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, antinociceptive, antioxidant, antipeptic ulcer, anti-scaries, antispasmodic, antiviral, cytotoxicity, genotoxicity, and utoerotonic 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.

© 2018 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/) DOI: http://dx.doi.org/10.22159/ajpcr.2018.v11i11.29108

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 suffrutesces. The genus consists of seven species restricted to temperate and subtropical Africa and southern Yemen [12]. Calvão 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 *Poelmanniopsis* 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. trifoliata* 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)
Asian J Pharm Clin Res, Vol 11, Issue 11, 2018, 75-82

Maroyi

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. [29].

PHOTOCHEMISTRY 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-11a-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, germaacene-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].

Table 1: Medicinal uses of Heteromorpha arborescens in tropical Africa

| Medicinal use                          | Parts of the plant used           | Country                                                                 | References |
|----------------------------------------|-----------------------------------|-------------------------------------------------------------------------|------------|
| Inflammation and pain (painful joints, | Bark, leaves, and roots           | Malawi, South Africa, Swaziland, and Zimbabwe                           | [3-6,11,29-32] |
| rheumatism, abdominal, general body,   |                                    |                                                                         |            |
| and back pains)                        |                                    |                                                                         |            |
| Aphrodisiac                            | Roots and root bark                | Botswana, Malawi, Mozambique, South Africa, and Zimbabwe                 | [3,4,33]   |
| Respiratory problems (asthma, chest    | Leaves and roots                   | Kenya, Lesotho, South Africa, and Zimbabwe                              | [3-6,16,30,32,34-37] |
| pains, coughs, and tuberculosis)       |                                    |                                                                         |            |
| Blood purifier                         | Leaves and roots                   | South Africa                                                            | [3,16]     |
| Purifying blood                         |                                    |                                                                         | [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]        |
| Contraceptive                          | Bark and leaves                    | South Africa                                                            | [3,6,32]   |
| 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                              | Malawi, South Africa, Uganda, Tanzania                                 | [4,6,16,32,36,48-50] |
| Fever and malaria                      | Bark and leaves and roots          | Tanzania                                                                | [42]       |
| Fungal infections                      | Roots                              | Eritrea, Kenya, Lesotho, South Africa, Swaziland, and Zimbabwe           | [3-6,11,16,29,31,32-34,36,45,46,52,53] |
| Gonorrhea                              | Milky exudate                      | Ethiopia                                                                | [51]       |
| Headache                               | Bark, charcoal, leaves, and roots  | Botswana, South Africa, Swaziland, and Zimbabwe                          | [44]       |
| Heart problems                         | Roots                              | Zimbabwe                                                                | [33]       |
| Induce appetite                        | Roots                              | Zimbabwe                                                                | [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                                              | [3,6,11,33] |
| 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 vermiﬁge) | Bark | South Africa | [3,5,60] |

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].

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.
| Phytochemical composition       | Values      | Plant parts                              | References |
|--------------------------------|-------------|------------------------------------------|------------|
| Acetic acid (%)                | 0.1         | Leaves and flowering parts               | [64]       |
| Alloaromadendrene (%)          | 0.1–0.2     | Leaves                                  | [65]       |
| Apiole (%)                     | 0.3–2.9     | Leaves                                  | [65]       |
| Bicyclgermacrene (%)           | 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-δ-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]    |
| δ-cadinene (%)                 | 0.4         | Leaves and flowering plants              | [64]       |
| δ-δ-carene (%)                 | 0.05–0.6    | Leaves                                  | [65]       |
| trans-carveol (%)              | 0.05        | Leaves and flowering plants              | [64]       |
| p-cymen-8-ol (%)               | 0.05–0.7    | Leaves                                  | [65]       |
| p-cymene (%)                   | 0.5–2.9     | Leaves and flowering plants              | [64,65]    |
| trans-dec-2-enal (%)           | 0.05        | Leaves and flowering plants              | [64]       |
| Dill apiolene (%)              | 0.6–3.8     | Leaves                                  | [65]       |
| trans-β-farnesene (%)          | 0.05        | Leaves and flowering plants              | [64]       |
| Geraniol (%)                   | 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 plants              | [64,65]    |
| α-humulene 1,2-epoxide (%)     | 0.05        | Leaves and flowering plants              | [64]       |
| Isoamyloisovalerate (%)        | 0.05–0.2    | Leaves                                  | [65]       |
| Limonene (%)                   | 2.4–15.7    | Leaves and flowering plants              | [64,65]    |
| Linalool (%)                   | 0.05–0.9    | Leaves and flowering plants              | [64,65]    |
| Linalyl acetate (%)            | 0.05        | Leaves and flowering plants              | [64]       |
| p-menth-2-en-1-ol (%)          | 0.05        | Leaves                                  | [65]       |
| trans-p-menth-2-en-1-ol (%)    | 0.05        | Leaves and flowering plants              | [64]       |
| 2-methylpent-2-enolic 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 plants              | [65]       |
| 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-norololid (%)            | 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]       |
| α-phellandrene (%)             | 0.05–1.3    | Leaves                                  | [65]       |
| β-phellandrene (%)             | 0.4–10.8    | Leaves and flowering plants              | [64,65]    |
| α-pinene (%)                   | 1.8–22.2    | Leaves and flowering plants              | [64,65]    |
| β-pinene (%)                   | 0.05–7.4    | Leaves and flowering plants              | [64,65]    |
| trans-pinocarveol (%)          | 0.1         | Leaves and flowering plants              | [64]       |
| trans-piperitol (%)            | 0.05        | Leaves and flowering plants              | [64]       |
| Sabicin (%)                    | 5.3–30.0    | Leaves and flowering plants              | [64,65]    |
| cis-sabinene hydrate (%)       | 0.05–0.2    | Leaves and flowering plants              | [64,65]    |
| trans-sabinene hydrate (%)     | 0.05        | Leaves and flowering plants              | [64]       |
| Spathulenol (%)                | 0.1–0.4     | Leaves and flowering plants              | [64,65]    |
| Terpinen-4-ol (%)              | 0.05–1.8    | Leaves and flowering plants              | [64]       |
| α-terpineol (%)                | 1.9–4.3     | Leaves                                  | [65]       |
| Terpinolene (%)                | 0.4–2.0     | Leaves and flowering plants              | [64,65]    |

(Contd...)
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 helmint, *Haemonchus contortus*. The extracts exhibited activities with median effective concentration (EC₅₀) values of 0.62 mg/ml for the egg hatch assay and EC₅₀ value of 0.64 mg/ml in the larval development assay. The results 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 helmint, *Haemonchus contortus*. The extracts exhibited activities with EC₅₀ values of 0.6 mg/ml to 2.9 mg/ml for the egg hatch assay and EC₅₀ 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 (IC₅₀) value of 53.8 µg/ml which was comparable to the IC₅₀ 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 µg/ml [68]. Nkomo and Kambiri [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. kristine*, *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 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 µl/g to 325.4 µl/g [74]. These antibacterial activities exhibited by extracts of *H. arborescens* support the traditional usage of the species as remedies for 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 *Caldosporium cucumerinum*. The two compounds, falcarioindol and pramisan, isolated from the leaves of *H. arborescens* were active to a concentration

---

**Table 2: (Continued)**

| Phytochemical composition | Values | Plant parts | References |
|---------------------------|--------|-------------|------------|
| α-terpine in (%)          | 0.2−0.9| Leaves and flowering parts | [64,65] |
| γ-terpine in (%)          | 0.05−3.0| Leaves and flowering plants | [64,65] |
| α-thujene in (%)          | 0.1    | Leaves and flowering plants | [64,65] |
| Torreyol (%)              | 0.05   | Leaves | [65] |
| trans-sabinene hydrate (%)| 0.05−0.2| Leaves and flowering plants | [64] |
| Tricylene (%)             | 0.05   | Leaves and flowering plants | [64] |
| cis-verbenol (%)          | 0.1    | Leaves and flowering plants | [64] |
| trans-verbenol (%)        | 0.05   | Leaves and flowering plants | [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] |
of 0.5 µg in C. cuniculatum 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 flavius, 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 flavius, 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. flavius, and A. niger with medium lethal concentration (IC₅₀) values ranging from 0.1 to 3.2 [47]. Adamu et al. [70] evaluated antifungal activities of acetic 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
Beucher 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 percent 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-epoxyoalan-11-en-3β-yl-[β-D-glucopyranosyl (1→2)]-[β-D-glucopyranosyl (1→3)]-β-D-fucopyranoside and 16β,23,28-trihydroxy-11α-methoxyoalan-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-epoxyoalan-11-en-3β-yl-[β-D-glucopyranosyl (1→2)]-[β-D-glucopyranosyl (1→3)]-β-D-fucopyranoside showed activity in the TPA and the serotonin paw edema tests, whereas 16β,23,28-trihydroxy-11α-methoxyoalan-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 lipopoly saccharide-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 IC₅₀ value of 8.50 µg/ml which was higher than IC₅₀ 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-picyrylhydrazyl (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 EC₅₀ 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 IC₅₀ value of 154.8 µg/ml which was much higher than IC₅₀ values of 33.3 µg/ml and 5.6 µg/ml exhibited by ascorbic acid and trolox, respectively, the two positive controls. The IC₅₀ values for ABTS assay were 95.7 µg/ml with ascorbic acid and trolox exhibiting IC₅₀ 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 carbamol. 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, nymphs, and adult *Psoroptes cuniculi* with lindane as a positive control. Only chloroform extract at a concentration of 1 μg/ml exhibited 100% morality and the control, lindane also showed 100% mortality [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 extract antagonizes 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 contraction of the rat diaphragm muscle in the presence of alcuronium. The contractile effects on the uterus appear to involve stimulation of serotonin HT₁ 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-(4,5-dimethyl thiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) cellular assay. The extracts exhibited moderate toxicity with LC₅₀ 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 EC₅₀ 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 extracts exhibited non-toxicity against both Vero and bovine dermis cells with the MTT assay. The extracts exhibited LC₅₀ value of 81.0 μg/ml which was much higher than LC₅₀ 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 LC₅₀ value of 81.0 μg/ml and therefore considered to be non-toxic in comparison to the reference drug doxorubicin in which exhibited LC₅₀ value of 8.3 μg/ml [74]. Madikizela and McGaw [62] 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 LC₅₀ 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.

ACKNOWLEDGMENTS

The author would like to express his gratitude to the National Research Foundation (NRF), South Africa and Govan Mbeki Research and Development Centre (GMRDC), University of Fort Hare for financial support to conduct this study.

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.

REFERENCES

1. Van Wyk BE. A review of African medicinal and aromatic plants. In: Nefdti M, Najia H, Máthé A, editors. Medicinal and Aromatic Plants of the World: Africa. Dordrecht: Springer; 2017. p. 19-60.
2. Van Wyk BE. The potential of South African plants in the development of new medicinal products. S Afr J Bot 2011;77:812-29.
3. Watt JM, Breyer-Brandwijk MG. The Medicinal and Poisonous Plants of Southern and Eastern Africa. Edinburgh: E and S Livingstone Ltd.; 1962.
4. Gelfand M, Mavi S, Drummond RB, Ndemera B. The Traditional Medical Practitioner in Zimbabwe: His Principles of Practice and Pharmacopoeia. Gweru: Manbo Press; 1985.
5. Hutchings A, Scott AH, Lewis G, Cunningham AB. Zulu Medicinal Plants: An Inventory. Pietermaritzburg: University of Natal Press; 1996.
6. Van Wyk BE, Van Oudshoorn B, Gericie N. Medicinal Plants of South Africa. Pretoria: Briza Publications; 2013.
7. Setshogo MP, Mberekci CM. Floristic diversity and uses of medicinal plants sold by street vendor in Gaborone, Botswana. Afr J Pl Sci 2011;5:69-74.
8. Meke GS, Mumba RF, BwanaI RJ, Williams VL. The trade and marketing of traditional medicines in Southern and Central Malawi. Int J Sustain Dev World Ecol 2017;24:73-87.
9. Botha J, Weiersbye IM. Ethnobotany and use of plants on mine properties in the Witwatersrand basin gold fields, South Africa. In: Fournie A, Tibbett M, Wiertz J, editors. Mine Closure. Perth: Australian Centre for Geomechanics; 2010. p. 325-42.
10. Bussmann RW. Ethnobotany of the samburu of Mt. Nyiru, South Turkana, Kenya. J Ethnobiol Ethnomed 2006;2:35.
11. Long C. Swaziland's Flora: SiSwati Names and uses. Swaziland: Swazi Centre for Geomechanics; 2010. p. 325-42.
12. Naftali M, Najia H, Máthé A, editors. Medicinal and Aromatic Plants of the World: Africa. Dordrecht: Springer; 2017. p. 19-60.
13. Calvillo CI, Tilney PM, Wyk BE, Downing SR. A molecular phylogenetic study of Southern African Apiaceae. Am J Bot 2006;93:1828-47.
14. Van Wyk AE, Van Wyk P. Field Guide to Trees of Southern Africa. Cape Town: Struik Publishers (Pty) Ltd.; 1997.
15. Neffati M, Najia H, Máthé A, editors. Medicinal and Aromatic Plants of the World: Africa. Dordrecht: Springer; 2017. p. 19-60.
16. Palgrave MC. Keith Coates Palgrave Trees of Southern Africa. 3rd ed. Cape Town: Struik Publishers (Pty) Ltd.; 2002.
17. Schmidt E, Lotter M, McCleland W. Trees and Shrubs of Mpumalanga and Kruger National Park. Johannesburg: Jacana; 2002.
18. Cannon JF. Umbelliferae. Conspectus Fl Angol 1970;4:340-3.
18. Cannon JF. Umbelliferae. In: Launert IE, editor. Flora Zambesiaca 4. London: Flora Zambesiaca Managing Committee; 1978. p. 578-81.
19. Townsend CC. Some notes on species of Heteromorpha (Umbelliferae). Kew Bull 1985;40:843-50.
20. Townsend CC. Umbelliferae. In: Polhill RM, editor. Flora of Tropical East Africa. Rotterdam: A.A. Balkema; 1989. p. 37-41.
21. Winter PJ, Van Wyk BE, Tilney PM. The morphology and development of the fruit of Heteromorpha (Apiaceae). S Afr J Bot 1993;59:336-41.
22. Winter PJ, Van Wyk BE. The taxonomic value of epidermal characters in the leaf of Heteromorpha and some related genera (Apiaceae). Bothalia 1994;24:187-94.
23. Setsibho MP, Venter F. Trees of Botswana: Names and Distribution. Pretoria: Southern African Botanical Diversity Network Report No. 18; 2003.
24. Da Silva MC, Izidine S, Amude AB. A Preliminary Checklist of the Vascular Plants of Mozambique. Pretoria: Southern African Botanical Diversity Network Report No. 30; 2004.
25. Burrows JE, Willis CK. Plants of the Nyika Plateau. Pretoria: Southern African Botanical Diversity Network Report No. 31; 2005.
26. Phiri PSM. A Checklist of Zambian Vascular Plants. Pretoria: Southern African Botanical Diversity Network Report No. 32; 2005.
27. Setsibho MP. Preliminary Checklist of the Plants of Botswana. Pretoria: Southern African Botanical Diversity Network Report No. 33. SABONET, 2005.
28. Hyde MA, Wursten BT, Ballings P, Palgrave CM. Heteromorpha arborescens (Spreng.) Cham. Schltdl. Var. Abyssinica (A. Rich.) H. Wolff. Flora of Zimbabwe: Species Information: Heteromorpha arborescens var. Abyssinica; 2018. Available from: https://www.zimbabweflora.co.zw/speciesdata/species.php?species_id=143100. [Last retrieved on 2018 Apr 21].
29. Arnold HJ, Guluman M. Pharmacopoeia of traditional medicine in Venda. J Ethnopharmacol 1984;12:35-74.
30. Bryant AT. Zulu Medicine and Medicine-Men. Cape Town: C. Struik; 1966.
31. McGaw LJ, Jäger AK, Van Staden J. Prostaglandin synthesis inhibitory activity in zulu, xhosa and sotho medicinal plants. Phytother Res 1997;11:113-7.
32. Lundgaard NH, Prior RM, Light ME, Stafford GI, Van Staden J, Prior RM. The effects of Heteromorpha trifoliata on gastrointestinal smooth muscle of the guinea pig. J Ethnopharmacol 1996;54:13-7.
33. Madikizela B, Kambizi L, McGaw LJ. An ethnobotanical survey of medicinal plants used to treat infectious diseases in the Rungwe district, Tanzania. Afr J Tradit Complement Altern Med 2010;7:253-7.
34. Spencer P. Samburu Notions of Health and Disease, and their Relationship to Inner Cleanliness. SOAS Research Online, No 8764; 2011;1:01-13.
35. Parry O, Duri ZJ, Zinyama E. The effects of Heteromorpha trifoliata on gastrointestinal smooth muscle of the guinea pig. J Ethnopharmacol 1996;54:13-7.
36. Chekole G, Asfaw Z, Kelbessa E. Euthanobital study of medicinal plants in the environs of Tara-gedam and Amba remnant forests of Libo Kemkem district, Northwest Ethiopia. J Ethnobiol Ethnomed 2015;11:44.
37. Gerstner J. A preliminary checklist of Zulu names of plants with short notes. Bantu Stud 1938;12:215-36, 321-42.
38. Adamu M, Bagla VP, Eloff JN. Fractionation of Heteromorpha arborescens from Mozambique. J Ethnopharmacol 2003.
39. Adamu M, Naidoo V, Eloff JN. Efficacy and toxicity of thirteen plant extracts from Heteromorpha arborescens. J Ethnopharmacol 2003.
40. Masika PJ, Van Averbeeck W, Sonandi A. Use of herbal remedies by small scale farmers to treat livestock diseases in central Eastern Cape Province, South Africa. J Safi Vet Assoc 2000;71:87-91.
41. Desta B. Ethiopian traditional herbal drugs. Part II: Antimicrobial activity of 63 medicinal plants. J Ethnopharmacol 1993;39:129-39.
42. Mwangi JW, Achola KJ, Lwande W, Hassanali A, Laurent R. Volatile compounds of antifungal compounds falcarindiol and sarisan from Heteromorpha trifoliata. Planta Med 1998;54:36-7.
43. Recio MD, Just MJ, Giner RM, Danilic M, Rios LR, Horstettmann K. Antibacterial activity in Zulu, Xhosa and Sotho medicinal plants. Phytother Res 1994;7:215-63.
44. Chekole G, Asfaw Z, Kelbessa E. Euthanobital study of medicinal plants in the environs of Tara-gedam and Amba remnant forests of Libo Kemkem district, Northwest Ethiopia. J Ethnobiol Ethnomed 2015;11:44.
45. Arnegardde1.pdf. [Last accessed on 2018 Mar 11].
46. Mwangi JW, Achola KJ, Lwande W, Hassanali A, Laurent R. Volatile components of Heteromorpha trifoliata (Wendl) Eckl. Zey. Flav Fragr J 1999;4:241-3.
47. Chagonda LS, Makanda CD, Chalchat JC. Essential oils of cultivated Heteropyxis natalensis (Harv.) and Cultivated Heteromorpha trifoliata (Wendl) Zey. Flav Fragr J 1999;4:241-3.
48. Deans SG, Kennedy AJ, Gundidza MG, Waterman PG, Gray AI. Antimicrobial activities of the volatile oil of Heteromorpha trifoliata. J Ethnopharmacol 1997;54:259-62.
49. Elisha IL, Dzoyem JP, McGaw LJ, Botha FS, Eloff JN. The anti-arithmetic, anti-inflammatory, antioxidant activity and relationships with total phenolics and total flavonoids of nine South African plants used traditionally to treat arthritis. BMC Complement Altern Med 2016;16:307.
50. Elisha IL, Dzoyem JP, McGaw LJ, Botha FS, Eloff JN. The anti-arithmetic, anti-inflammatory, antioxidant activity and relationships with total phenolics and total flavonoids of nine South African plants used traditionally to treat arthritis. BMC Complement Altern Med 2016;16:307.
51. McGaw LJ, Jäger AK, Van Staden J. Antibacterial, anthelmintic and anti-smoaky activity in Southern African medicinal plants. J Ethnopharmacol 2000;72:247-63.
52. Adamu M, Naidoo V, Eloff JN. Efficacy and toxicity of thirteen plant extracts from Heteromorpha arborescens used in ethnoveterinary medicine in South Africa on egg hatching and larval development of Haemonchus contortus. BMC Vet Res 2013;9:38.
53. Adamu M, Naidoo V, Eloff JN. The antibacterial activity, antioxidant activity and selectivity index of leaf extracts of nine South African tree species used in ethnoveterinary medicine to treat helminth infections. BMC Vet Res 2010;14:50.
54. Elisha IL, Dzoyem JP, Botha FS, Eloff JN. The efficacy and safety of South African medicinal plants in controlling Bacillus anthracis.
sterne vaccine strain. BMC Complement Altern Med 2016;16:5.

73. Elisha IL, Botha FS, McGaw LJ, Eloff JN. The antibacterial activity of extracts of nine plant species with good activity against *Escherichia coli* against five other bacteria and cytotoxicity of extracts. BMC Complement Altern Med 2017;17:133.

74. Elisha IL, Jambalang AR, Botha FS, Buys EM, McGaw LJ, Eloff JN, et al. Potency and selectivity indices of acetone leaf extracts of nine selected South African trees against six opportunistic *Enterobacteriaceae* isolates from commercial chicken eggs. BMC Complement Altern Med 2017;17:90.

75. Madikizela B, McGaw LJ. Scientific rationale for traditional use of plants to treat tuberculosis in the Eastern region of the OR Tambo district, South Africa. J Ethnopharmacol 2018;224:250-60.

76. Adamu M, Naidoo V, Eloff JN. Some Southern African plant species used to treat helminth infections in ethnoveterinary medicine have excellent antifungal activities. BMC Complement Altern Med 2012;12:213.

77. Beuscher N, Bodinet C, Neumann-Haefelin D, Marston A, Horstettmann K. Antiviral activity of African medicinal plants. J Ethnopharmacol 1994;42:101-9.

78. Recio MD, Giner RM, Manez S, Rios JL, Horstettmann K. Screening of tropical plants for anti-inflammatory activity. Phytother Res 1995;9:571-4.

79. Nkomo M, Nkeh-Chungag BN, Kambizi L, Ndebia EJ, Sewani-Rusike C, Iputu JE, et al. Investigation of the antinociceptive and anti-inflammatory properties of *Heteromorpha arborescens* (*Apiaceae*). Afr J Tradit Complement Altern Med 2011;8:412-9.

80. Osim EE, Maredza T, Rao PV, Nhandara B, Adayanju B, et al. *Heteromorpha trifoliata* (*Dombwe*) accelerates acetic acid induced peptic ulcers: A preliminary study in the rats. Cent Afr J Med 1999;45:35-40.

81. Katerere D, Parry O. Pharmacological actions of *Heteromorpha trifoliata* (*“dombwe”*) on rat isolated muscle preparations. Cent Afr J Med 2000;46:9-13.

82. Maroyi A. *Dicoma anomala* son: A review of its botany, ethnomedicine, phytochemistry and pharmacology. Asian J Pharm Clin Res 2018;11:70-7.

83. Zaidi FB, Ahmed S, Makkad M. Role of effective project management in reducing drug development cost. Asian J Pharm Clin Res 2017;10:53-6.