

# A Review of Plants Used in South African Traditional Medicine for the Management and Treatment of Hypertension

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## ABSTRACT

South Africa contains 9% of the world's higher plants, and despite its rich biodiversity, it has one of the highest prevalence of hypertension in Africa. This review provides information on medicinal plants embraced in South Africa for hypertension management, with the aim of reporting pharmacological information on the indigenous use of these plants as antihypertensives. This review not only focuses on the activity of antihypertensive medicinal plants but also reports some of its phytochemical constituents and other ethnopharmacological and therapeutic properties. Information obtained from scientific and or unpublished databases such as Science Direct, PubMed, SciFinder, JSTOR, Google Scholar, Web of Science, and various books revealed 117 documented antihypertensive plant species from 50 families. Interestingly, Asteraceae topped the list with 16 species, followed by Fabaceae with 8 species; however, only 25% of all plant species have demonstrated antihypertensive effects originating from both *in vitro* and *in vivo* studies, lending credence to their folkloric use. Only 11 plant species reportedly possess antihypertensive properties in animal models, with very few species subjected to analytical processes to reveal the identity of their bioactive antihypertensive compounds. In this review, we hope to encourage researchers and global research institutions (universities, agricultural research councils, and medical research councils), particularly those showing an interest in natural products, for the need for concerted efforts to undertake more studies aimed at revealing the untapped potential of these plants. These studies are very important for the development of new pharmaceuticals of natural origin useful for the management of hypertension.

## ABBREVIATIONS

ACE	angiotensin-converting enzyme
CVD	cardiovascular diseases
CCD	congestive cardiac diseases
CHD	coronary heart diseases
HBP	high blood pressure
HTN	hypertension
KZN	KwaZulu-Natal
SA	South Africa

## Introduction

HTN (HBP)—a silent killer that provides no symptoms, signs, or warnings—is defined according to the World Health Organization and Naish et al. [1] as a medical condition that results in a persistent rise in blood pressure (BP) within the arteries of an individual. HBP or HTN, expressed as systolic (maximum pressure) or minimum pressure (diastolic) measurements, may be a result of unclassified lifestyle or genetic factors (such as excessive salt intake, smoking, or alcohol), which account for about 90–95% of the total HBP [2], although there are less common secondary causes—for

example, narrowing of the kidney arteries [2] or the use of birth control pills (represented by unconfirmed hypotheses). The BP of a normotensive individual is in the range of 100–140 mmHg systolic and 60–90 mmHg diastolic pressures (although different values apply to children) [3]. Exceeding the normal or accepted values of these measurements has been linked to increased risk of CVD and many chronic complications that include but are not limited to CHD, stroke, cardiac arrest, CCD, renal insufficiency, and myocardial infarction [4, 5].

Globally, more than 1 billion people suffer from HTN, with an estimated 1.25 billion by 2025 [6]. In addition, HTN and its related diseases are gradually becoming major causes of disability [7]. To date, HBP has been regarded as a disease of developed countries; however, in recent years, the prevalence of HTN is speedily growing in low- and middle-income countries (LMIC) as well as continents like Africa [8], where poverty, exposure to infectious diseases (e.g., HIV, malaria, tuberculosis), and inadequate awareness of disease treatment and control are the order of the day. Today, 1 out of every 5 adults in LMIC suffers from HBP, and it has been projected that by 2025 this ratio will balloon to 3 out of every 4 adults [9]. Similarly, in sub-Saharan Africa, the incidence of HTN has increased tremendously, particularly during the last 20–30 y, with 40% (approximately 20 million) of the entire adult population living with the disease [10]. This translates to about 80 million people (of the overall 650 million populations) in 2000 (within the region), with the possibility of this number increasing to 150 million by 2025 [9]. Intriguingly, HTN constitutes a major health concern in SA, as HBP and its related conditions (CVD, diabetes, and stroke) remain the second highest cause of mortality after sexually transmitted diseases [11], with more than 6.3 million adult sufferers (particularly black South Africans) [12]. Moreover, further epidemiological information in terms of age and prevalence revealed the average incidence of HBP to be 59% among blacks, 55% among Indians, and 50% among whites, with females (11.2%)—most importantly those between the ages of 15 and 34—recording a higher prevalence than males (7%) of the 34–65 age bracket [12, 13].

The treatment or control of HBP aims to lower the maximum (systolic) and minimum (diastolic) pressures below 140/90 mmHg (normal BP). This is achieved through nonpharmacological (lifestyle modification) and pharmacological (drug therapy) approaches. Lifestyle modification rallies around maintaining body weight (<25 kgm<sup>-2</sup>), regular exercise (30 min daily), restricting excessive salt consumption (limiting intake to <2400 mg/d), and the regulation of alcohol intake (limiting intake to 2 standard drinks for men and 1 for women) [12]. It is noteworthy that a number of investigations buttressed the relevance of these modifications in HTN management [14, 15]. Pharmacologically, the use of orthodox drugs is encouraged to control HBP via nitric oxide, as well as neural and renal endocrine mechanisms when lifestyle modification fails to achieve the desired results [16]. Antihypertensive agents including diuretics (relaxation of blood vessels/expulsion of excess fluids/salt), beta blockers such as atenolol (inhibition of adrenaline action to control heart rate), calcium channel blockers (arterioles relaxation and heart beat regulation), ACE (an important enzyme within the renin-angiotensin cascade) inhibitors such as lisinopril (limiting the arteries production of

angiotensin/altering narrowing of the arteries), and vasodilators such as aspirin (which relaxes the blood vessels for ease of blood flow within the circulatory system) are embraced individually or in combination to manage HBP and related conditions [7, 12]. Experimentally, HBP may be evaluated *in vitro* (ACEI assays) and/or *in vivo* (Dahl-salt stress assays). However, the adoption of these synthetic moieties in HTN management has presented a number of challenges in recent years, including serious financial implications, unavailability to buy, numerous side effects attributed to altered renal function, angioedema (severe swelling below the skin surface), dry cough, weakness, and headaches [17]. As such, there is an urgent call for an appropriate substitute in phytotherapy, which is adjudged to be safe, effective, inexpensive, and pose little or no side effects in HTN control [18].

Medicinal plants (MPs), otherwise known as medicinal herbs, are employed in herbal medicine for their usefulness in promoting health, affording brief relief of symptoms or providing therapeutic uses. They produce a number of compounds (phytoconstituents) that play important roles in their biological functions, such as protecting them from predation (e.g., insects, fungi, herbivores mammals). Herbal medicine or phytotherapy is an age-old tradition practiced globally and involves the use of whole plants or plant parts (leaves, flowers, fruits, stems, roots, or rhizomes) to maintain the general well-being of an individual [19]. Globally, 60% of the developed and 80% of the developing and underdeveloped populations of the world now rely on herbal therapy for their health care needs [20]. Of particular interest is Africa, where an estimated 60–90% of the entire population makes use of phyto-medicine in the management of ailments, including HTN [21], based in part on the availability and affordability of these medicines as compared to popular or conventional biomedicines [22].

Besides being endowed with rich cultural biodiversity, SA accounts for 9% of the higher plants worldwide, with well over 30,000 plant species [23]. It is no surprise that over 3000 species of these plants are currently used by more than 200,000 traditional healers in the treatment, cure, or management of many diseases [24]. It is noteworthy that more than 60–80% of the entire population, particularly those of rural settlements, adopt the use of medicinal herbs in various forms as medicines for the maintenance of health. Research efforts examining the pharmacological activities of MPs have been ongoing for decades in SA. While a number of the potential effects of these plants against many diseases such as diabetes, cancer, malaria, and other infectious ailments have been scientifically validated, very few of them have been evaluated for their hypotensive as well as antihypertensive efficacies [12], despite their traditional use and continuous documentation. In line with the aforementioned, there is a need for more research efforts (*vis-à-vis* the rapid prevalence of HBP) from government, scientific/academic institutions, and research agencies toward affirming their efficacy and determining the safety profile of documented antihypertensive plants in order to stem the growing prevalence of HBP. Hence, this review has been prepared to report the antihypertensive or hypotensive MPs used in SA to encourage the financing of additional studies to explore those with unproven pharmacological or biological properties, as well as to evaluate and isolate their active compounds as potential drug candidates.

## Results and Discussion

### Antihypertensive MPs in SA

According to Watt and Brewer-Brandwijk [25], Hutchings et al. [26], van Wyk et al. [24], van Wyk and Gericke [23], Thring and Weitz [27], Mofette [28], Olorunnisola et al. [29], Moteetee and van Wyk [30], Semenya et al. [31], de Wet et al. [32], and David et al. [33], more than 100 MPs are traditionally used and ethnobotanically documented in SA for the management of HTN (► **Table 1**). It is noteworthy that, for the purpose of this review, random selection of these plants was considered. Moreover, some plants without formal documentation of their medicinal properties use are also included in the list based on their reported antihypertensive potential.

#### *Adenopodia spicata* (E.Mey.) C. Presl

*A. spicata* is an endemic plant of southern Africa that belongs to the Leguminosae (or Fabaceae) family. There are 7 species of the genus *Adenopodia* (*gymnantha*, *oaxacana*, *patens*, *rotundifolia*, *scelerata*, *schlechteri*, and *spicata*) distributed in the northern neotropics, particularly Mexico (southern and western) and Central America. The prominent common names include stekel-splinterboontjie (Afrikaans), ibobo, umlungumabele, ubobo (Zulu), spiny splinter-bean (English), and umbambangwe, and they are traditionally used for treating chest or breast pain, syphilis, and HTN [26]. The prominent chemical components are saponins, and the *in vitro* antihypertensive activity of the plant against ACE (an enzyme responsible for the conversion of angiotensin I to angiotensin II that plays a role in HBP) has been reported, where it showed 97% and 72% inhibition of the enzyme using aqueous and ethanolic leaf extracts, respectively, each at a concentration of 25 µg/mL (► **Table 2**) [34].

#### *Agapanthus africanus* (L.) Hoffmanns.

*A. africanus*, a member of the Amaryllidaceae (or Agapanthaceae) family, is also called blue lily, Cape agapanthus, fynbos agapanthus (English), kleinblouelei (Afrikaans), ubani (Zulu), and isicakathi (Xhosa). The plant is widely distributed on the Cape of Good Hope (eastern), SA, and grows up to 25–70 cm long. Its folkloric usage includes treatment for chest pains, cough, and heart disease, as well as to induce or ease labor [24,26]. Oxytocic, *in vivo* antifungal, and antihypertensive activity of the aqueous and ethanolic leaf extracts (25 µg/mL) against ACE (► **Table 2**) have been reported with 63% and 44% inhibition, respectively [34]. Active constituents include spirostane (found to induce apoplastic peroxidase activity) and furostane, as well as several other saponins and saponinins [24].

#### *Agave americana* (L.)

*A. americana* is a flowering plant of the Asparagaceae family indigenous to Mexico and the United States, particularly Texas, Arizona, and New Mexico, but is now grown in many continents and nations of the world such as Africa (Kenya, Nairobi, Western Cape, SA), Australia, China, India, and Thailand. Its common names include century plant, agave, agave cactus, American agave aloe, or American aloe (despite not being related to the genus *Aloe*), blougaring-

boom, Amerikaanse aalwee, kaalgaarboom, Amerikaanse aalwyn, blou-aalwee, gareboom, makaalwyn (Afrikaans), lekhala (Sotho), and xikwenga (Tsonga). It is traditionally used in the treatment of HTN by the Bapedi traditional healers [31], as well as having other ornamental uses. Its chemical constituents include but are not limited to isolated cantalaponin-1 ((25R)-5 $\alpha$ -spirostan-3 $\beta$ ,6 $\alpha$ ,23 $\alpha$ -triol-3,6-di-O- $\beta$ -D-glucopyranoside) and (25R)-3 $\beta$ ,6 $\alpha$ -dihydroxy-5 $\alpha$ -spirostan-12-one 3,6-di-O-beta-D-glucopyranoside [35], while pharmacological evidence of its anti-inflammatory, antileishmanial, antifungal, antitumor (in MTT assays), cytotoxic, antimicrobial, antioxidant, antiulcer, antibacterial, and irritant properties have been reported [35,36]. Additionally, the antihypertensive effect of an ethanolic leaf extract (25 µg/mL) of the plant has been verified against ACE and found to inhibit the activity of the enzyme by 82%, in addition to a 72% inhibition by aqueous leaf extract (► **Table 2**) [34].

#### *Alepidea amatymbica* Eckl. & Zeyh.

*A. amatymbica* is included in the Apiaceae family, with local names such as larger tinsel flower (English), kalmoes (Afrikaans), iqwili (Xhosa), iKhathazo (Zulu), and lesoko (Sotho). There are close to 30 species of the genus *Alepidea* existing in southern Africa, with a few species distributed in Kenya and Ethiopia. Interestingly, 3 subspecies of *A. amatymbica* are available. Traditionally, the plant is used for the treatment of colds, cough, malaria, rheumatism, wound healing, asthma (when combined with *Cannabis sativa* L. [Cannabaceae]), influenza, and abdominal cramps [24], while its application as an antimicrobial, antihypertensive, diuretic [37], antioxidant, anti-inflammatory, antitrypanosomal, antibacterial, antimicrobial, antifungal, antihypertensive, antiplasmodial, anti-HIV, and anthelmintic are also documented. Wintola and Afolayan reported on the cytotoxicity of the plant and its safety profile in a comprehensive review [38].

#### *Allium sativum* (L.)

*A. sativum* is a member of the Amaryllidaceae family native to Central Asia and Iran (northeastern region). Commonly referred to as garlic, it is the second most widely used plant in the genus *Allium* next to onion, *Allium cepa* L. *A. sativum* contains as its phytochemical constituents sulfur compounds (like allylpropyl, aliin, allicin, s-allylcysteini, ajoene, and vinylthiols), peptides, terpenoids, phenols, saponins, amino acids including arginine, minerals such as selenium, and enzymes like myrosinase and peroxidase, as reported by Tesfeya and Mengesha [39]. The plant is indigenously used as a spice to flavor foods and to aid digestion, as well in the control of numerous ailments such as heart problems [25], fever, diabetes, breast cancer, stroke, and arthritis and as an immune system enhancer. Of particular interest is the thorough review of its pharmacological properties (antibacterial, antifungal, antiparasitic, antiviral, antihypertensive, antiatherosclerotic, antithrombotic, antioxidant, antimutagenic, antihyperglycemic, antilipidemic, antihelminthic, diuretic, digestive, hepatoprotective, radioprotective, cardioprotective, antiprotozoal, antimicrobial, anti-inflammatory, antitubercular, immunomodulatory, analgesic, and wound healing), as well as its cytotoxic and safety profile from different nations of the world including Spain, India, and Ethiopia [39–41], among others. Additionally, its biological importance as an antidiabetic

► **Table 1** South African MPs documented for HBP control.

Name	Family	Common name (Zulu/Afrikaans)	Plant type	Part(s) used	Evidence of documented HBP use	Ethnobotanical indications on HBP	References
<i>Achyranthes aspera</i>	Amaranthaceae	Isinama	Herb	Roots	[26]	NS	[26]
<i>Acokanthera oppositifolia</i>	Apocynaceae	inHlungunyembe	Shrub	Leaves, roots stem	[24]	Maceration	[24]
<i>Adenopodia spinata</i>	Fabaceae	Ubobo	Shrub	Leaves, roots	[26]	Maceration	[26, 34]
<i>Agapanthus africanus</i>	Amaryllidaceae	Ubani	Herb	Leaves, roots	[26]	Maceration, infusion	[26, 34]
<i>Agathosma betulina</i>	Rutaceae	Regteboegoe	Shrub	Leaves, stem	[29]	Infusion	[29]
<i>Agave americana</i>	Asparagaceae	Unknown	Shrub	Leaves	[31]	Decoction	[26, 31, 34]
<i>Albertisia delagoensis</i>	Menispermaceae	Umgandaganda	Shrub	Rhizome, leaves, stem, root	[32]	Decoction	[32]
<i>Alepidea amatymbica</i>	Apiaceae	iKhathazo	Shrub	Rhizomes, roots	[24]	NS	[24]
<i>Allium sativum</i>	Amaryllidaceae	Unknown	Herb	Flower bud	[25, 27]	NS	[27]
<i>Aloe ferox</i>	Asphodelaceae	iNhlaba	Shrub	Leaves/sap	[27, 28, 33, 110]	NS	[33]
<i>Aloe marlothii</i>	Asphodelaceae	inhlaba umhlaba	Herb	Leaves, roots	[32]	Decoction	[32]
<i>Aloe striatula</i>	Asphodelaceae	Unknown	Shrub	NS	[28]	NS	[28]
<i>Amaranthus dubius</i>	Amaranthaceae	Unknown	Herb	Leaves	FPR	Maceration	[18]
<i>Amaranthus hybridus</i>	Amaranthaceae	Unknown	Herb	Leaves	FPR	Maceration	[18]
<i>Arachis hypogaea</i>	Fabaceae	Amakinati	Herb	Leaves, seed	[32]	Decoction	[33]
<i>Artemisia afra</i>	Asteraceae	Mhlonyane	Shrub	Leaves	[27, 33]	Infusion	[27, 33]
<i>Asystasia gangetica</i>	Acanthaceae	Isihobo	Herb	Leaves	FPR	Maceration	[18]
<i>Ballota africana</i>	Lamiaceae	Kattekruide	Shrub	Leaves	[24, 25, 33]	Infusion	[27, 33]
<i>Cadaba aphylla</i>	Brassicaceae	Bobbejaanarm	Shrub	Leaves, stem	[33]	Infusion	[33]
<i>Canabis sativa</i>	Cannabaceae	Nsangu	Herb	Leaves	[24, 29–30, 32]	Infusion, decoction	[29, 32]
<i>Carpobrotus dimidiatus</i>	Mesembryanthemaceae	Ikhambi lamabulawo	Herb	Leaves, stem, fruit	[32]	Decoction	[32]
<i>Catha edulis</i>	Celastraceae	Umhlwazi	Shrub	Leaves	[26]	Maceration	[26, 34]
<i>Catharanthus roseus</i>	Apocynaceae	Unknown	Herb/ sub-shrub	Roots, flower, seeds	[32]	Decoction	[32]
<i>Chrysocoma ciliata</i>	Asteraceae	Kaalsiektebos	Shrub	Leaves, roots	[33]	Decoction	[33]
<i>Cinnamomum camphora</i>	Lauraceae	Uroselina	Tree	Gum	[24]	NS	[24]
<i>Cissampelos capensis</i>	Menispermaceae	Fynblaarklimop	Shrub	Roots	[24, 29]	Infusion	[29]
<i>Citrullus lanatus</i>	Curcubitaceae	Bitterwaatlemoen	Herb	Fruit, seed, leaves	[32]	Decoction	[32]
<i>Citrus limon</i>	Rutaceae	Ulamula	Shrub/ small tree	Peel of fruit, pulp, root	[32]	Decoction	[32]
<i>Citrus maxima</i>	Rutaceae	Upapamuzi	Tree	Fruit	[32]	N/A (taken raw)	[32]
<i>Cladostemon kirkii</i>	Capparaceae	umThekwini	Shrub/ small tree	Root, stem, bark	[32]	Maceration, decoction	[32]
<i>Clausena anisata</i>	Rutaceae	Umnukambhiba	Shrub	Leaves, roots	[26]	Maceration, decoction	[26, 34, 65]
<i>Commelina africana</i>	Commelinaceae	Idangabane	Herb	Whole plant	[26, 30]	Decoction ( <i>T. capensis</i> )	[30]
<i>Commelina benghalensis</i>	Commelinaceae	Idangabane	Herb	Whole plant	[26]	Poultice	[26]

cont.

► Table 1 Continued

Name	Family	Common name (Zulu/Afrikaans)	Plant type	Part(s) used	Evidence of documented HBP use	Ethnobotanical indications on HBP	References
<i>Convolvulus capensis</i>	Convolvulaceae	Skaapklimop	Shrub	Bulb	[33]	Decoction	[33]
<i>Conyza scabrida</i>	Asteraceae	Umanzimnyama	Shrub	Leaves	[27]	Infusion	[24, 27]
<i>Crinum macowanii</i>	Amaryllidaceae	Umdube	Herb	Bulbs, leaves, whole plants	[24]	NS	[24]
<i>Crassula muscosa</i>	Crassulaceae	Skoenvetebos	Herb	Leaves, stem, roots, flowers	[33]	Decoction	[33]
<i>Dicerthamnium rhinocerotis</i>	Asteraceae	Ranosterbos	Small shrub	Leaves, stem	[33]	NS	[33]
<i>Dicoma anomala</i>	Asteraceae	Umuna	Herb	Leaves, roots	[24, 28]	NS	[24, 28]
<i>Dicoma capensis</i>	Asteraceae	Koorsbossie	Herb	Leaves, twigs, roots	[24]	NS	[24]
<i>Dietses iridioides</i>	Iridaceae	isishuphe somfula	Herb	Leaves, roots, rhizomes	[26]	Maceration, infusion	[26, 34, 65]
<i>Diosma oppositifolia</i>	Rutaceae	Bitterboegoe	Shrub	Leaves, stem, flowers	[33]	NS	[33]
<i>Dipcadi brevifolium</i>	Hyacinthaceae	Ikhakakha	Herb	Bulb	[26]	Decoction	[26]
<i>Dombeya rotundifolia</i>	Malvaceae	iNhliziyonkhulu	Tree	Leaves, roots	[26]	Maceration	[26, 34]
<i>Drimia elata</i>	Asparagaceae	Undongana-zibomvana	Herb	Bulb	[26]	NS	[26]
<i>Ekebergia capensis</i>	Meliaceae	Essenhout	Tree	Leaves, bark	[26]	NS	[26]
<i>Elephantorrhiza elephantina</i>	Fabaceae	Intolwane	Sub-shrub	Leaves, rhizome	[26, 29, 30]	Infusion	[29]
<i>Elytropappus rhinocerotis</i>	Asteraceae	renosterbos	Shrub	Leaves	[27]	Infusion	[27]
<i>Eriobotrya japonica</i>	Rosaceae	Unknown	Shrub/ small tree	Leaves	[31]	Infusion	[31]
<i>Eriocephalus africanus</i>	Asteraceae	Kapokbos	Shrub	Leaves	[24, 25, 27, 30]	Infusion	[27]
<i>Euclea undulata</i>	Ebenaceae	Inkunzane	Shrub/ small tree	Bark, roots, whole plant	[24]	Infusion	[24]
<i>Euryops abrotanifolius</i>	Asteraceae	Bergharpuisbos	Shrub	Leaves, stems	[33]	NS	[33]
<i>Galinsoga parviflora</i>	Asteraceae	Unknown	Herb	Leaves	FPR	Maceration	[18]
<i>Geranium incanum</i>	Geraniaceae	Vrouetee	Grass or small herb	Leaves, stem	[29]	Decoction	[29]
<i>Gethyllis spp</i>	Amaryllidaceae	Koekoemakranka	N/A	Seeds, pod	[27]	Maceration	[27]
<i>Helichrysum crispum</i>	Asteraceae	Hotnotskooigoed	Herb	Leaves	[25, 27]	Infusion	[27]
<i>Helichrysum odoratissimum</i>	Asteraceae	Imphepho	Herb	Leaves, roots	[29]	Infusion	[29]
<i>Hoodia gordonii</i>	Apocynaceae	Bobbejaangaap	Herb	Leaves, stem	[110]	NS	[110]
<i>Hyphaene coriacea</i>	Arecaceae	iLala	Tree	Roots	[32]	NS	[32]
<i>Hypoxis argentea</i>	Hypoxidaceae	Inongwe	Herb	Corm, tuber	[32]	Decoction	[32]
<i>Hypoxis colchicifolia</i>	Hypoxidaceae	Ilabatheka	Herb	Bulb	[29]	NS (chewed)	[29]
<i>Hypoxis hemerocallidea</i>	Hypoxidaceae	Inkomfe	Grasses or small herb	Corm, roots	[29, 32]	Decoction	[29, 32]
<i>Justicia flava</i>	Acanthaceae	Impela	Herb	Leaves	FPR	Maceration	[18]
<i>Lantana camara</i>	Verbenaceae	Ubukhwebezane	Shrub	Roots	[31]	Infusion/decoction	[31]

cont.

► **Table 1** Continued

Name	Family	Common name (Zulu/Afrikaans)	Plant type	Part(s) used	Evidence of documented HBP use	Ethnobotanical indications on HBP	References
<i>Leonotis leonurus</i>	Lamiaceae	Umfincafincane	Shrub	Leaves, roots, flowers, whole plant	[27, 33]	Decoction	[27, 33]
<i>Lessertia frutescens</i>	Fabaceae	Umnwele	Shrub	Leaves, shoot	[29, 33, 110]	Decoction	[29]
<i>Leucosidea sericea</i>	Rosaceae	Umtshitshi	Small tree	NS	[28]	NS	[28]
<i>Lichtensteinia lacera</i>	Apiaceae	Kalmiswortel	Herb	Leaves, stem	[33]	Infusion	[33]
<i>Lippia javanica</i>	Verbanaceae	Umsuzwane	Shrub	Leaves	[32]	Decoction	[32]
<i>Medicago sativa</i>	Fabaceae	Unknown	Herb	Whole plant	[31]	Decoction	[28, 31]
<i>Mentha aquatica</i>	Lamiaceae	Unknown	Herb	Leaves, stem, seed	[28, 30]	Infusion	[28, 30]
<i>Mentha longifolia</i>	Lamiaceae	ufuthana lomhlanaga	Herb	Leaves, stem	[30, 33]	Decoction	[33]
<i>Mesembryanthemum</i> spp.	Aizoaceae	Unknown	N/A	Leaves, stem	[26]	Maceration, decoction	[26, 34]
<i>Momordica balsamina</i>	Curcurbitaceae	Intshungu	Herb	Leaves	[32]	Decoction	[32, 75]
<i>Momordica charantia</i>	Curcurbitaceae	Unknown	Herb	Whole plant	FPR	Maceration	[75]
<i>Momordica foetida</i>	Curcurbitaceae	Intshungu	Herb	Leaves, stem	[26]	NS	[26]
<i>Musa acuminata</i>	Musaceae	Ihliziyo	Herb	Flower bracts	[32]	Decoction	[32]
<i>Ocimum basilicum</i>	Lamiaceae	Unknown	Herb	Leaves, stem	[29]	Infusion	[29]
<i>Oldenlandia affinis</i>	Rubiaceae	Umampeshane	Herb	Root	[26]	Decoction	[26]
<i>Olea europaea subsp. africana</i>	Oleaceae	Umnquma	Tree	Leaves, roots	[23, 24, 26–29]	Decoction	[29]
<i>Opuntia ficus</i>	Cactaceae	Umthelekisi	Shrub/tree	Roots	[31]	Decoction	[31]
<i>Oxygonum sinuatum</i>	Polygonaceae	Unknown	Herb	Leaves	FPR	Maceration	[18]
<i>Ozoroa engleri</i>	Anacardiaceae	Isifico	Tree	Roots, bark, leaves	[32]	Decoction	[111]
<i>Pentanisia prunelloides</i>	Rubiaceae	Icimamlilo	Herb	Rhizome, corm, roots	[24, 26]	NS	[26]
<i>Persea americana</i>	Lauraceae	Unknown	Tree	Leaf, pulp, fruit, root	[31]	Decoction	[31]
<i>Peucedanum galbanum</i>	Apiaceae	Droedas	Shrub	Leaves	[24]	Infusion	[24]
<i>Physalis viscosa</i>	Solanaceae	Unknown	Herb	Leaves	FPR	Maceration	[18]
<i>Protorhus longifolia</i>	Anacardiaceae	Uzintwa	Tree	Bark, leaves	[26]	Maceration	[26, 34]
<i>Psidium guajava</i>	Myrtaceae	Koejawel	Shrub/ small tree	Leaves, roots	[31, 32]	Decoction	[31, 32]
<i>Pyrenacantha kaurabassana</i>	Icacinaceae	Unknown	Shrub	Bulb, tuber	[32]	Decoction	[32]
<i>Ptaeroxylon obliquum</i>	Rutaceae	umThathi	Tree	Roots	[24, 32]	Maceration	[26, 32]
<i>Rapanea melanophloeos</i>	Myrsinaceae	iKhubalwane	Tree	Bark	[26]	NS	[26]
<i>Rauvolfia caffra</i>	Apocynaceae	umHlambamanzi	Tree	Bark, stem, whole plant	[24]	NS	[24]
<i>Rhoicissus digitata</i>	Vitaceae	umNangwazi	Shrub	Tubers, bulb	[29]	Infusion	[29]
<i>Rhus chirindensis</i>	Anacardiaceae	Umhlabamvudu	Tree	Leaves, roots, bark, twigs, fruits	[26]	Maceration	[34]

cont.



► Table 1 Continued

Name	Family	Common name (Zulu/Afrikaans)	Plant type	Part(s) used	Evidence of documented HBP use	Ethnobotanical indications on HBP	References
<i>Ricinus communis</i>	Euphorbiaceae	Umhlakuva	Shrub	Leaves	[32]	Decoction	[32]
<i>Ruta graveolens</i>	Rutaceae	Unknown	Shrub	Leaves	[24, 25, 27, 29]	Infusion	[27, 29]
<i>Salvia africana-caerulea</i>	Lamiaceae	Wildesalie	Shrub	Twig, leaves	[28, 33]	Infusion	[33]
<i>Sarcophyte sanguinea</i>	Balanophoraceae	Umvumbuka	Herb	Whole plant, Stem, root	[32]	Infusion, decoction	[32]
<i>Sarcostemma viminale</i>	Apocynaceae	Umbelebele	Shrub	Stem, aerial parts, twigs	[32]	Infusion	[32]
<i>Sceletium tortuosum</i>	Aizoaceae	Tandtrekbos	Herb	Leaves, roots	[33]	NS	[33]
<i>Schkuhria pinnata</i>	Asteraceae	Ruhwahwa	Herb	Whole plant	[29]	Infusion, decoction	[31]
<i>Sclerocarya birrea</i>	Anacardiaceae	Maroela	Tree	Bark, leaves, stem-bark, stem	[26]	Decoction	[26]
<i>Scolopia mundii</i>	Salicaceae	iHlambahlale	Tree	Bark	[26]	NS	[26]
<i>Searsia burchellii</i>	Anacardiaceae	Karookoeniebos	Shrub/ small tree	Leaves, stem, roots	[33]	Infusion	[33]
<i>Senecio bupleuroides</i>	Asteraceae	Isiqandamatshana	Shrub	NS	[26]	NS	[26]
<i>Senecio inornatus</i>	Asteraceae	Uhlabo	Herb/small shrub	Root	[26]	Decoction	[26]
<i>Senecio serratuloides</i>	Asteraceae	Ichazampukane	Herb	Leaves, stem	[32]	Decoction	[32]
<i>Spermacoce natalensis</i>	Rubiaceae	Umabophe	Herb	Bark, roots, leaves	[26]	NS	[46]
<i>Stangeria eriopus</i>	Zamiaceae	Umfigwani	Cycad	Root, leaves	[26]	NS	[34]
<i>Strychnos madagascariensis</i>	Strychnaceae	umKwakwa	Tree	Seeds, bark, roots, fruit	[32]	NS (crush to powder for swallowing)	[32]
<i>Teedia lucida</i>	Scrophulariaceae	Hlwenya	Herb/dwarf shrub	NS	[28]	NS	[28]
<i>Tephrosia capensis</i>	Fabaceae	Unknown	Small shrub	Root	[26]	Decoction	[28]
<i>Tetradenia riparia</i>	Lamiaceae	Ibozane	Shrub/tree	Leaves, seeds	[32]	Decoction	[32]
<i>Trichilia emetica</i>	Meliaceae	Umathuzini	Tree	Leaves, fruits, roots, bark, stem	[32]	Poultice, decoction	[32]
<i>Trifolium africanum</i>	Fabaceae	Wildeklawer	Herb	Whole plant	[28, 30]	Infusion	[30]
<i>Trifolium burchellianum</i>	Fabaceae	Usithathi	Herb	Leaf, stem, roots	[28, 30]	Infusion (combined with <i>M. aquatica</i> )	[30]
<i>Tulbaghia acutiloba</i>	Alliaceae	Ishaladi Lezinyoka	Herb	Bulb, flower, Whole plant	[28, 30]	Infusion, decoction	[30]
<i>Tulbaghia violacea</i>	Alliaceae	wilde knoffel	Herb	Rhizome, bulb, leaves, roots	[24, 26–29, 33]	Infusion, decoctions	[27, 29, 33]
<i>Turraea floribunda</i>	Meliaceae	Umadlozane	Tree	Bark, leaves, roots	[26]	Infusions	[26]
<i>Urtica urens</i>	Urticaceae	Unknown	Herb	Leaves	[30]	Decoction	[30]
<i>Valeriana capensis</i>	Valerianaceae	Wildebaldjerjan	Herb	Rhizomes, roots	[24]	NS	[24]
<i>Vangueria infausta</i>	Rubiaceae	umTulwa	Shrub/ small tree	Bark, leaves	[32]	Maceration, infusion	[32]
<i>Warburgia salutaris</i>	Canellaceae	Isibhaha	Tree	Bark, root	[110]	NS	[110]

FPR: from pharmacological report; NS: not stated or specified; N/A: not applicable

► **Table 2** MPs with reported antihypertensive activity.

Name	Pharmacological activities		Assay type(s)	Method(s)/ inducing agent	Part(s) used	Medium for extraction	Conc. tested	Province(s) or location	References
	Antioxidant,	Antidiabetic							
<i>Acokanthera oppositifolia</i>	Antioxidant		<i>In vitro</i>	DPPH, ABTS, FRAP	Stem	Methanol	0.1 mg/mL	Eastern Cape	[112]
<i>Adenopodia spicata</i>		Antihypertensive	<i>In vitro</i>	ACEI assay	Leaves, root	Aqueous, ethanol	25 µg/mL	KZN	[34]
<i>Agapanthus africanus</i>		Antihypertensive	<i>In vitro</i>	ACEI assay	Leaves, root	Aqueous	25 µg/mL	KZN	[34]
<i>Agathosma betulina</i>	Antioxidant		<i>In vitro</i>	ABTS, DPPH	Leaves	Hot water, DCM	1, 3, 5, 10, 20 µg/mL	Pretoria	[113]
		Antidiabetic	<i>In vitro</i>	α-amylase, α-glucosidase					
<i>Agave americana</i>	Antioxidant		<i>In vivo</i>	ORAC, TEAC, FRAP		Aqueous, ethanol, acetone		Cape Town	[114]
		Antihypertensive	<i>In vitro</i>	ACEI assay	Leaves	Aqueous, ethanol	25 µg/mL	KZN	[34]
<i>Alepidia amatymbica</i>		Antihypertensive, cardiovascular, diuretic	<i>In vivo</i>	Sodium thiopentone (rats model)	Rhizome	Hexane, methanol, DCM	20 mg/kg body weight	KZN	[38, 115]
		Antihypertensive	<i>In vitro</i>	ACEI	Leaves	Aqueous, methanol	0.1 g/mL	KZN	[18]
<i>Amaranthus dubius</i>		ACE inhibitory activity	<i>In vitro</i>	ACEI	Leaves	Aqueous, methanol	0.1 g/mL	KZN	[18]
<i>Artemisia afra</i>		Antidiabetic	<i>In vivo</i>	STZ-induced rat model	Leaves	Aqueous	50, 100, 200 mg/kg	Eastern Cape	[116]
<i>Asystasia gangetica</i>		Cardioprotection	<i>In vivo</i>	ISP	Leaves	Aqueous	100, 200 mg/kg	Eastern Cape	[117]
		Antihypertensive	<i>In vitro and In vivo</i>	ACEI	Leaves	Aqueous and methanol	0.1 g/mL	KZN	[18]
<i>Carpobrotus dimidiatus</i>			<i>In vivo</i>	Sodium pentobarbitone		Aqueous	10, 25, 50, 100, 200, 400 mg/mL	Western Cape	[46]
	Antioxidant		<i>In vitro</i>	DPPH, FRAC	Leaves	Aqueous methanol (50%)	10, 20, 30, 40, 50, 60, 70 µg/mL	KZN	[108]
<i>Catha edulis</i>		Antihypertensive	<i>In vitro</i>	ACEI assay	Leaves	Aqueous, ethanol	25 µg/mL	KZN	[34]
<i>Citrus lemon</i>	Antioxidant		<i>In vitro</i>	DPPH, nitric oxide, reducing power,	Peel of fruits	Ethanol, acetone	0.025, 0.05, 0.1, 0.2, 0.5 µg/mL	Eastern Cape	[54]

continued



▶ **Table 2** Continued

Name	Pharmacological activities		Assay type(s)	Method(s)/ inducing agent	Part(s) used	Medium for extraction	Conc. tested	Province(s) or location	References
	Antioxidant,	Antidiabetic							
<i>Clausena anisata</i>			<i>In vivo</i>	HRM	Leaves	Aqueous	50, 100, 200, 400 mg/bw	Limpopo	[59]
		Antidiabetic	<i>In vivo</i>	STZ-rat model	Roots	Methanol	100, 200, 400, 800 mg/kg bw	KZN	[58]
<i>Crinum macowanii</i>		Cardiovascular	<i>In vivo</i>	Normotensive rats	Whole plants	Aqueous	0.05, 0.10, 0.15, 0.20 mg/kg	Western Cape	[62–63]
<i>Dicoma anomala</i>	Antioxidant	Antidiabetic	<i>In vivo</i>	STZ-rat model	Root	Aqueous	125, 250, 500 mg/kg	Free State	[118]
<i>Diets iridioides</i>			<i>In vivo</i>	ISP-rat	Root	Aqueous	same	Same	[119]
			<i>In vitro</i>	ACEI assay	Leaves, root	Aqueous	25 µg/mL	KZN	[34]
<i>Dombeya rotundifolia</i>			<i>In vitro</i>	ACEI assay	Leaves, root	Aqueous	25 µg/mL	KZN	[34]
<i>Ekeberghia capensis</i>		Cardiovascular, vasorelaxant, bradycardia	<i>In vivo</i>	Inactin-induced normotensive rats and Dahl salt stress rats	Leaves	Ethanol	18 mg/kg i. v. and 120 mg/kg p. o	KZN	[120]
<i>Euclea undulata</i>		Hypoglycemic	<i>In vitro</i>	α-amylase, α-glucosidase, glucose uptake (GU)	Whole plant	Acetone	50 µg/mL and 16–250 µg/mL CU	Gauteng (Pretoria)	[120]
			<i>In vivo</i>	STZ-rat model	Bark	Acetone	50, 100 mg/kg b.w	Gauteng (Pretoria)	[121]
<i>Hypoxis hemerocallidea</i>		Cardiovascular, anti-hypertensive	<i>In vitro</i>	Isolated muscle experiment	Fresh corm	Aqueous	12.5, 25, 50, 100, 200, 400 mg/mL	KZN	[75]
			<i>In vivo</i>	Sodium 5-ethyl-(1-methylbutyl)-2-thiobarbiturate-induced Dahl salt-stress rats	As above	Same as above	25, 50, 100, 200, 400 mg/kg b.w	KZN	[75]
<i>Justicia flava</i>		Antihypertensive	<i>In vitro</i>	ACEI assay	Leaves	Aqueous, methanol	0.1 g/mL	KZN	[18]

continued

▶ **Table 2** Continued

Name	Pharmacological activities		Assay type(s)	Method(s)/ inducing agent	Part(s) used	Medium for extraction	Conc. tested	Province(s) or location	References
	Antioxidant,	Antidiabetic							
<i>Leonotis leonurus</i>	Antioxidant	Antihypertensive, cardiovascular	<i>In vitro</i>	DPPH, ABTS radical scavenging assays	Leaves	Acetone, Aqueous, methanol	0.02, 0.05, 0.1, 0.5, 0.75, 1 mg/mL	Eastern Cape	[122]
		Antidiabetic	<i>In vivo</i>	STZ-rats model	Leaves	Aqueous	50, 100, 200, 400, 800 mg/kg b.w.	KZN	[123]
				As above			125, 250, 500 mg/kg b.w.		
					Leaves	Aqueous	0.5–7.0 mg/kg	Eastern Cape	[123]
				Sodium pentobarbitone induced rats		Methanol	25, 50, 100, 200, 400, 800 mg/kg	Western Cape	
<i>Lessertia frutescens</i>	Antioxidant	Cardiovascular	<i>In vitro, In vivo</i>	Dahl salt hypertensive rats	Leaves				[124]
		Normotensive, antihypertensive	<i>In vivo</i>	Sodium pentobarbitone induced rats	Leaves	Aqueous	1, 2 mg/mL	KZN	[123]
		Normotensive	<i>In vivo</i>		Whole plant	Decoction		Western Cape	[64]
					Shoot	Aqueous	50, 100, 200, 400, 800 mg/kg	KZN	[100]
						Leaves	Hot water	0.1 g/mL	Eastern Cape
<i>Lippia javanica</i>	Antioxidant		<i>In vitro</i>	DPPH, ABTS, FRAC	Leaves	Aqueous, Aqueous-methanol (70%)	1, 2, 3, 4, 5 mg/mL, 0.3 g/mL	Gauteng	[126]
			<i>In vitro</i>	ACEI assay	Leaves, stem	Aqueous, ethanol	25 µg/mL	KZN	[34]
<i>Mesembryanthemum spp</i>		Antihypertensive	<i>In vitro</i>						
<i>Momordica charantia</i>	Antioxidant	Hypoglycaemic	<i>In vivo</i>	STZ-induced rats	Whole plant	Aqueous	50, 100, 200, 400, 800 mg/kg	KZN	[75]
			<i>In vivo</i>	High fat diet	Leaves	As above	As above	As above	[75]
<i>Momordica foetida</i>	Antioxidant		<i>In vitro</i>	sodium 5-ethyl-(1-methylbutyl)-2-thiobarbiturat-induced Dahl salt-stress rats	As above				
			<i>In vitro</i>	DPPH, ABTS, Reducing power, metal chelating	Leaves	Methanol	0.1 mg/mL	KZN	[127]
<i>Oxygonum sinuatum</i>	Antidiabetic		Cell lines	Chang, 3T3 L1, C2C12 cells	Whole plant	DCM-methanol (1 : 1), Water	NS	Eastern Cape	[128]
			<i>In vitro</i>	ACEI	Leaves	Aqueous, methanol	0.1 g/mL	KZN	[18]

continued

▶ Table 2 Continued

Name	Pharmacological activities		Assay type(s)	Method(s)/ inducing agent	Part(s) used	Medium for extraction	Conc. tested	Province(s) or location	References
	Antioxidant, Antidiabetic	Antihypertensive, cardiovascular							
<i>Pentanissia prunelloides</i>	Antioxidant		<i>In vitro</i>	DPPH, Superoxide anion, Hydroxyl radical, Metal chelating	Root	Aqueous, ethanol, hydro-ethanol (1 : 1), hexane	6.25, 12.5, 25, 50, 100 µg/mL	Free State	[129]
<i>Physalis viscosa</i>		Antidiabetic	<i>In vitro</i>	Alpha (amylase and glucosidase)					
<i>Protorhus longifolia</i>	Antioxidant	Antihypertensive	<i>In vitro</i>	ACEI	Leaves	Methanol, aqueous	0.1 g/mL	KZN	[18]
<i>Psidium guajava</i>			<i>In vitro</i>	DPPH, ABTS, metal chelating, Reducing power	Bark	Hexane, chloroform, ethyl acetate, methanol, aqueous	0–5 mg/100 mL	KZN	[89]
		Antihypertensive	<i>In vitro</i>	ACEI	Leaves	Aqueous, ethanol	25 µg/mL	KZN	[34]
		Hypoglycemic	<i>In vivo</i>	STZ-induced rats and Dahl salt-stress rats	Leaves	Aqueous	50, 100, 200, 400, 800 mg/mL	KZN	[93]
<i>Rauvolfia caffra</i>	Antioxidant		<i>In vitro</i>	FRAP, DPPH,	Stem, bark	DCM, methanol, ethyl acetate, ethanol	1 mg/mL	Limpopo	[96]
<i>Rhus chirindensis</i>			<i>In vivo</i>	Spontaneously hypertensive rats	Whole plants	DCM, methanol, ethyl acetate	15, 300, 500 mg/kg b.w		
<i>Sclerocarya birrea</i>			<i>In vitro</i>	ACEI	Leaves	Aqueous, ethanol	25 µg/mL	KZN	[34]
		Hypoglycemic	<i>In vivo</i>	STZ	Stem-bark	Aqueous	25, 50, 100, 200, 400, 800, 1600 mg/mL	KZN	[100]
<i>Senecio serratulloides</i>			<i>In vitro</i>	ACEI	Leaves	Aqueous, ethanol	25 µg/mL	KZN	[34, 101]
<i>Stangeria eriopus</i>	Antioxidant		<i>In vivo</i>	Dahl salt sensitive rats	Stem bark	Aqueous	25, 50, 100, 200, 400 mg/mL	KZN	
<i>Trichilia emetica</i>	Antioxidant	Antihypertensive	<i>In vitro</i>	DPPH, FRAC	Leaves	Aqueous methanol (50%)	10, 20, 30, 40, 50, 60, 70 µg/mL	KZN	[112]
			<i>In vitro</i>	ACEI	Leaves	Aqueous, ethanol	25 µg/mL	KZN	[34]
			<i>In vitro</i>	DPPH	leaves	Aqueous, methanol		Gauteng	[130]

continued

▶ **Table 2** Continued

Name	Pharmacological activities		Assay type(s)	Method(s)/ inducing agent	Part(s) used	Medium for extraction	Conc. tested	Province(s) or location	References	
	Antioxidant, Antidiabetic	Antihypertensive, cardiovascular								
<i>Tulbaghia violacea</i>	Antioxidant		<i>In vitro</i>	DPPH, reducing power, H <sub>2</sub> O <sub>2</sub>	Rhizome	Methanol	0.02, 10, 20, 30, 40, 50 µg/mL	Eastern Cape	[29]	
	Antidiabetic		<i>In vivo</i>	STZ	Rhizome	Aqueous	60, 120 mg/kg	KZN	[103]	
				ACEI				0.1 g/mL	KZN	
		Antihypertensive	<i>In vitro</i>		Leaves	Methanol, aqueous		60 mg/kg		[18]
			<i>In vivo</i>	Human Angiotensin I, II acetate salt hydrate	Leaves	Methanol			Western Cape	[104]
			Normotensive rats	Leaves			5, 10, 20, 40, 80, 160 mg/kg	Western Cape	[105]	

ACEI: angiotensin converting enzyme inhibitor; STZ: streptozotocin; ABTS: 2, 2'-azino-bis (3-ethylbenzothiazoline-6)-sulphonic acid; DPPH: 1, 1-diphenyl-2-picrylhydrazyl; FRAC: ferrous-reducing antioxidant capacity; ORAC: oxygen radical absorbance capacity; TEAC: Trolox equivalent antioxidant capacity; ISP: isoproterenol; DCM: dichloromethane; KZN: KwaZulu-Natal

agent against streptozocin-induced diabetic Wistar rats was reported when it lowered blood glucose levels after 14 d of administration at 3 concentrations (0.1, 0.25, 0.5 g/mg body weight) [42]. Furthermore, its antibacterial, analgesic, prophylactic, antioxidant, antimicrobial, phytotoxic, and anticoccidial properties, as well as its promotion of fertility and reduction of red blood cells' osmotic fragility, have been mentioned prominently in previous studies.

#### *Amaranthus dubius* Mart ex. Thell.

*A. dubius* is a member of the Amaranthaceae family, with the common name of spleen amaranth. The plant was domesticated in South America and lately instituted in Europe, Asia, and Africa. Medicinally, the plant is used as an antidote for kidney problems, anemia, fever, hemorrhage, stomach troubles [43], and HTN [18], while the potential active phytoconstituents in the plant include but are not limited to ascorbic acid, thiamine, riboflavin,  $\beta$ -carotene, iron, calcium, alkaloids, tannins, saponins, and glycosides. The methanolic extract of the plant showed good inhibition (67%) against ACE (▶ **Table 2**), indicating antihypertensive activity *in vitro* according to Ramesar et al. [18].

#### *Amaranthus hybridus* (L.)

*A. hybridus* is also a member of the Amaranthaceae family endemic to eastern North America, with distribution in other continents such as Asia (Thailand, India, Japan, Lebanon, Pakistan, Indonesia, and Jordan), Africa (SA, Ethiopia, Kenya, Tanzania, and Zambia), and South America (Argentina, Brazil, Peru, and Colombia). The common names (local and international) include green or slim amaranth (English), terere (Kenya), blede, quelite (Spanish), amarante hybride (French), caruru-de-folha-larga (Portuguese), caruru-branco, caruru-roxo (Brazil), bastard-amarant, gruenaeh-riger amarant (Germany), honagaogeito (Japan), and basterdamarant (Netherlands). Aside from being used medicinally as a cure for diarrhea, anemia, menstrual/intestinal bleeding, wound healing, and for burnt or itchy skin [43] with the presence of cardiac glycosides, steroids, flavonoids, and terpenoids as inherent active ingredients, the plant is also cultivated for its nutritive value (protein, vitamins, and minerals) and is consumed in SA and some other African countries as a leafy vegetable. Pharmacologically, *A. hybridus* has been reported to possess antimicrobial, hepatoprotective, anticarcinogenic, and antioxidant activities, as well as *in vitro* antihypertensive activity, when an aqueous extract of the plant was tested at a concentration of 0.1 g/mL against ACE in a South African study [18] (▶ **Table 2**).

#### *Asystasia gangetica* (L.) T. Anderson subsp. *micrantha* (Nees) Ensermu

*A. gangetica*, locally called creeping foxglove (English) or isihobo (Zulu), is associated with the Acanthaceae family (<http://pza.sanbi.org/asystasia-gangetica>). It is a fast-growing herbaceous groundcover plant that extends from 300–600 mm. Based on the information available about its distribution, it is located in tropical areas from Asia to SA (Eastern Cape, KZN, Limpopo, and Mpumalanga) and other southern African countries like Namibia, Botswana, and Swaziland. In fact, the South African subspecies differs from that of the Asian subspecies and has prominent pink flowers. Because of its nutritive value, the leaves are consumed

as a spinach [43], while it is also used in traditional medicine for the management of asthma in many regions of Nigeria. Its active phytoconstituents include flavonoids, phenols, alkaloids, cardiac glycosides, tannins, and terpenoids [44], with 5, 11-epoxymegastigmane glucoside and megastigmane glucoside as some of the isolated compounds. In Nigeria, the antibacterial, antifungal, bronchospasmolytic, antihyperlipidaemic, and anthelmintic activities of *A. gangetica* have been reported. Other pharmacological activities include but are not limited to anti-inflammatory, antihyperglycemic, antioxidant, and cytotoxic [44,45]. Interestingly in a SA study, *A. gangetica* inhibited the activity of ACE *in vitro* [18], while also reducing the BP level and heart rate of spontaneously hypertensive rats when varying concentrations (10–400 mg/kg body weight) of the aqueous extract were administered orally [46] (► **Table 2**).

#### *Catha edulis* (Vahl.) Endl.

*C. edulis*, a member of the Celastraceae family, is a very attractive shrub with glowing green leaves that grows up to 10-m high. Widely distributed in tropical Africa including Ethiopia, SA (KZN, Eastern Cape, Mpumalanga, and Limpopo), and the Arabian Peninsula, the local names are bushman's tea (English), boesmanstee (Afrikaans), umhlwazi (Zulu), iqgwaka (Xhosa), and khat (Arabic). Besides its other uses as firewood, furniture, insect repellent, and fencing poles, it medicinally functions against respiratory diseases, relieving fatigue and sleeplessness, and is also useful as an antidote against cough, asthma, and other chest illnesses [24], as well as for stimulating the heart [26]. In SA, it is regarded as a drug because its active ingredient, cathinone (an alkaloid which is closely related to ephedrine and amphetamine), is listed in the Drug Act. Other polyphenolic compounds including tannins, flavonoids, terpenes, sterols, and essential oils are present [47], from which compounds such as cathidine, cathiduline, norephedrine, and cathinone are isolated. Similarly, the essential oil has also been found to contain carvotanacetone, trans-pulegol, and 2,5-dimethoxy-p-cymene. Pharmacologically, its effect is similar to amphetamine, and it is thus referred to as a natural amphetamine [48]. Other properties include hyperthermia, analgesic, hyperactivity, anorexia, cardiovascular, antimicrobial, antifungal, antibacterial, cytotoxic, antimicrobial, anti-inflammatory, antioxidant, antiulcer, hepatotoxic, and nephrotoxic. In addition, its *in vitro* antihypertensive properties were established by a study conducted in KZN in which aqueous and ethanolic leaf extracts of the plant at 25 µg/mL inhibited the activity of ACE by 48% and 82%, respectively (see ► **Table 2**) [34].

#### *Catharanthus roseus* (L.) G. Don

The common names of this Apocynaceae family plant include Madagascar periwinkle, rose periwinkle, Cape periwinkle, old maid, bright-eyes, and vinca (English). The plant is endemic to Madagascar but may be found in other areas of Africa, such as Kenya, Uganda, Tanzania, and SA [32] as an ornamental or a MP. The plant is traditionally used for treating diabetes, eye inflammation, rheumatism, malaria, and HBP [32]. Vinblastine and vincristine are alkaloids isolated from the herb and are chemotherapeutic agents used for managing various types of cancer [49]. The anti-oxidant, antidiabetic, anthelmintic, antineoplastic, antidiarrheal,

antimicrobial, anticancer, antiulcer, wound healing, hypolipidemic, memory enhancing, and hypotensive activities of the plant were mentioned in a recent review by Nisar et al. [50]. Moreover, in an experiment to evaluate the antihypertensive effect, which was conducted by Naznin et al. using the ethanolic leaf extract of the plant [51], the results showed that the BPs of adrenaline-induced hypertensive rats were lowered when a dose of the extract (30 mg/155 g body weight) was administered to the animals daily for 1 wk, indicating its hypotensive effect. Furthermore, the safety profile of the plant has also been established [52].

#### *Citrus limon* (L.) Osbeck

*C. limon* is commonly named lemon (English) or ulamula (Zulu), and belongs to the Rutaceae family. It is a spiny, all-year-round shrub or small tree that may grow up to 6 m in height. The plant is thought to have originated in Asia and today is one of the most widely homegrown fruit trees. Aside from being rich in vitamin C, which assists in warding off infections, it is traditionally used to treat scurvy, sore throats, fevers, rheumatism, HBP, and chest pain [32]. Moreover, the detected phytochemicals include but are not limited to phenolic acids, flavonoids, triterpenoids, carotenoids, essential oils, and tannins [53], while a series of pharmacological benefits such as anticancer, hypoglycemic, anti-obesity, antimicrobial, antiviral, antihyperlipidemic, antihypercholesterolemic, hypotensive, anti-inflammatory, analgesic, and hepatoprotective [54] have been reported.

#### *Citrus maxima* (Burm.) Merr

*C. maxima*, another Rutaceae family plant is commonly referred to as pummelo (English) or upapamuzi (Zulu). *C. maxima* is a low-branching evergreen tree 5–10 m in height, though it may sometimes grow as tall as 15 m. It is native to Southeast Asia but has distribution in tropical and subtropical regions such as Thailand, southern China, Japan, Indonesia, Malaysia, the Philippines, and the United States. The plant is a natural (nonhybrid) citrus fruit and is the largest of all the citrus species, bearing a great resemblance to the grapefruit, though it is larger, not bitter, and possesses a thicker rind. Traditionally, it is used in the treatment of cough, fever, gastric ailments, HTN, hemorrhage, and epilepsy [32,55]. In a comprehensive review by Vijaylakshmi and Radha [55], its pharmacological properties including antioxidant, antidiabetic, analgesic, anti-inflammatory, antidepressant, anticonvulsant, antitumor, hypnotic, hepatoprotective, antibacterial, antihypercholesterolemic, and hypotensive have been reported. Interestingly, a report by Oboh et al. [56] established the antihypertensive effect of the juice extract of the plant, which inhibited ACE (► **Table 2**) by more than 50%. In addition, the juice reduces the plasma total cholesterol, triglycerides, and low-density lipoprotein-cholesterol levels of rats fed a high cholesterol diet, with subsequent increase in the high-density lipoprotein-cholesterol.

#### *Clausena anisata* (Willd.) Hook. f. ex Benth

*C. anisata* is a member of the Rutaceae family and is locally called isifudu, isifuthu, umsanka, umnukambhiba (Zulu), basternieshout, perdepis, baster-perdepis (Afrikaans), umnukambiba, umnukandiba (Xhosa), and horsewood, or false horsewood (English). The plant is not endemic to SA, but is widely distributed in Eastern

Cape, Free State, KZN, Limpopo, Mpumalanga, and Western Cape. Traditionally, it is used as a remedy for heart diseases [57], tape worm, rheumatism, fever, bad breath, as a blood purifier, and for diseases of the liver [26]. The active phytoconstituents are terpenoids, sesquiterpenes, fatty acids, alkaloids, coumarins, limonoids, essential oils, phenolics, tannins, and saponins [57], with numerous compounds (e.g., limonene, myrcene, umbelliferone, clausanitin, and mupamine) isolated from various parts of the plant (roots, pericarp, root bark, and leaves). Five known compounds have been isolated from the essential oil:  $\beta$ -pinene (32.8%), sabinene (28.3%), germacrene-D (12.7%), estragole (6.4%), and linalool (5.9%), which are found to possess larvicidal action against *Anopheles stephensi* (Culicidae) Liston, *Aedes aegypti* (Culicidae) Linn., and *Culex quinquefasciatus* (Culicidae) Say. When different concentrations of the extract were administered to streptozotocin-induced diabetic rats, their blood glucose levels were restored, demonstrating the plant's hypoglycemic effects [58]. The antioxidant and anti-inflammatory activities of acetone extracts of the plant against lipoxygenase and nitric oxide synthase enzymes; the analgesic, antifungal, antiplasmodial, and antibacterial activity of clausenol (carbazole alkaloids) isolated from the plant; and the activity of crude plant extracts against bacterial and fungal isolates and HIV, as well as their antioxidant, cytotoxic, wound healing, antimalarial, anticonvulsant, anthelmintic, and antimicrobial properties, are available in scientific journals. Interestingly, *C. anisata* was reported to lower BP at a dose of 400 mg/kg in a hypertensive rat model in a 40-d experimental study [59], suggesting its antihypertensive effects.

#### *Crinum macowanii* Baker

*C. macowanii* is a deciduous, summer-growing bulb about 600–2500 cm long, with a fleshy perennial root. This Amaryllidaceae family plant with common names such as river crinum, river lily, sabie crinum, Cape coast lily (English), riverlelie, boslelie, sabielelie (Afrikaans), intelezi (Xhosa), and umdube (Zulu) is indigenous (with 19 other species) to southern Africa, particularly SA (Eastern Cape, Free State, KZN, Mpumalanga, Gauteng, North West, and Limpopo), despite being the most widely distributed of the *Crinum* species. The plant is traditionally embraced as a remedy for kidney and bladder infections, tuberculosis, fever, scrofula, micturition, rheumatic fever, itchy rashes, boils, acne, and venereal ailments [23], as well as for the stimulation of milk production in women and cattle. The active constituents are alkaloids, with more than 11 isolated compounds such as lycorine (major compound), macowine, crinamidine, powelline, crinine, buphanidrine, krepowine, cheryline, undulatine, 4a-dehydroxycrinamabine, and 1-epideacetylbowdensine [60], and it has been reported to have antitumor, analgesic, and hypotensive potential [61]. Other activities include cytotoxic, antimalarial, antiviral against exotic RNA viruses, antifungal, genotoxic, mutagenic, and nematocidal. Additionally, dose-dependent increases in heart rate, as well as systolic and diastolic pressures were observed when anaesthetized normotensive Wistar rats were pretreated with i.v. infusion of the aqueous extract of the plant either singly or in combination with cardioactive substances such as atropine, atenolol, reserpine, prazosin, and verapamil. The effects of the extract on the tested parameters were on par with those of the known cardioactive sub-

stances (except for verapamil in systolic and diastolic pressures), indicating the cardiovascular effects of the plant [62]. Similarly, hippadine (another compound isolated from the plant) at various doses (0.05, 0.10, 0.15, 0.20 mg/kg) has also been reported to lower systolic and diastolic BPs, as well as mean arterial BP, suggesting its antihypertensive [63] and cardiovascular [64] effects.

#### *Dietes iridioides* (L.) Sweet ex Klatt

The rhizomatous *D. iridioides* is an evergreen herb that extends up to 600 mm in height and is sword-shaped with dark-green leaves in a loose fan. It is a member of the Iridaceae family, with local names such as wood iris (English), indawo-yehlathi, isiqiki-sikato-koloshe, and isishuphe somfula (Zulu), and is widely spread from Eastern Cape through KZN to Gauteng in the green forests or cleared bush of SA and Ethiopia. Infusions of the inner contents of the rhizomes are orally taken to stop dysentery [26]. Similarly, the rhizomes are used during childbirth and for HTN control [65], while they may also serve as constituents of tonics used in goats and sheep. The *in vitro* antiprotozoal and antihypertensive effects were suggested by Duncan et al., who reported that it inhibited the activity of ACE when evaluated with other Zulu plants [34] (► **Table 2**).

#### *Dombeya rotundifolia* Hochst

Wild pear (English), drolpeer (Afrikaans), iNhliziyonkhulu (Zulu), mohlalaphala (Northern Sotho), motubane (Tswana), and nsihaphukuma (Tsonga) are local names for *D. rotundifolia*, a member of the Malvaceae family. It is a deciduous, fast-growing, and frost- and drought-resistant tree that grows up to 10 m in height but is usually between 3 and 6 m. Medicinally, the inner bark is used to treat weakness of the heart. Other uses of various parts of the plant are to treat intestinal ulceration, stomach troubles, and sharp stomach pains, fever, diarrhea, palpitation, nausea, enemas for dyspepsia, and to induce labor [24, 26]. Its identified chemical moieties include but are not limited to saponins, tannins, and cardiac glycosides [66], with a few isolated compounds such as lauric, myristic, stearic, and palmitic acids with antibacterial activity. Similarly, reports of lupeol and  $\beta$ -sitosterol being isolated from the bark of the stem have been documented [67]. Reported biological activities are antibacterial, anti-inflammatory [66], anthelmintic, antidiarrheal, and abortifacient. Furthermore, Duncan et al. [34] suggested that ethanolic extracts of the plant leaf have antihypertensive effects based on their inhibition of ACE (83%) (► **Table 2**).

#### *Ekebergia capensis* Sparrm.

*E. capensis* is an evergreen tree in the Meliaceae family with the potential to grow as high as 15 m, existing in different habitats ranging from high altitude evergreen forests to riverine forests, and from sea level to approximately 1500 m above sea level. Commonly called Cape ash, dogplum (English), essenhout (Afrikaans), mmidibidi (Northern Sotho), umnyamatsi (Southern Sotho), and nyamaru (Tswana), *E. capensis* grows in southern Mozambique, Zimbabwe, Swaziland, Uganda, Ethiopia, Congo, and SA, especially Eastern Cape, KZN, and Limpopo. It is used to treat various disease conditions, such as dysentery, heartburn, cough, acute gastritis, headache, scabies, abscesses, boils, and acne. Moreover, the antimicrobial, antituberculous, antitrypanosomal, cytotoxic,



antimicrobial, anti-inflammatory, mutagenic, antimutagenic, antimalarial, and uterogenic potential of the plant have been affirmed. Similarly, Kamadyaapa et al. [68] reported that acute intravenous (18 mg/kg) and subchronic oral (120 mg/kg) administration of ethanolic leaf extracts of the plant resulted in a hypotensive effect on anaesthetized normotensive rats, while it also prevented the onset of HBP in weanling Dahl salt stress rats [69], suggesting a vasorelaxing action mediated via endothelium-derived relaxing factor-dependent or independent pathways, as well as a hypotensive effect mediated by regulating the total peripheral resistance of the vascular smooth muscles [70]. The chemical constituents of *E. capensis* are glycosides, polyphenols, tannins, triterpenes (major), and saponins. Further efforts to isolate the photoactive compounds yielded oleanonic acid; 2,3,22,23-tetrahydroxy-2,6,10,15,19,23-hexamethyl-6,10,14,18-tetracosatetraene; oleanolic acid, ekeberin A; proceranolide; kaempferol-3-*O*- $\beta$ -D-glucopyranoside; 3-*epi*-oleanolic acid; quercetin-3-*O*- $\beta$ -D-glucopyranoside and 2-hydroxymethyl-2,3,22,23-tetrahydroxy-6,10,15,19,23-pentamethyl-6,10,14,18-tetracosatetraene from triterpenoids, some of which have been found to possess antimalarial, cytotoxic, hypoglycemic, and antihypertensive activities [71, 72].

#### *Galinsoga parviflora* (Cav.)

*G. parviflora* is an herbaceous plant from the Asteraceae family. It is endemic to South America but is well distributed in tropical, subtropical, and temperate regions of the world. Locally called chickweed, gallant soldier, or kew weed (English), the herb is about 60–75 cm tall, with oppositely clustered leaves that are toothed at the margins. Isolated compounds identified within the plant are apigenin, 7- $\beta$ -d-glucoside, luteolin, phytol, stigmasterol,  $\beta$ -sitosterol, fumaric acid, uracil emanating from flavonoids and so on [73]. It is used as flavoring in the preparation of ajiaco soup, a very common and popular soup to the people of Colombia, Cuba, and Peru, and is also used in fruit salads. Medicinally, it is used for curing sores, colds, and wound healing. Pharmacologically, the plant possesses antibacterial, anti-inflammatory, wound healing, antioxidant, and allelopathic effects, as well as having established antihypertensive activity, as a methanolic extract inhibited the activity of ACE by 56% in a study conducted by Ramesar et al. [18] (► **Table 2**).

#### *Hypoxis hemerocallidea* Fisch., C. A. Mey. & Ave-Lall

*H. hemerocallidea*, honored as the “miracle muti” and “wonder potato” by the majority of South African herbal users, is a very beautiful, tuberous, perennial member of the Hypoxidaceae family, with a yellow star-like flower that signifies the onset of spring and summer rains. Commonly referred to as starflower and other names [74], the plant is medicinally employed in SA as an antidote for various human and veterinary diseases and is likely the most highly researched plant in Africa. It is useful against numerous ailments such as heart weakness, stroke, HBP [29], cancer, testicular tumors, infertility (male and female), headaches, dizziness, urinary tract infections, psychiatric disorders, and burns [26], while the prominent phytoconstituents include but are not limited to phytosterol glucosides ( $\beta$ -sitosterol), diglucoside hypoxoside, aglycone rooperol, sterols, and sterolins [25, 26]. Interestingly,

several pharmacological indications such as antioxidant, antibacterial, anticonvulsant, antiviral, antidiarrheal, antinociceptive, anti-inflammatory, antidiabetic, uterolytic, anti-HIV, anticancer, and cardiovascular effects of the plant have been reported in our recent review and those of others [74]. The cardiovascular effects as reported by Ojewole et al. [75] were revealed when the aqueous corm extract (12.5–400 mg/mL) of the plant produced prominent inotropic and chronotropic responses on the myocardial contractility of excised guinea pig muscles. This finding was corroborated in an animal model when the extract (25–400 mg/kg) lowered the systemic arterial BP and heart rate of Dahl salt-stress hypertensive rats, indicating the antihypertensive effect of the extract (► **Table 2**).

#### *Justicia flava* (Vahl) Vahl

*J. flava*, a perennial herb or shrub, is a member of the Acanthaceae family locally called yellow justice (English), geelgarnaalbos (Afrikaans), and impela (Zulu), and is widely distributed from tropical east Africa to SA (North West, Eastern Cape, KZN, Limpopo, Gauteng). In folkloric medicine, it is used to treat cough, stomach pain, diarrhea, fevers, dysentery, and convulsions [26]. The active constituents are  $\beta$ -sitosterol, stigmasterol, campesterol,  $\beta$ -sitosterol- $\beta$ -D-glucoside, and salicylic acid. In addition, its isolated compounds such as lignans, justicinol, helioxanthin, (+)-isolariciresinol, docosanoic acid, podophyllotoxin and  $\beta$ -sitosterol- $\beta$ -D-glucoside, orosunol, 8-demethyl-orsunol [26, 76] have been tested and shown to possess antiviral and antitumor activities. Similarly, the aqueous leaf extract of the plant was reported to inhibit the activity of ACE (by 53%) in an *in vitro* study conducted in KZN (► **Table 2**), suggesting the antihypertensive potential of the plant [18].

#### *Mesembryanthemum* species

The genus *Mesembryanthemum* in the family Aizoaceae comprises 25 species endemic to the northern hemisphere and southern Africa. The most common of the 25 species are *Mesembryanthemum crystallinum* (Linn.) and *Mesembryanthemum nodiflorum* (Linn.). The former is a robust succulent herb or dense prostrate shrub of up to 1 m wide. However, in terms of morphology, *nodiflorum* resembles *M. crystallinum*, except smaller in virtually all parts. It is used medicinally to treat bad dreams, heart weakness, HBP, stomach, and other gastrointestinal ailments, swellings, dropsy, and general body pain [26, 34]. The antihypertensive activity of the plant has been investigated following the work of Duncan et al. [34], in which the aqueous leaf and ethanolic stem extracts of the plant inhibited the activity of ACE by 90% and 57%, respectively (► **Table 2**).

#### *Momordica balsamina* (L.)

*M. balsamina* belongs to the Cucurbitaceae family, with balsam pear (English), laloentjie (Afrikaans), intshungu, intshungwana yehlathi (Zulu), and mohodu (Sotho) as its common names. The plant is a climbing perennial herb containing a prostrate or climbing stem (5 m high), and is native to tropical Africa, Asia, Arabia, India, and Australia, but may be found in most provinces in SA (except Western Cape), as well as Namibia, Botswana, and Swaziland among other Africa countries. Besides the fact that most of its parts are consumed as a food source, it is indigenously used to

treat stomach and intestinal ailments [26], as well as diabetes, headaches, boils, sores, HBP, burns, and wounds. [32,77]. The phytochemical screening of various parts of the plant have established the presence of major secondary metabolites such as alkaloids, flavonoids, saponins, terpenes, and steroids attributed to numerous medicinal activities including anti-HIV, hepatoprotective, antiplasmodial, antimicrobial, antidiarrheal, anti-inflammatory, antidiabetic, analgesic, antiseptic, antioxidant, antibacterial, and antihypertensive [77].

#### *Momordica charantia* (L.)

*M. charantia* is a tropical and/or subtropical plant belonging to the Cucurbitaceae family with common names such as bitter melon, bitter gourd, bitter squash, or balsam pear (English). The plant is indigenous to India but is widely distributed in Asia, Africa, and the Caribbean, owing to its edible fruits. It grows up to 5 m in height, bears simple, alternate leaves (4–12 cm) with 3–7 deeply differentiated lobes. Medicinally, it is used as a treatment for stomach ailments, diabetes, cough, respiratory diseases, skin diseases, wounds, ulcers, gout, rheumatism, HBP, menstrual problems, cancer, and HIV/AIDS [78], while its active constituents consist of triterpenes, protein, steroids, polyphenols, alkaloids, lipids, and inorganics [79]. The pharmacological implications of the plant as an antioxidant, antidiabetic, anticancer, antitumor, antiviral, antimicrobial, antigenotoxic, anthelmintic, antimalarial, antineoplastic, antiulcerative, and immunomodulatory were extensively reviewed in an updated report by Gupta et al. [80]. In a South African study, the hypoglycemic and hypotensive effects of *M. charantia* were presented by Oyewole et al. [75], wherein aqueous extract of the whole plant at concentrations of 50, 100, 200, 400, and 800 mg/kg were found to restore the normal plasma glucose level of streptozotocin-induced diabetic Wistar rats in a dose-dependent manner, while similarly reducing the systemic BP and heart rates of Dahl salt-stress hypertensive rats, suggesting its antihyperglycemic and antihypertensive activities (► **Table 2**).

#### *Ocimum basilicum* (L.)

*O. basilicum* is a characteristic herb ascribed to the Lamiaceae family. Its local names are basil, great basil, Saint-Joseph's wort, royal herb, and king of herbs, and it is native to India. *O. basilicum* is a perennial herb that grows to a length of 0.5 m and has monoecious flowers (i.e., possessing both male and female reproductive organs). Medicinally, the plant is used for a plethora of ailments such as digestive and nervous system ailments, colic and indigestion, nausea, abdominal cramps, snake bites, skin diseases, gonorrhea, diarrhea, earache, dysentery, itching, malaria, and menstrual dysfunction [81]. The essential oil and other phytochemicals contain linalool, eugenol,  $\alpha$ -cubebene, caryophyllene, rosmarinic, estragole, and methyl cinammate [82], which are bioactive as anticonvulsants, hypnotics, antimicrobials, and antifungals, as well as anti-sickling agents [82]. Interestingly, the radical scavenging, antioxidant, antiseptic, insecticidal, and anti-sickling activities of the extracts from *O. basilicum* are reported in previous studies. Additionally, an updated and exhaustive review of its pharmacological properties such as analgesic, anti-inflammatory, hypoglycemic, hepatoprotective, antihyperlipidemic, antiulcerative, cardioprotective, stimulatory, sedative, hypnotic, anticonvulsant,

memory retention, stroke preventive, antimicrobial, antiviral, antimycobacterial, chemo-modulatory, immuno-modulatory, anticancer, anti-osteoporotic, antihypertensive, and antithrombotic, as well as a safety profile of the plant, have been reported by Miraj and Kiani [83].

#### *Olea europaea* (L.) subsp. *africana* (Mill.) P. S. Green

The Oleaceae family houses the genus *Olea*, of which the species *europaea* is a member, and has common names such as wild olive (English), olienhout (Afrikaans), mohlware (South Sotho, North Sotho), umnquma (Xhosa, Zulu, and Swati), mutilwari (Venda), and motlware (Tswana). It is a small to medium-sized tree growing between 5 m, and to as tall as 18 m. It is predominant in SA, where it was previously referred to as *O. africana* and is a small-fruited subspecies of the commercial olive [24]. While the plant is widespread in Eastern Cape, KZN, Western Cape, Mpumalanga, Northern Cape, Limpopo, North West, and Gauteng, it is medicinally used to lower BP [23,26,29], enhance renal function, alleviate colic, to act as diuretics, tonics, and antidiarrheals, and to treat sore throats [26]. The phytochemicals include but are not limited to isolated flavonoids, essential oils, flavone glycosides, biphenols, sugars, sterols, triterpenoids, secoiridoids, and phenolic compounds including oleuropein (major),  $\alpha$ -pinene, rutin, ursolic acid, oleanoic acid, uvaol, apigenin, and luteolin, which have anticancer, antidiabetic, antimicrobial, antiatherosclerotic, antihypertensive, antioxidant, cardiovascular, antidysrhythmic, and antihyperlipidemic properties [71,84]. Moreover, the pharmacological investigations on the various parts of the plant from different regions of the world were revealed in a complete review presented by Hashim et al., and included antidiabetic, anticancer, antimicrobial, antioxidant, antihypertensive, cardioprotective, anti-inflammatory, gastroprotective, and neuroprotective activities [84].

#### *Opuntia ficus-indica* (Mill)

Indigenous to Mexico, *O. ficus-indica*, the most common, domesticated, and studied member of the Cactaceae family [85], is locally referred to as Indian fig, mission prickly pear (English) boereturksvy or grootdoringturksvy (Afrikaans), and umthelekisi (Zulu). It is a succulent, branched shrub or tree growing up to 3 m with a sturdy trunk. Besides being widespread in other places such as Australia, southern Europe, Africa (SA, Uganda, and Kenya), and southern, northern, and central America, the plant is ethnobotanically used to cure gonorrhoea and HBP by Bapedi traditional healers of the Limpopo Province [31] in SA, as well as diabetes, ulcers, burns, and asthma in different parts of the world. The chemical constituents include but are not limited to sugars (glucose and galactose), flavonoids, phenols, vitamins (ascorbic acid, vitamin A, B, K), and minerals (Ca, Mg, Na, P) from various parts of the plant [86], with compounds such as quercetin, kaempferol, piscidic acid, sinapoyl-glucose, rutin, and catechin [85] isolated to provide hypoglycemic, antiatherosclerotic, and antihyperlipidemic effects [85]. Pharmacologically, the antiulcer, anti-inflammatory, neuroprotective, anticancer, antiviral, antidiabetic, antioxidant, antihyperlipidemic, antihypertensive, antimicrobial, wound healing (cicatrising), antiatherogenic, antihyperinsulinemic, and hepatoprotective effects of the plant have been reviewed and reported by Kaur et al. [86], in addition to other available reviews.

### *Oxygonum sinuatum* (Hochst. & Steud. Ex Meisn.) Dammer

*O. sinuatum*, otherwise known as *Ceratogonum sinuatum* among others names, belongs to the Polygonaceae family. It is a less erect, branched herb widely distributed in eastern and southern Africa including South Sudan, Angola, Ethiopia, Uganda, Kenya, Congo, and SA. Irrespective of its acceptance as an edible vegetable in some parts of the continent, it is employed for the treatment of boils, tonsillitis, and fungal infections (eyes, legs). Moreover, its antihypertensive activity has been reported by Ramesar et al., along with that of 16 other Zulu nutritive MPs [18], when 50 microliters (0.1 g/mL) of the aqueous leaf extract inhibited the activity of ACE by 59% (► Table 2).

### *Persea americana* (Mill)

The Lauraceae family houses the genus *Persea* of which the species *americana* is a member. *P. americana* is referred to as avocado, with numerous synonyms including but not limited to *Persea edulis* (Raf.), *Persea gigantea* (L. O. Williams), and *Persea gratissima* (C. F. Gaertn.). *P. americana*, thought to have originated in Mexico and central America, is a fast-growing tree or shrub popular for its edible, green-fleshed fruits. It grows up to 40 m tall, but most are no taller than 20 m. Medicinally, the plant is used to treat ulcers, diabetes, and HTN [31], while the active constituents include but are not limited to terpenoids, glycosides, flavonoids, and coumarin [87]. The pharmacological relevance of the plants as anti-inflammatory, vasorelaxant, analgesic, hypotensive, anticonvulsant, antiviral, wound healing, antiulcer, antihepatotoxic, antioxidant, hypoglycemic, antimalarial, antithrombotic, antihypercholesterolemic, antiarthritic, cardiovascular, haemopoietic, and antihyperlipidemic, as well as its safety profile, have been reported by Yasir et al. [87] and Tcheghebe et al. [88] in their exhaustive reviews. Moreover, in addition to the above-mentioned pharmacological activities, the immunomodulatory, antimicrobial, cytotoxic, and antioxidant effects are also reported.

### *Physalis viscosa* (L.)

*P. viscosa* is a rhizomatous perennial herb in the Solanaceae family with local names including starhair ground cherry, stellate ground cherry, grape ground cherry (English), and arrebenta-cavalo (Portuguese). Native to South America and widely distributed on other continents, *P. viscosa* is endowed with a hairy stem and grows up to 400 mm in length. Medicinally, it is used for urine suppression, fever, gout, wounds, anemia, and as a diuretic, while the antihypertensive effect is affirmed in a study conducted by Ramesar et al., when the methanolic leaf extract *in vitro* inhibited ACE by 60% [18].

### *Protorhus longifolia* (Bernh. Ex C. Krauss) Engl.

*P. longifolia* is a tree in the Anacardiaceae family with common names such as red beech, purple currant, red Cape beech (English), rooiboekenhout, rooimelkhout (Afrikaans), ikhubalo, isifuce (Xhosa), umkomiso, and uzintlwa (Zulu). It is a fast-growing, single-stemmed, evergreen garden plant that grows up to 15 m in height, with the ability to withstand frost and drought. *P. longifolia* is indigenous to Swaziland and SA, with major distribution in Eastern Cape, KZN, Limpopo, and Mpumalanga. Traditionally, its use for the treatment of HBP, heartburn, internal bleeding, diarrhea

(both in humans and cattle), dysentery, lightning shock, cramps, and swollen legs has been documented [26,65]. The antiplatelet aggregation, antioxidant, cytotoxic, antimycobacterial and antimicrobial effects of the crude extract are reported [89], while a lanosteryl triterpene isolated from the plant has also shown anti-hyperlipidemic, antihyperglycemic, anticoagulant, anti-inflammatory, and cardioprotective effects [90]. Additionally, the antihypertensive property of aqueous (64%) and ethanolic (77%) leaf extracts against ACE has also been reported [34].

### *Psidium guajava* (Linn.)

*P. guajava* is a member of the Myrtaceae family called Koejawel in Afrikaans. It is an evergreen shrub or tree with hairy branchlets growing up to 10 m high. It is endemic to the Caribbean, Central America, and South America, and is used medicinally for inflammation, diabetes, HTN, diarrhea, rheumatism, ulcers, wounds, pain, fever, and lung ailments [31,91]. The chemical constituents include tannins, essential oils, sterols, flavonoids, phenolics, saponins, triterpenes, carbohydrates, fats, proteins, and vitamins, while the compounds isolated from various parts of the plant, such as  $\alpha$ -pinene, limonene,  $\beta$ -pinene,  $\beta$ -sitosterol, ascorbic acid, thiamine, nerolidol, 3-caryophyllene, and so on [91], have been established. Similarly, Gutierrez et al. [91] submitted its antidiarrheal, antimicrobial, anti-inflammatory, antimalarial, antitussive, antioxidant, hepatoprotective, antigenotoxic, antimutagenic, antiallergic, anticancer, cardiovascular, hypotensive, antihyperglycemic, analgesic, antinociceptive, and wound healing effects, as well as the safety profile of *P. guajava* in a comprehensive review, which has been updated recently by Díaz de Cerio et al. [92]. In another study, Ojewole [93] established the hypoglycemic and hypotensive effects of the plant when an aqueous extract, orally administered caused a dose-dependent (50–800 mg/kg body weight) normoglycemic and antihyperglycemic effect, as well as a significant reduction in systemic arterial BPs and heart rates in streptozotocin-induced diabetic and Dahl salt-stress hypertensive rats.

### *Ptaeroxylon obliquum* (Thunb.) Radlk.

Sneezewood (English), nieshout (Afrikaans), and umThathi (Xhosa, Zulu) are the local given names of *P. obliquum*, a member of the Rutaceae family. Endemic to the southern African countries, including Zimbabwe, Mozambique, and SA, particularly Eastern Cape, Western Cape, Mpumalanga, KZN, and Limpopo, sneezewood trees are endowed with oppositely arranged leaves with 3–8 leaflets clearly asymmetrical in shape. Medicinally, the plant is used to alleviate headaches, repel moths, cure heart diseases, and for wound healing (in both cattle and humans, particularly after circumcision), myiasis [24], cough, dysentery, malaria, itching, and chest pain, among other uses. Its antibacterial, broad-spectrum immune modulation, antioxidant, antifungal, mosquitoicidal, cytotoxic, and hypotensive [94] effects have been documented.

### *Rauvolfia caffra* (Sond.)

*R. caffra*'s common names include but are not limited to quinine tree (English), kinaboom (Afrikaans), umJelo (Xhosa), and umHlambamanzi (Zulu). It is a fast-growing, evergreen tree of

about 300 cm in height. In terms of distribution, roughly 60 species of the genus *Rauvolfia* exist, 7 of them are found predominantly in Africa, 3 in Madagascar, and *caffra*, which is found primarily in southern Africa, particularly Swaziland, and most provinces in SA (Eastern Cape, KZN, Mpumalanga, Limpopo, Gauteng, and North West). Its indigenous usages are wound healing and to treat coughs, diarrhea, stomach ailments, and HBP [95], while it also possesses alkaloids, terpenoids, flavonoids, and polyphenols as some of its chemical components [96], as well as reserpine, which has been demonstrated to have HBP-lowering effects [97]. Its various pharmacological properties such as antioxidant, antimycobacterial, antimicrobial, molluscicidal, anticancer, anti-inflammatory, antitrypanosomal, and antimalarial, as well as antihypertensive activity when various doses (15, 300, 500 mg/kg bw) of the plant extracts (methanolic, ethyl acetate, and dichloromethane) brought down the systolic and diastolic BP in spontaneously-hypertensive rats [96] are reported.

#### *Rhus chirindensis* (Baker) f.

*R. chirindensis*, otherwise referred to as *Searsia chirindensis* (Baker f.) Moffett, is an average-sized semi-deciduous tree (about 10 m in height) belonging to the Anacardiaceae family. The plant is native to SA and found along the coastal belt sparing from the Cape through KZN to other parts of southern Africa such as Swaziland, Mozambique, Tanzania, and Zimbabwe. Its common names include red currant (English), bostaaibos (Afrikaans), muvhadelaphanga (Venda), umhlabamvudu (Zulu), and umhlokothi (Xhosa). Traditionally, *R. chirindensis* has been applied in the treatment of measles, cough, chest pain, syphilis, convulsions, and epilepsy in most rural populations of SA, as well as in the management of HBP [26]. Pharmacologically, the anticonvulsant, analgesic, anti-inflammatory, hypoglycemic, antioxidant, cytotoxic, anti-HIV, and antibacterial activities of the plant have been reported [98]. The ethanolic leaf extract of the plant has been confirmed to possess antihypertensive activity when it inhibits the activity of ACE by 85% [34].

#### *Sclerocarya birrea* (A.Rich.) Hochst. subsp. *caffra* (Sond.) Kokwaro

This member of the Anacardiaceae family is commonly referred to as jelly plum, cat thorn, cidar tree, marula (English), morula (Sotho), mufula (Tshivenda), mufuna, mupfura, mushomo (Shona), ukanyi (Tsonga), umganu (Ndebele), and maroela (Afrikaans), with distribution in the Miombo woodlands of southern Africa (KZN, Limpopo and Mpumalanga, Zimbabwe, Mozambique, and Ethiopia), the Sudano-Saharan region of West Africa and Madagascar. It is a medium-large sized deciduous tree that grows as high as 12 m. Besides its major phytochemical components, such as phenolics, saponins, flavonoids, essential oils, and tannins [99], the traditional uses (such as treatment of HTN [26]) of various parts of the plant have been documented in various nations of Africa [99]. The bark is used for dysentery, diarrhea, rheumatism, malaria, hemorrhoids, and to determine the sex of an unborn child. The leaves are used for curing gonorrhoea, while the fruits are edible—eaten raw or turned into a delicious jelly or used to make a local alcoholic drink, mukumbi (by the Venda people), which is now a commercialized liquor. Interestingly, numerous

pharmacological properties have been thoroughly reviewed by Ojewole et al. [99], including anticonvulsant, antihypertensive, antibacterial, antifungal, antihelminthic, antiplasmodial, hypoglycemic, analgesic, anti-inflammatory, antidiarrheal, antioxidant, as well as in the treatment of renal and skeletal muscle disorders. The aqueous extract of the stem-bark of the plant orally administered at various concentrations (25–1600 mg/mL) lowered the blood glucose level of diabetic streptozotocin Wistar rats in a dose-dependent manner, with 800 mg/mL exhibiting optimal reduction, and reduced the systemic arterial BP as well as the heart rates of hypertensive rats [100, 101].

#### *Stangeria eriopus* (Kunze) Baill

A perennial member of the Zamiaceae family, it is locally referred to as Stanger's cycad, natal grass cycad (English), bobbejaakos (Afrikaans), imfingo (Zulu), and umfingwani (Xhosa). *S. eriopus* is a slow-growing perennial plant consisting of large fern-like leaves (0.25–2.0 m); a swollen, carrot-shaped tuberous root; and an upper stem that reveals branches with up to 10 heads. The plant is also monoecious (male and female reproductive organs existing on separate plants) and coniferous, with its cones giving rise to each point of growth. The male cone is cylindrical in shape and tapers at the tip reaching a diameter of 3–4 cm at maturity (yellowish-brown), while the female cone is 18 × 8 cm in diameter and is egg-shaped or ellipsoidal to conical with a rounded tip, turning a dark-green color at maturity. It is endemic to the east coast of SA (KZN, Eastern Cape) and southern Mozambique, and is used to treat headaches, internal parasites in cattle, and HTN [24, 26, 34], with macrozamin (methylazoxymethanol glycoside) as its major phytoconstituent [102]. Pharmacologically, the activity of its aqueous leaf extract against ACE has been reported in the work of Duncan et al. [34], establishing its *in vitro* antihypertensive effect with 55% inhibition.

#### *Tulbaghia violacea* Harv.

*T. violacea* is a member of the Alliaceae family, with common names such as wild garlic (English), wildeknoeflok, and wilde knoefel (Afrikaans), is a rapid-growing, bulbous plant extending to 0.5 m in height (25 cm wide). This plant, among the other 29 *Tulbaghia* species, is endemic to southern Africa particularly SA (Eastern Cape, KZN, Limpopo) and Zimbabwe, with various indigenous applications. It is used as an aphrodisiac, as well as to treat sinus conditions, headaches, cough, colds, asthma, tuberculosis (pulmonary), intestinal worms, HTN, and cancer of the esophagus [24, 27, 29, 30, 33], owing to its numerous pharmacological and biological properties. Besides the fact that it possesses sulfur-containing compounds (e.g., alliin), showing much resemblance to *Allium ursinum* (Amaryllidaceae) Linn. in odor, the leaves and flowers are consumed as a leafy green vegetable, and it is worth noting that it may also be used as a seasoning. The antioxidant, cytotoxic, antiparasitic, antimicrobial, antibacterial, anthelmintic, antiamebic, antidiabetic, hypolipidemic, anti-HIV, antithrombotic, androgenic, anticancer, and antihypertensive properties [18, 29, 34, 103] of the plant have been reported, as has the safety profile. In fact, in a study by Raji et al. [104, 105], a methanolic leaf extract of the plant at various concentrations (5, 10, 20, 40, 60, 80, 160 mg/kg b.w.) lowered the BP (systolic, diastolic), mean ar-



terial pressure and heart rate of ageing male normotensive and adult male spontaneously hypertensive rats in a dose-dependent manner, suggesting its antihypertensive effects. Similarly, Ramesar and others [18] reported the inhibition of ACE using aqueous (68%) and methanolic (71%) extracts of the plant in an *in vitro* study. Additionally, Duncan et al. [34] submitted that aqueous extracts of the leaf and bark inhibited ACE by 72% and 49%, respectively, while ethanolic leaf extracts inhibited the activity of the enzyme by 61%.

### ***Turraea floribunda* Hochst.**

Honeysuckle tree, wild honeysuckle tree (English), kanferfoelieboom (Afrikaans), umdlozana (Swazi), and umadlozane (Zulu) are the common names of *T. floribunda*, a member of the Meliaceae family. It is a fast-growing, slender, small to medium-sized deciduous tree that grows to between 10–15 m in height and is single or multi-stemmed and loosely branched. Found in rocky areas in woodland and forested ravines, its global distribution includes countries like Congo, Uganda, Mozambique, Kenya, Zimbabwe, Malawi, Tanzania, Swaziland, Uganda, and SA, especially Eastern Cape, KZN. Medicinally, it can be used to manage rheumatism, dropsy, heart disorders, malaria, including its use as a purgative, enema, and emetic (use in trance by the Sangomas) [106]. Besides the presence of limonoids, turraflorins, tetranortriterpenoids, and phytoconstituents [107, 108], pharmacologically, the antitrypanosomal, larvicidal, antioxidant, anti-inflammatory, anticholinesterase, mutagenic, antimalarial, and antibacterial properties of the plant have been reported. Notwithstanding the above properties, an aqueous leaf extract of the plant showed weak inhibition (45%) of ACE in a study conducted by Duncan et al. [34], thus established its weak antihypertensive effect.

## Discussion

The use of MPs and or phytotherapy against a variety of human diseases is no longer considered an archaic practice, as its global acceptance continues to rise. This is attributed to their assumed safety, efficacy, cost-effectiveness and minimal side effects [17, 18]. Interestingly, their role in the treatment of CVD, including HTN, have contributed greatly to cardiovascular studies [109], owing to the challenging prevalence and burden of HTN, as well as the ineffectiveness and/or expense of antihypertensive single drug therapy, among others. The information in this review has been gathered from numerous sources and includes over 100 MPs whose various parts (particularly leaves and roots) or whole plants are prepared (mostly by maceration or decoction) and applied on a regular basis for the management of HBP by traditional healers residing, practicing and/or hailing from different tribes (Zulu, Xhosa, Sotho) across the republic of SA. It is noteworthy that 27 of these plants have been identified as having BP-lowering effects through either *in vitro* or *in vivo* studies or evaluated with both, despite the evaluation of almost half of all plants reviewed reflecting that 17 of these plants inhibit the activity of ACE using *in vitro* assays, others have been further confirmed in animal (Dahl-salt stress and or sodium thiopentone-induced) studies as potential antihypertensives. Additionally, most of the assays described and corroborated the use of polar solvents—primarily

water, methanol and ethanol (► **Table 2**)—by indigenous traditional healers as the most effective medium for extracting active components from plants. Similarly, the detection of saponins, tannins, flavonoids and alkaloids in most of the plants with reported antihypertensive effects suggests that these phytochemicals may be responsible for their BP-reducing effects. Moreover, the isolation of alkaloids having reported antihypertensive effects from these plants—including but not limited to hippane, lycorine (*C. macowanii*) and reserpine (*R. caffra*)—supports the latter submission.

Notwithstanding the *in vitro* evaluations of the plants, it is imperative to submit that such testing cannot be used to confirm the pharmacological activity of a MP unless it is buttressed by an *in vivo* study. It is therefore pertinent that more efforts be made by stakeholders (researchers, scientists, medicinal practitioners, institutes, and pharmaceutical companies) toward confirming the pharmacological effect of these indigenously used antihypertensive MPs. In addition, those that have remained unassessed should be evaluated *in vitro* to investigate their pharmaceutical properties and gain additional insights into their potential pharmaceutical uses, leading to the development of effective, safe, and perhaps novel moieties or formulations to curb the prevalence of HBP.

Toxicity studies provide the assessment of safety profiles for MPs or drug substances (formulations), and may be acute, subacute, chronic, or subchronic. However, despite the pharmacological activities of many MPs and the general assumption that they are safer than conventional medicines in the treatment and/or management of diseases, there are compelling arguments regarding their safety, as some of them are understood to cause ill-effects in experimental animals. Intriguingly, plants such as *Aloe ferox*, *Hoodia gordonii*, *C. roseus*, and *Artemia afra* have not only established their potential in alleviating HBP, but are also reported to be nontoxic [52, 116], suggesting that they may be studied in clinical trials, thus presenting an excellent prospect for the development of pharmaceuticals to control HTN.

### Future studies

Based on our observations in the present review, the following studies are proposed:

- Intensified efforts to subject traditional antihypertensive plants to initial *in vitro* and *in vivo* pharmacological activity screening.
- Isolation and elucidation of bioactive compounds against HTN to confirm that they are responsible for the elicited effects. Thus far, most of the MPs with BP-lowering effects have not been subjected to isolation processes, an area requiring urgent attention.
- The global or general acceptance of MPs as an alternative therapy to orthodox medicine requires that the drug moieties discovered should be able to pass all the rigorous processes of drug development. Hence, there is need for all the plants already demonstrated as safe and effective in reported studies to be subjected to rigorous clinical trials for subsequent drug formulation and eventual commercialization.

In conclusion, HTN is a disease attributed to an increased risk of many chronic complications such as CHD, CCD, stroke, cardiac arrest, renal insufficiency, myocardial infarction, and so on. However, the current management of HBP with synthetic antihypertensives is characterized by various side effects such as dizziness, blurred vision, skin rash, muscle cramps and tiredness, while the use of phytotherapy has continued to receive wider interest and publicity owing to their therapeutic properties and minimal side effects. This review highlights that many documented antihypertensive MPs have not been adequately explored or pharmacologically proven. Hence, there is a need for the government to sponsor additional research to establish the efficacy and safety of these plants as alternative options to curb or manage HBP.

## Methodology

Exhaustive literature search was used for this review on Google Scholar and research articles from scientific databases such as Science Direct, PubMed, JSTOR, and Medicine were adopted. Most of the articles used centers between 2000 to 2018 and more than 700 journals, over 20 dissertations/theses, and 5 books were retrieved, with emphasis being placed on the antihypertensive activities of the MPs when keywords such as SA, MPs, HTN, hypotension, HBP, and antihypertensive as well as languages particularly Zulu, Xhosa, Sotho, and Afrikaans were provided to browsing engine. Information on other pharmacological activities of the documented plants aside their antihypertensive properties (► **Tables 1 and 2**) were sourced from 458 peer-reviewed articles.

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## Conflict of Interest

The authors declare no conflicts of interest.

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