimene (%)	7.1–19.8	Leaves	[65]
Octanal (%)	0.2	Leaves and flowering plants	[64]
2-pentylfuran (%)	0.05	Leaves and flowering parts	[64]
α-phellandrene (%)	0.05–1.3	Leaves	[65]
β-phellandrene (%)	0.4–10.8	Leaves and flowering parts	[64,65]
α-pinene (%)	1.8–22.2	Leaves and flowering parts	[64,65]
β-pinene (%)	0.05–7.4	Leaves and flowering parts	[64,65]
trans-pinocarveol (%)	0.1	Leaves and flowering parts	[64]
trans-piperitol (%)	0.05	Leaves and flowering parts	[64]
Sabinene (%)	5.3–30.0	Leaves and flowering parts	[64,65]
cis-sabinene hydrate (%)	0.05–0.2	Leaves and flowering parts	[64,65]
trans-sabinene hydrate (%)	0.05	Leaves and flowering parts	[64]
Spathulenol (%)	0.1–0.4	Leaves and flowering parts	[64,65]
Terpinen-4-ol (%)	0.05–3.8	Leaves and flowering parts	[64,65]
α-terpineol (%)	1.9–4.3	Leaves	[65]
Terpinolene (%)	0.4–2.0	Leaves and flowering parts	[64,65]

(Contd...)

Table 2: *(Continued)*

Phytochemical composition	Values	Plant parts	References
α-terpinene (%)	0.2–0.9	Leaves and flowering parts	[64,65]
γ-terpinene (%)	0.05–3.0	Leaves and flowering plants	[64,65]
α-thujene (%)	0.1	Leaves and flowering plants	[64,65]
Torreyol (%)	0.05	Leaves and flowering plants	[64]
trans-sabinene hydrate (%)	0.05–0.2	Leaves	[65]
Tricyclene (%)	0.05	Leaves and flowering plants	[64]
cis-verbenol (%)	0.1	Leaves and flowering plants	[64]
trans-verbenol	0.05	Leaves and flowering parts	[64]
Total flavonoid content (mg QE/g)	275.5±5.0	Leaves	[67]
Total phenolic content (mg gallic acid equivalent/g)	255.5±4.6	Leaves	[67]

in two different assays. Ethanol and water extracts exhibited activities at concentrations of 2 mg/ml after 2 h and the 7-day incubation periods [68]. Adamu *et al*. [69] evaluated anthelmintic activities of leaf acetone extracts of *H. arborescens* using the egg hatch assay and the larval development test on the helminth, *Haemonchus contortus*. The extracts exhibited activities with median effective concentration (EC_{50}) values of 0.62 mg/ml for the egg hatch assay and EC_{50} value of 0.64 mg/ml in the larval development assay. The extracts resulted in 100% inhibition at concentrations as low as 3.13 mg/ml and the best inhibitory activity was at 0.39 mg/ml with 36.3% inhibition. The activities in the larval development test were generally lower than the egg hatch assay [69]. Adamu *et al*. [70] evaluated the anthelmintic activities of crude, butanol, ethyl acetate, chloroform, and hexane leaf extracts of *H. arborescens* using the egg hatch assay and the larval development test on the helminth, *Haemonchus contortus*. The extracts exhibited activities with EC_{50} values of 0.6 mg/ml to 2.9 mg/ml for the egg hatch assay and EC_{50} values of 0.6 mg/ml to 3.3 mg/ml in the larval development assay [70]. These anthelmintic activities exhibited by *H. arborescens* extracts corroborate the traditional usage of leaves and roots of the species against intestinal worms in Lesotho [35], South Africa [3,6,16,30,36], and Swaziland [11].

Antiarthritic activities

Elisha *et al*. [67] evaluated the antiarthritic activities of acetone leaf extracts of *H. arborescens* using an anti-protein denaturation assay. The extracts exhibited good *in vitro* antiarthritic activities with half maximal inhibitory concentration (IC_{50}) value of 53.8 µg/ml which was comparable to the IC_{50} value of 32.4 µg/ml exhibited by the positive control diclofenac sodium [67]. The promising activities of the extracts support the traditional claims of use of the species as remedies for rheumatism and other chronic inflammatory conditions.

Antibacterial activities

Desta [51] evaluated antibacterial activities of aqueous, dichloromethane, methanol, and petroleum ether milky exudate extracts of *H. arborescens* against *Staphylococcus aureus, Salmonella gallinarum, Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa,* and *Klebsiella pneumoniae* using the agar plate well diffusion method with neomycin as a positive control. Aqueous, dichloromethane, and methanol extracts exhibited activities against *S. aureus, S. gallinarum, E. coli,* and *P. aeruginosa*, with the zone of inhibition exhibited by the aqueous extract against *S. aureus* greater than that of neomycin, the standard antibiotic [51]. Deans *et al*. [66] evaluated antibacterial activities of the essential oil isolated from *H. arborescens* against 25 bacterial species. The essential oil exhibited activities against all tested microbes with zone of inhibition ranging from 4.0 mm to 15.3 mm [66]. McGaw *et al*. [68] evaluated antibacterial activities of hexane, ethanol, and waterleaf extracts of *H. arborescens* against *Bacillus subtilis, S. aureus, E. coli,* and *Klebsiella pneumoniae* using the disc diffusion assay and microdilution assay. Only ethanol extract exhibited activities with minimum inhibitory concentration (MIC) value of 0.78 mg/ml [68]. Nkomo and Kambizi [47] also evaluated the antibacterial activities of methanol and water root extracts of *H. arborescens* against *Bacillus cereus, E. coli, K. pneumoniae, Micrococcus kristinae, P. aeruginosa, Serratia marcescens, Shigella flexneri, S. aureus, Staphylococcus epidermidis,* and *Streptococcus faecalis*. The methanolic extracts were active against all the bacterial strains with MIC values ranging from 0.1 mg/ml to 10.0 mg/ml while water extracts were active against *M. kristinae, S. aureus,* and *S. epidermidis* with MIC values ranging from 0.1 mg/ml to 10.0 mg/ml [47]. Adamu *et al*. [71] evaluated the antibacterial activities of the leaf acetone extract of *H. arborescens* against *S. aureus, P. aeruginosa, E. coli,* and *Enterococcus faecalis* using a serial microdilution method with gentamicin as the positive control. The extracts exhibited activities with MIC values ranging from 0.63 mg/ml to 1.25 mg/ml [71]. Adamu *et al*. [70] evaluated antibacterial activities of butanol, ethyl acetate, chloroform, and hexane leaf extracts of *H. arborescens* against *S. aureus, E. faecalis, P. aeruginosa,* and *E. coli* using a serial microplate dilution method with gentamicin as a positive control. The extracts showed activities with MIC values ranging from 0.16 mg/ml to 2.5 mg/ml and gentamicin, the control exhibited MIC value of 0.01 mg/ml [70]. Elisha *et al*. [72] evaluated the antibacterial activities of acetone leaf extracts of *H. arborescens* against *Bacillus anthracis* Sterne strain using the microplate serial dilution method with gentamicin as a positive control. The extracts exhibited activities with MIC value of 0.2 mg/ml and total antibacterial activity of 163 ml/g [72]. Elisha *et al*. [73] evaluated the antibacterial activities of acetone leaf extracts of *H. arborescens* against *S. aureus, E. faecalis, B. cereus, E. coli, Salmonella typhimurium,* and *P. aeruginosa* using a microplate serial dilution technique with gentamicin as the positive control. The extracts exhibited activities with MIC values ranging from 0.16 mg/ml to 0.52 mg/ml [73]. Elisha *et al*. [74] evaluated the antibacterial activities of acetone leaf extracts of *H. arborescens* against *Stenotrophomonas maltophilia, K. pneumoniae, Salmonella serotype Typhimurium, Proteus mirabilis, Enterobacter cloacae,* and *E. coli* using a serial microdilution method with gentamicin as a positive control. The extract exhibited activities with MIC values ranging from 0.08 mg/ml to 0.31 mg/ml and total antibacterial activity values ranging from 84.0 ml/g to 325.4 ml/g [74]. These antibacterial activities exhibited by extracts of *H. arborescens* support the traditional usage of the species as remedy for diseases caused by bacterial pathogens such as boils [40], dysentery [3,6,32,36], gonorrhea [51], skin infections [39], and stomach problems [6,16,46].

Antimycobacterial activities

Madikizela and McGaw [75] evaluated the antimycobacterial activities of aqueous, acetone, and ethanol leaf extracts of *H. arborescens* against *Mycobacterium aurum, Mycobacterium bovis, M. bovis* BCG, *Mycobacterium gordonae, Mycobacterium fortuitum, Mycobacterium smegmatis, Mycobacterium tuberculosis,* and *M. tuberculosis* H37RV using a microdilution method. The extracts showed activities against tested pathogens with MIC values ranging from 0.08 mg/ml to 5.0 mg/ml [75]. These antimycobacterial activities exhibited by *H. arborescens* extracts corroborate medicinal usage of the species as herbal medicine for tuberculosis in both humans and animals [3,30,37,59].

Antifungal activities

Research by Villegas *et al*. [61] revealed that the petroleum ether leaf extract of *H. arborescens* was fungicidal in a TLC bioassay for *Cladosporium cucumerium*. The two compounds, falcarindiol and sarisan isolated from the leaves of *H. arborescens* were active to a concentration

of 0.5 µg in *C. cucumerium* bioassay [61]. Desta [51] evaluated antifungal activities of aqueous, dichloromethane, methanol, and petroleum ether milky exudate extracts of *H. arborescens* against *Candida albicans* using the agar plate well diffusion method with nystatin as a positive control. The aqueous and methanol extracts showed weak-to-moderate activities with zone of inhibition smaller than that exhibited by nystatin [51]. Deans *et al*. [66] evaluated antifungal activities of the essential oil isolated from *H. arborescens* against *Aspergillus flavus, Aspergillus niger, Aspergillus ochraceus,* and *Aspergillus parasiticus*. The essential oil exhibited activities against all tested microbes [66]. Nkomo and Kambizi [47] evaluated the antifungal activities of methanol and water root extracts of *H. arborescens* against *Aspergillus flavus, A. niger, C. albicans,* and *Penicillium notatum*. Both extracts did not show any activities against *C. albicans*, but extracts exhibited activities against *P. notatum, A. flavus,* and *A. niger* with medium lethal concentration (LC_{50}) values ranging from 0.1 to 3.2 [47]. Adamu *et al*. [76] evaluated antifungal activities of acetone leaf extracts of *H. arborescens* against *Aspergillus fumigatus, Cryptococcus neoformans,* and *C. albicans* using the serial microplate dilution method. The extracts exhibited activities with MIC values ranging from 0.16 mg/mL to 1.25 mg/mL [76]. Adamu *et al*. [70] evaluated antifungal activities of crude, butanol, ethyl acetate, chloroform, and hexane leaf extracts of *H. arborescens* against *C. albicans, Candida neoformans,* and *Aspergillus fumigatus* using the serial microplate dilution method with amphotericin B as a positive control. The extracts showed activities with MIC values ranging from 0.08 mg/ml to 2.5 mg/ml and amphotericin B, the control exhibited MIC value of 0.01 mg/ml [70].These antifungal activities exhibited by *H. arborescens* extracts validate the traditional use of the species against fungal infections and ringworm in South Africa and Tanzania [33,42].

Antiviral activities

Beuscher *et al*. [77] evaluated the antiviral activities of dichloromethane, ethanol, and methanol root bark extracts of *H. arborescens* against poliovirus, herpes simplex virus, and rhinovirus using the plaque reduction assays. The ethanol and methanol extracts showed activities against poliovirus at a concentration range of 10 µg/ml to 50 µg/ml while dichloromethane extract showed activities against rhinovirus at a concentration range of 25 µg/ml–50 µg/ml [77].

Anti-inflammatory activities

Recio *et al*. [78] evaluated anti-inflammatory activities of methanol leaf and ethanol stem bark extracts of *H. arborescens* by administering extracts topically on tetradecanoylphorbol acetate (TPA)-induced mouse ear edema and orally on carrageenan-induced mouse paw edema. The leaf and stem bark extracts were active when assayed topically (ear edema test) showing a percentage reduction in edema of 64% and 77%, respectively. 3 h after carrageenan injection, the methanol leaf extracts showed anti-inflammatory activities with a percent reduction in edema of 44% [78]. Similarly, Recio *et al*. [62] evaluated anti-inflammatory activities of two saikosaponins isolated from methanol extracts of *H. arborescens* leaves, 16β,23-dihydroxy-13,28-epoxyolean-11-en-3β-yl-[β-D-glucopyranosyl (1→2)]-[β-D-glucopyranosyl (1→3)]-β-D-fucopyranoside and 16β,23,28-trihydroxy-11α-methoxyolean-12-en-3β-yl-[β-D-glucopyranosyl (1→2)]-[β-D-glucopyranosyl (1→3)]-β-D-fucopyranoside using TPA-induced mouse ear edema assay, ethylphenylpropiolate (EPP) mouse ear edema, the serotonin paw edema, and carrageenan paw edema tests. The compound 16β,23-dihydroxy-13,28-epoxyolean-11-en-3β-yl-[β-D-glucopyranosyl (1→2)]-[β-D-glucopyranosyl (1→3)]-β-D-fucopyranoside showed activity in the TPA, EPP, and the serotonin paw edema tests, whereas 16β,23,28-trihydroxy-11α-methoxyolean-12-en-3β-yl-[β-D-glucopyranosyl (1→2)]-[β-D-glucopyranosyl (1→3)]-β-D-fucopyranoside was active only in the mouse ear edema model. Both compounds had only a slight effect against a carrageenan paw edema model [62]. McGaw *et al*. [41] assessed anti-inflammatory activities of aqueous and ethanol leaf extracts of *H. arborescens* by evaluating the presence of prostaglandin synthesis inhibitors using the cyclooxygenase-1 (COX-1) assay. An ethanolic extract exhibited good COX-1 inhibitory activities (85–88%), whereas water extract was less active (32–75%) in comparison to 75% inhibitory activity exhibited by the standard indomethacin (0.5 µg) [41]. Lundgaard *et al*. [32] evaluated the COX-1 inhibition activities of acetone, aqueous, dichloromethane, ethyl acetate, methanol, and petroleum ether root, bark, and leaf extracts of *H. arborescens* using the COX-1 assay. The organic extracts of roots had good activities, the petroleum ether extract of the twigs also had high inhibitory activities, while the leaves, in general, did not show much activity and water extracts of all the three plant parts were inactive [32]. Nkomo *et al*. [79] evaluated the anti-inflammatory activities of aqueous and methanol root extracts of *H. arborescens* using inflammatory pain assay, the albumin-induced hind paw edema model, and the carrageenan-induced hind paw edema model. Both extracts produced a significant reduction of edema induced by albumin and carrageenan [79]. Elisha *et al*. [67] evaluated the anti-inflammatory activities of acetone leaf extracts of *H. arborescens* by determining the inhibition of nitric oxide production in lipopolysaccharide-activated RAW 264.7 macrophages as well as 15-lipoxygenase enzyme inhibition. The extracts inhibited nitric oxide production in a dose-dependent manner in the LPS-stimulated RAW 264.7 macrophages with *H. arborescens* inhibiting NO production by 89.5% at a concentration of 30 µg/ml. The extract exhibited weak activities against 15-lipoxygenase activity with IC_{50} value of 85.0 µg/ml which was higher than IC_{50} value of 53.7 µg/ml exhibited by the positive control quercetin [67]. These findings seem to justify the use of the plant in traditional medicine in the management of pain and inflammation-related diseases such as painful joints, rheumatism, abdominal, back, and general body pains [3-6,11,29-32].

Antinociceptive activities

Nkomo *et al*. [79] evaluated the antinociceptive activities of aqueous and methanol root extracts of *H. arborescens* using the hot plate, abdominal constriction, and formalin tests. Both extracts produced significant inhibition of thermal nociception induced by a hot plate. On chemical nociception induced by intraperitoneal acetic acid and subplantar formalin injection, both extracts significantly decreased the number of writhing episodes and the licking time in a dose-dependent manner. Treatment with the extracts at the same doses produced a significant pain inhibition of the carrageenan-induced inflammatory pain [79]. These findings seem to justify the use of the plant in traditional medicine in the management of pain and inflammation-related diseases.

Antioxidant activities

Adamu *et al*. [71] evaluated the antioxidant activities of the leaf acetone extract of *H. arborescens* using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2′-azino-bis (3-ethyl-benzthiazoline-6-sulfonic acid) radical scavenging assays. The extract exhibited trolox equivalent antioxidant capacity (TEAC) value of 0.2 and EC_{50} value of 4.4 using ABTS and DPPH, respectively [71]. Elisha *et al*. [67] evaluated the antioxidant activities of acetone leaf extracts of *H. arborescens* using the DPPH and ABTS radical scavenging assays and ferric reducing antioxidant power (FRAP) assay. The extracts showed weak antioxidant activity with IC_{50} value of 154.8 µg/ml which was much higher than IC_{50} values of 3.3 µg/ml and 5.6 µg/ml exhibited by ascorbic acid and trolox, respectively, the two positive controls. The IC_{50} values for ABTS assay were 95.7 µg/ml with ascorbic acid and trolox exhibiting IC_{50} values of 2.9 µg/ml and 6.8 µg/ml, respectively. The TEAC and FRAP values were 0.07 and 0.06, respectively [67].

Anti-peptic ulcer activities

Osim *et al*. [80] evaluated the effects of *H. arborescens* aqueous root bark extract on acetic acid-induced ulcers, food intake, water intake, weight gain, and gastric acid secretion in female Sprague-Dawley rats. Following consumption of the extract, food intake, daily water intake, and weekly weight gain were not significantly different in the test and control groups. The extract had no significant effect on gastric acid secretion stimulated by histamine, gastrin, and carbachol. However, histological examination revealed traces of ulcer at the sites where ulcers were induced previously. Osim *et al*. [80] concluded that *H. arborescens* accelerates the healing of acetic acid-induced peptic ulcer in rats. These findings validate the use of *H. arborescens* in the treatment of peptic ulcer in humans in Kenya [56] and Zimbabwe [57].

Anti-scabies activities

Heyndrickx *et al*. [38] evaluated anti-scabies activities of chloroform, ethanol, hexane, and waterleaf extracts of *H. arborescens* against the larvae, nymphae, and adult Psoroptes cuniculi with lindane as a positive control. Only chloroform extract at a concentration of 1 μgcm^2 exhibited 100% morality and the control, lindane also showed 100% morality [38]. These findings corroborate the traditional usage of *H. arborescens* leaves as herbal medicines against scabies in Rwanda [38].

Antispasmodic activities

Parry *et al*. [56] investigated the antispasmodic activities of aqueous root bark extract of *H. arborescens* on various smooth gastrointestinal muscle preparations performed on the isolated guinea pig ileum preparation. The extract had no contractile or relaxant effect on guinea pig gastrointestinal smooth muscle, trachea, and tenia coli nor did it affect the spontaneously beating atrium. However, the extract antagonized ileal contractions induced by acetylcholine, histamine, serotonin, and potassium chloride in a concentration-dependent manner. The extracts antagonize the effects of various agonists by either preventing calcium influx into the smooth muscle cell or inhibiting the calcium-induced calcium release mechanism or preventing the release of calcium from the sarcoplasmic reticulum or by preventing the binding of calcium to calmodulin [56]. These findings could explain its rational use in traditional medicine to alleviate abdominal spasms.

Uterotonic activities

Katerere and Parry [81] evaluated the uterotonic activities of aqueous root bark extract of *H. arborescens* on Sprague-Dawley rat uterine and skeletal muscles. The extract contracted the rat uterus and the contractions were not antagonized by atropine but were blocked by both cyproheptadine and verapamil. The extract also induced a contracture of the rat diaphragm muscle in the presence of alcuronium. The contractile effects on the uterus appear to involve stimulation of serotonin HT_2 receptors, leading to an increase in calcium influx into the smooth muscle cell [81].

Cytotoxicity activities

Adamu *et al*. [69] evaluated cytotoxicity activities of leaf acetone extracts of *H. arborescens* using the 3-5-dimethyl thiazol-2-yl-2, 5-diphenyl tetrazolium bromide (MTT) cellular assay. The extracts exhibited moderate toxicity with LC_{50} value of 0.04 mg/ml and selectivity index value of 0.07 [69]. Adamu *et al*. [70] evaluated cytotoxicity activities of crude, butanol, ethyl acetate, chloroform, and hexane leaf extracts of *H. arborescens* using the MTT assay on Vero cells with berberine chloride (Sigma) as a positive control. The EC_{50} values exhibited by the extracts ranged from 0.04 mg/ml to 2.1 mg/ml [70]. Elisha *et al*. [73] evaluated the cytotoxicity activities of acetone leaf extracts of *H. arborescens* on Vero kidney cells using the MTT reduction assay with doxorubicin as a positive control. The extract was non-toxic with LC_{50} value of 81.0 μg/ml which was much higher than LC_{50} value of 8.3 μg/ml exhibited by the control doxorubicin [73]. Elisha *et al*. [74] evaluated the cytotoxicity activities of acetone leaf extracts of *H. arborescens* using the MTT assay on Vero cells with doxorubicin as a positive control. The extracts exhibited LC_{50} value of 81.0 μg/ml and therefore considered to be non-toxic in comparison to the reference drug doxorubicin which exhibited LC_{50} value of 8.3 μg/ml [74]. Madikizela and McGaw [63] evaluated the cytotoxicity activities of aqueous and ethanol leaf extracts of *H. arborescens* against Vero monkey kidney and bovine dermis cells using the MTT assay. The tested extracts were non-cytotoxic against both Vero and bovine dermis cells with LC_{50} values ranging from 0.9 mg/ml to 5.6 mg/ml, and the selectivity index values ranging from 1.3 to 69.9 [63].

Genotoxicity activities

Madikizela and McGaw [75] evaluated the genotoxicity activities of aqueous, acetone, and ethanol leaf extracts of *H. arborescens* against *Salmonella typhimurium* TA98 and TA100. The ethanol extracts showed clear mutagenicity against TA100 with numbers of revertant colonies greater than twice that of the negative controls for the 5 mg/ml, the highest concentration tested, however, decreasing with decreasing concentrations of extracts [75].

CONCLUSION

H. arborescens is an important medicinal plant species throughout its distributional range in tropical Africa. The pharmacological evaluations carried so far, corroborate some of the documented medicinal uses of the species. There are still research gaps regarding phytochemistry of the species and it, therefore, seems premature to draw firm conclusions about the alleged therapeutic effects of *H. arborescens*. Previous research by Maroyi [82] and Zaidi *et al*. [83] revealed that the development of pharmaceutical drugs and health-promoting products from herbal medicines is a complicated process. Therefore, more detailed research is needed aimed at assessing several plant parts of the species used as traditional medicines, evaluating their chemical compounds, biological, and toxicological activities. Detailed clinical trials are also required aimed at evaluating the efficacy of crude extracts of *H. arborescens* or compounds isolated from the species.

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AUTHOR'S CONTRIBUTION

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

CONFLICTS OF INTEREST

The author declares that there are no conflicts of interest regarding the publication of this paper.

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