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Review Article

The Pharmacology and Therapeutic Value of Conventional Antihypertensive Drugs in the Management of Hypertension: An Ethno-Botanical Review of Commonly Used Antihypertensive Medicinal Plants in Arsi Zone, South-East Ethiopia

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ABSTRACT

Plants have been used to treat a wide range of diseases throughout the history of human beings and this practice continues to date. In traditional methods, plant materials are tested for pharmaceutical purposes. Natural products from plants remain vital in drug discovery where they can be used directly as drugs or serve as leads to new drugs by providing chemical entities. Hypertension (HTN) is a progressive cardiovascular disease characterized by persistently elevated systemic blood pressure. If left uncontrolled, HTN will become the major cause of human suffering as well as imposing severe economic and service burdens on health systems. Today on the market there are large armamentaria of conventional antihypertensive drugs, however, the major concerns that often delay treatment allude to higher costs, unavailability and inaccessibility, undesired side effects of antihypertensive drugs and reduced patient compliance to consume more than a pill per day. The search for natural, cheaper, and nontoxic compounds is becoming necessary. In the past, the drug discovery of the biological compounds from plant materials and the process of identifying the structures of active compounds from the extracts were problematic. In Ethiopia, the long history of using traditional medicinal plants for combating various ailments can be confirmed by referring to the medico-religious manuscripts in the country. Herbal medicines have been also commonly used and remain. Symptoms of HTN can be also resolved by herbals.

Keywords: Antihypertensive drugs; Hypertension; Medicinal plants

INTRODUCTION

Traditional medicine refers to any ancient, culturally based healthcare practice different from scientific medicine [1]. Plants have been used to treat a wide range of diseases throughout the history of human beings and this practice continues to date. This is mainly because most of these herbals are accessible, affordable and the extracted chemicals have little or no side effects compared to drugs synthesized in the laboratory [2]. Natural products from plants remain vital in drug discovery where they can be used directly as drugs or serve as leads to new drugs by providing chemical entities [3]. The approach to new drugs through natural products has proved to be the single most successful strategy for the discovery of new drugs [4]. Currently, a large number of medicinal plants have found their way as raw materials of modern biopharmaceutical industry. Besides their use in fighting various ailments at local level, different medicinal plants are used as export commodities, which generate considerable income [5].

In traditional methods, plant materials are tested for pharmaceutical purposes. If any evidence of activity is observed, the extract is fractioned, and the active compound is isolated and identified. Each step of decomposition and isolation is usually guided by biological tests, which are referred to as bioassay-guided fractionation (Figure 1) [6]. Sometimes, a direct product isolation method, regardless of bioactivity, is also used, which leads to the isolation of a number of natural compounds suitable for measuring any biological activity. However, this process can be slow and inefficient, and also does not guarantee isolation of lead compounds from screening would be in chemically successful or even recordable [7].

The beginning of the development of herbal medicines was concurrent with the development of chemistry and isolation, purification, and determination of plant compounds [8]. Naturally

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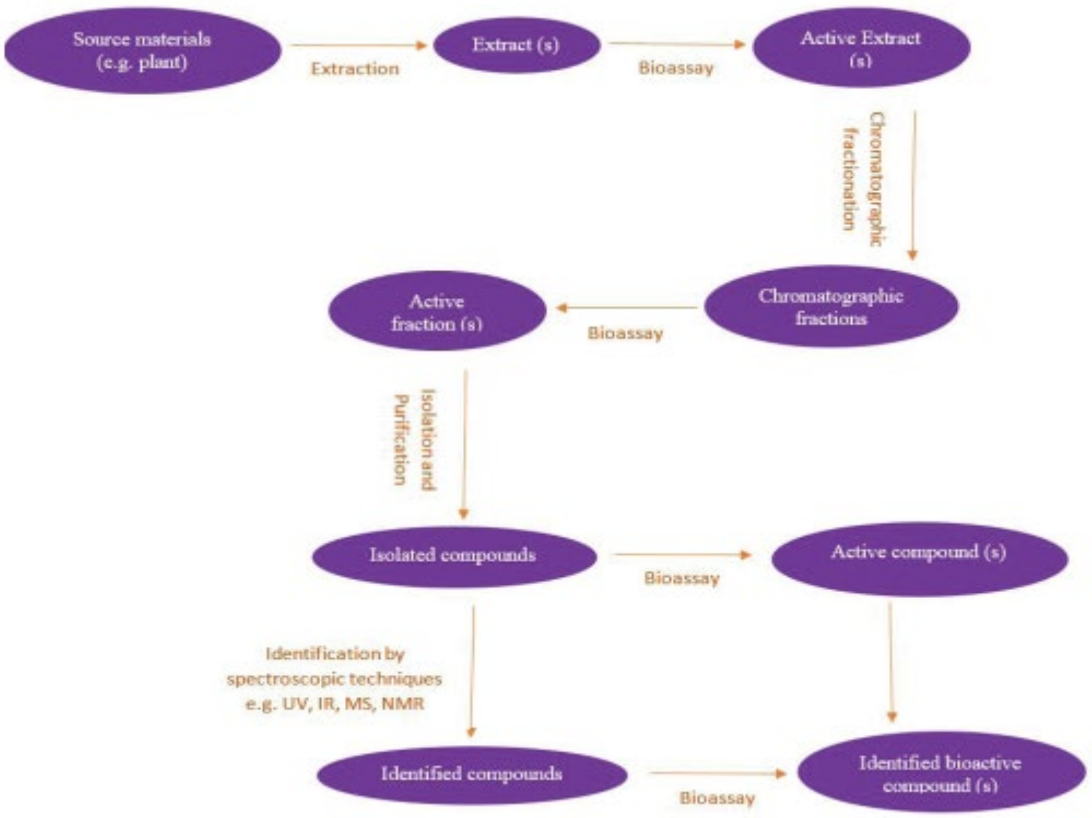

Figure 1: The traditional process of discovering natural drugs [6].

occurring compounds may be divided into two broad categories. The first class of compounds is known as primary metabolites which include nucleic acids, common amino acids, sugars, and high molecular weight polymeric materials such as cellulose, lignin and proteins which form the cellular structures. Most primary metabolites exert their biological effects within the cell or organism that is responsible for their production. The second class of compounds is secondary metabolites. Such compounds are characteristic of a limited range of species and occur in plants with high structural diversity. The major classes of secondary metabolites including tannins, glycosides, flavonoids, alkaloids, terpenoids, steroids, quinones, and saponins are among others and play a significant role in drug discovery. Secondary metabolites have often attracted the interest of researchers because of their biological effects on other organisms [9,10].

In the past, the drug discovery of the biological compounds from plant materials and the process of identifying the structures of active compounds from the extracts were problematic depending on the complexity of the compounds and might take weeks, months or even years. Nowadays, the rate of bioassay-guided fractionation has been significantly enhanced by the development of precision instruments such as high-performance liquid chromatography (HPLC/MS), liquid chromatography mass spectrometry (LC/MS), magnetic field and nuclear magnetic resonance (NMR) is a recent major breakthrough for the categorization of compounds that are extremely limited in quantity in their organisms of origin [11]. Despite the success of research to produce medicinal plants over the past few decades, future efforts face many challenges. Standardization of raw materials is an important issue for the plant industry [12]. Herbaceous plants can be easily infected during growth, processing and collection. Contamination and pollution with heavy metals are two main problems with herbal drugs [13]. The other challenge facing medicinal plants is also the loss of medicinal plant species due to the non-principled use of these resources [6]. According to the International Union for Conservation of Nature, there are between 50,000 and 80,000 flowering plant species that are used for pharmaceutical purposes around the world. Among these numbers, about 15,000 species are exposed to a risk of extinction due to high harvesting and destruction of habitats [14] and 20% of their wildlife resources are decreasing due to growing human populations and excessive consumption of plants [15].

LITERATURE REVIEW

The pharmacology and therapeutic value of conventional antihypertensive drugs in the management of hypertension

Hypertension (HTN) is a progressive cardiovascular disease characterized by persistently elevated systemic blood pressure of at least SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg [16, 17]. From a pathophysiological perspective, it is obvious that HTN is not purely an increase of blood pressure (BP) values, but a rather a sophisticated web of neurohormonal and haemodynamic interactions [18]. Depending on the underlying causes of the condition, HTN is categorized into 2 types: primary (essential) and secondary HTN. The majority (90%) of patients with HTN have 'primary' or 'essential' HTN where no identifiable underlying causes are exactly found but likely to be a consequence of a combination of both genetic and environmental factors [19, 20]. The remaining minority (up to 10%) have 'secondary' HTN which has identifiable organic causes such as endocrine, neurologic, renal, and vascular diseases, medical conditions (i.e., obstructive sleep apnea), pregnancy, and drug-induced [21, 22].

HTN is one of the most important public health problems in the world. HTN remains the leading cause of death globally, accounting

for 10.4 million deaths per year [23]. By 2030, the annual death toll is estimated to reach 23.5 million people [24]. Complications of HTN also account for 9.4 million deaths worldwide. It is responsible for at least 45% of deaths due to CHF [25], 49% of deaths due to ischemic heart disease [26], and 54% of deaths due to stroke [27]. HTN is the leading preventable risk factor for premature death and disability worldwide [28]. HTN is responsible for 143 million disabilities worldwide [29,30]. HTN is also a major player in the onset of diseases such as atherosclerosis, stroke, peripheral artery disease, heart failure, and coronary artery disease, as well as it can also lead to kidney damage, dementia, or blindness [31,32]. It has been considered as the first and the most common risk factor for CKD and ESRD [33]. The association with comorbidities such as dyslipidemia, prothrombotic state, and autonomic dysfunction contributes to an increase in morbidity and mortality [34]. The risk of cataract and hypertensive retinopathy was also found to be increased in populations with HTN independent of glycaemic risk, obesity, or lipids [35]. It also increases the risk and progression of diabetic retinopathy [36]. There is evidence that raised BP inversely correlates with cognitive function and that hypertension is associated with an increased incidence of dementia [37].

According to the World Economic Forum, NCDs are not only an important public health problem in both economically developed and developing nations [38]; rather, it will also have a big economic impact as a significant proportion of the productive population becomes chronically ill and stays at home, leaves their jobs, or die, leaving their families in poverty [39,40]. The global direct medical costs of HTN are estimated at $370 billion per year, with health care savings from effective management of blood pressure projected at roughly $100 billion per year [41]. High blood pressure costs the USA about $131 billion each year, averaged over 12 years from 2003 to 2014 [42]. This total includes the cost of health care services, medications to treat HTN, and missed days of work [43]. Over the period 2011 – 2025, the cumulative lost output in LMICs associated with NCDs is projected to be US$ 7.28 trillion [44]. HTN accounts for nearly half of the cost [45]. If left uncontrolled, HTN will become a major cause of human suffering as well as imposing severe economic and service burdens on health systems.

HTN is common and readily detectable; the key factor for the prevention and control of the epidemic of HTN is the identification and treatment of its major risk factors. Today on market there are many standard antihypertensive drugs ranging from diuretics (Indapamide, Furosemide, Amiloride), sympathoplegic agents (clonidine, reserpine), renin inhibitor (Aliskiren), ACEI (Enalapril, Captopril, Quinapril), ARBs (Losartan, Irbesartan, Olmesartan), Ca^{2+} channel blockers (Nifedipine, Verapamil, Diltiazem), α-adrenergic blockers (Prazosin, Doxazosin), β-adrenergic blockers (Nebivolol, Atenolol) to vasodilators (Minoxidil, sodium nitroprusside), which are used to manage blood pressure levels in hypertensive patients [46-48]. The objective of antihypertensive treatment is to achieve optimal blood pressure levels during therapy to reduce HTN-related complications. However, the frequent side effects that come with the use of these synthetic antihypertensive drugs, including dry mouth, dizziness, visual disorders, headache, cough, emotional distress, gastrointestinal disturbance, peripheral circulatory symptoms like cold hands and feet, swollen ankles, are by far their biggest disadvantages *[49,50].* These distressing side effects can lead to noncompliance and adversely affect health-related quality of life. These antihypertensive drugs also increase the risk of developing new diseases which worsen the situation and result in suboptimal control of high blood pressure [51]. Clinically, various antihypertensive drugs have been used to manage HTN and to alleviate symptoms. However, the efficacy of these drugs is only 40-60% and usually two or more antihypertensive drugs from different categories are needed to be combined to achieve the optimal results and thus, this ultimately increases the cost of treatment and side effects [52,53]. In ALLHAT, 60% of those BP was controlled to < 140/90 mmHg received two or more agents, and only 30% overall were controlled with one drug [54]. Furthermore, HTN prevalence is still increasing as a result of the awareness, control, and treatment of the disease are very weak [55]. Despite the fact that the detection of raised BP is very simple and cheap, only 34% of HTN is managed [56]. The major concerns that often delay treatment allude to higher costs [48], unavailability and inaccessibility [57], undesired side effects of antihypertensive drugs [48,56] and reduced patient compliance to consume more than a pill per day [31]. Therefore, newer antihypertensive agents are needed to expand therapeutic options, increase treatment efficacy, decrease side effects, and enhance patient adherence [57]. In addition, the search for natural, cheaper, and nontoxic compounds is becoming necessary [58-60].

Phytotherapeutic roles of commonly used medicinal plants for the management of hypertension in Arsi zone of Ethiopia

It is estimated that 70 – 80% of people worldwide rely chiefly on traditional, largely herbal medicines to meet their primary healthcare needs [61,62]. Traditional medicine plays an important role in primary health care in Ethiopia, where an estimated 80% of human illnesses and 90% of livestock diseases are being treated with plant materials, minerals, and animal products [63]. In Ethiopia, the long history of using traditional medicinal plants for combating various ailments can be confirmed by referring to the medico-religious manuscripts in the country [64]. Modern studies on traditional medicinal plants in Ethiopia started in 1973 [65]. Ever since this time, during the last four decades, considerable researchers have been doing investigations on MPs, especially on local knowledge of traditional MPs [66-71].

Although many people nowadays use herbal medicines as a constituent of primary health care, there are still many concerns about the safety and efficacy of using plants. While herbal medicines can potentially contribute to the advancement of healthcare, many major challenges need to be addressed before effective adherence of herbal medicines to traditional medicine. The lack of accurate translation and interpretation of the texts and research findings on plants by scientists around the world is one of the main challenges in this field. In fact, to realize the effective integration of plants into a medical system, researchers and practitioners should be trained in both modern and traditional medicine in the use of plant compounds. In addition, to build credibility for the use of plants in conventional medicine, the empirical arguments should be converted into evidence-based arguments. Finally, several questions about safety, accurate dose, duration of treatment, side effects, acute and chronic toxicities as well as the standardization of herbal medicines and natural products should be answered. If these issues are resolved, medicinal plants can be used as a safe, effective, and affordable form of health care [6]. Medicinal herbs have a hopeful future since there are about half a million plants around the world, most of them have not yet been studied in medical

practice, and current and future studies on medical activities can be effective in treating diseases [73]. The use of medicinal plants has a long history; however, the use of the whole plant or raw materials for treatment or experimentation has many drawbacks, including changes in the plant's compounds in different climates, simultaneous development of synergistic compounds that lead to adverse effects of antagonists, or other unexpected changes in bioactivity, and changes or loss of bioactivity due to the variability and accumulation, storage and preparation of raw materials; therefore, advancing towards the isolation of compounds and the use of pure substances with bioactivity, instead of the plant benefits, has certain benefits including convenient examination of therapeutic effects and determination of toxic doses to control the quality of the therapeutic formulation [72].

Herbal medicines have been commonly used and remain so instead of synthetic drugs because of their possible fewer side effects like weakness, tiredness, drowsiness, impotence, cold hands and feet, depression, insomnia, abnormal heartbeats, skin rash, dry mouth, dry cough, stuffy nose, headache, dizziness, swelling around eyes, constipation or diarrhea, fever or anaemia alone and associated with pressure medicines [74,75]. Symptoms of HTN like headaches, palpitations, fatigue, flushed face, blurry vision, nosebleeds, strong need to urinate, often ringing in ears, and dizziness can be resolved by herbals [76]. Herbals do not also interfere with medications including diuretics, blood thinners, β-blockers, and calcium channel blockers [77]. Many scientific studies also suggest different life style changes such as stress reduction, proper diet, regular exercise, limited salt intake, smoking cessation, limited alcohol intake, and the use of appropriate herbal medicines in the management of HTN [78,79].

The *Rumex* species

The Polygonaceae, commonly known as the knotwood or smartweed family, are a family of flowering plants and comprise about 1200 species containing 50 genera. Among which largest ones are *Eriogonum* (2410 species), *Rumex* (200 species), *Cocoloba* (120 species) and *Persicaria* (100 species), etc. This family is wildly distributed in North Temperature Zones although it can be found worldwide [80]. Plants belonging to the Polygonaceae are known to produce a large number of biologically important secondary metabolites, such as anthraquinones, naphthalenes, stilbenoids, steroids, flavonoid glycosides, leucoanthocyanidins and phenolic acids [81-85]. The name *Rumex* originated from the Latin word for dart, alluding to the shape of the leaves [86]. Roots, seeds, leaves, fresh plant juice, aerial parts, etc. are the parts generally used. Different species of *Rumex* genus contain various types of pharmacological activities, e.g. anti-inflammatory, antioxidant, cytotoxic, antifertility, purgative, antidiarrhoeal, antifungal, antipyretic, antiviral activities [87-92]. Traditionally, one species of *Rumex* genus named *Rumex abyssinicus*, has been also used for hypertension and pain relief. This plant also possesses antibacterial and diuretic properties [89]. Important chemical constituents of *Rumex* include anthraquinones, naphthalenes, tannins, flavonoids, phenolic acids, stilbenoids, triterpenes, carotenoids, etc. *Rumex hymenosepalus* contains Leucodelphinidin and Leucopelargonidin which are antitumorous substituents. Neopodin, a substance found in *Rumex japonicas,* has an inhibitory effect on osteoclasts [93]. *Rumex nepalensis* Spreng is another species that is widely used for various actions like antifungal, antibacterial, purgative. This species has moderate cytotoxicity and high phytotoxic activity [94]. The methanolic extract of *Rumex hastatus* D. Don species has many biological effects including antioxidant, antinociceptive, anti-diarrhoeal, and cytotoxic potential [95,96]. *Rumex dentatus, Rumex acetosa, Rumex crispus*, *Rumex patientia*, and *Rumex obtusifolius* are also some of the plants highly used for various pharmacological actions [97]. The juice of *Rumex nervosus* is used in Ethiopia for seizure bleeding roves to be the single most successful strategy for the discovery of new drugs [4].

Cymbopogon citratus

Cymbopogon citratus is an aromatic perennial plant of the Poacae family, with long slender green leaves. It is widely distributed and extensively used worldwide [98-101]. Several studies evaluating the phytochemical composition of *C. citratus* have shown the presence of saponins, tannins, anthraquinones, flavonoids, phenols, and alkaloids, in addition to terpenes, aldehydes, alcohols, and esters [102-105]. Furthermore, trace amounts of other components have been detected, including myrcene, geranial, geraniol, limonene, burneol, citronellol, nerol, α-terpineol, elemicin, catechol, luteolin, 6-C and 7-C-glycosides, caffeic acid, apigenin, luteolin, kaempferol, quercetin, chlorogenic acid, and geranyl acetate [102-105]. Fumesol, furfurol, isopulegol, isovaleranic aldehyde, L-linalool, methylheptenone, n-decyclic aldehyde, nerol, terpineone, p-coumaric acid, and valeric esters have also been isolated in some studies [102-105]. Cheel et al. [106] have reported the presence of isoscoparin, swertia japonin, and orientin in *C. citratus*, along with numerous other phytochemicals reported recently by Bharti et al. [107]. *C. citratus* also contains electrolytes and minerals (including sodium, potassium, calcium, copper, magnesium, manganese, selenium, phosphorus, iron, and zinc), vitamins (including folate, niacin, pyridoxine, riboflavin, and vitamins A, C, and E), and macronutrients (carbohydrates, proteins), and a small amount of fat [108]. Growing evidence suggests that these phytochemical components are responsible for the wide range of biological and therapeutic actions of *C. citratus*. The consumption of infusions and decoctions made from *C. citratus* has been a common practice in various countries since the discovery of the medicinal value of the plant throughout recorded history [98-100]. It is most frequently consumed for recreational and medical/therapeutic purposes [99], much like green, black, and red (rooibos) teas, herbal tea blends, and coffee. Many consumers prefer *C. citratus* tea to other beverages, because of its physicochemical characteristics, including taste; distinctive lemony smell, color, strength, and intensity [98], while many others consume *C. citratus* tea or decoction for physiological reasons [99,100]. It is used in herbal medicine for a wide range of applications based on its antibacterial [109], antifungal [110], antiprotozoal [111], anti-carcinogenic [112], anti-inflammatory [113], antioxidant [114], cardio-protective [115], antitussive, antiseptic, and anti-rheumatic activities. It has also been used to inhibit platelet aggregation [116], treat diabetes [117], dyslipidemia, gastrointestinal disturbances [118], anxiety [119], malaria [120], flu, fever, and pneumonia [102], as well as in aromatherapy. In addition to its therapeutic uses, *C. citratus* is also consumed as a tea, added to nonalcoholic beverages and baked food, and used as a flavoring and preservative in confections and cuisines. In cosmetics, essential oils are used as fragrances in the manufacture of perfumes, soaps, detergents, and creams [121, 122].

Cymbopogon citratus Stapf

Cymbopogon citratus Stapf. (Lemon grass) is an important medicinal and aromatic perennial tall grass having rhizomes and densely

tufted fibrous roots. It belongs to the Poaceae family which is renowned as an oil rich family. Green slightly leathery leaves appear in dense clusters on short underground stems [123]. The plant is a native herb of India and is cultivated in other tropical and subtropical countries [124]. Lemongrass can tolerate a wide range of soils and climatic conditions. However, vigorous growth is obtained on well-drained sandy loam soil with high fertility and exposed to sunlight [125]. It is reported to possess antibacterial [109], antifungal [123], antiprotozoal, anti-carcinogenic, anti-inflammatory, antioxidant, cardio-protective, antitussive, anti-septic, and antirheumatic activities [102]. It has also been used to inhibit platelet aggregation [116], treat diabetes [117], dyslipidemia, gastrointestinal disturbances [123], anxiety [119], malaria [120], flu, fever, and pneumonia [102], as well as in aromatherapy. In addition to its therapeutic uses, *C. citratus* is also consumed as a tea, added to nonalcoholic beverages and baked food, and used as a flavoring and preservative in confections and cuisines. In cosmetics, essential oils are used as fragrances in the manufacture of perfumes, soaps, detergents, and creams [126].

Calpurnia Aurea

Calpurnia aurea is a genus of flowering plants within the family of Fabaceae. The genus comprises shrubs or small trees in or along the margin of forests in many parts of Ethiopia and widely distributed in Africa from Cape Province to Eritrea and which also occurs in Southern India [127]. Literature survey brings to light that all parts of the plant species have been used for different human and animal diseases [128]. *Calpurnia aurea* from Ethiopia is known locally as "digitta" (Amharic), "Hitsawits" (Tigrigna). The plant is used in traditional medicine of Ethiopia to treat diverse medical conditions. In native countries like Ethiopia, traditionally, the leaves and powdered roots of *Calpurnia aurea* are used for the treatment of syphilis, malaria, rabies, diabetes, lung TB, hypertension, diarrhoea, leishmaniasis, elephantiasis, fungal diseases, different swellings, stomach-ache, abscesses, bowel, bladder disorders, to induce uterine contractions [129], used as an insecticide to kill lice [130], and tapeworm, trachoma, ringworm, as well as vomiting, headache and eye diseases [131-134], to destroy maggots, to destroy bedbugs, to relieve itches, used as a fish-poison or as a cure for dysentery, exhibit activity against amoebiasis and giardiasis, cough and snake bite [128,135].

The Thymus Species

The genus *Thymus* L. belongs to the Lamiaceae family and consists of over 400 species of herbaceous annuals and perennial plants that are extensively used for medicinal and nonmedicinal purposes. These plants are widely distributed throughout the Old World [136,137] and have been used for many centuries in traditional medicine due to their antiseptic, carminative, antiviral, and antioxidant properties [138]. *Thymus* species are also interesting as a source of pentacyclic triterpenoids with several properties, such as anti-inflammatory, hepatoprotective, antimicrobial, anti-HIV-1 activity, antiulcer, gastroprotective, hypoglycemic, anti-hyperlipidemic activity, and specific cytotoxicity against a variety of tumor cell lines [139-141]. Furthermore, interests focusing mainly on selected chemotypes for the cosmetic and food industries, among others, lead to the loss of other species in nature, such as *Thymus cariensis* Hub.-Mor. & Jalas, *Thymus cilicicus* Boiss. & Balansa, *Thymus sipyleus* Boiss., *Thymus pulvinatus* Čelak., and *Thymus cherlerioides* Vis [142]. These species should be preserved to make available access to a wide range of genetic diversity. On the other hand, as the plant has a low propagation rate in nature, a suitable method to obtain a high number of plants is needed [143].

Diuretics are substances that promote the production of urine and elimination of ions such as sodium from the body. Numerous studies now exist affirming the diuretic effects of traditional medicines [144]. The leaf of T. schimperi is traditionally used for urinary retention and hypertension and is reported to show diuretic activity with increased ionic content of urine in rats [145]. Moreover, there is also scientific evidence that aqueous leaf extract of *T. serrulatus* possesses *in vitro* vasodilatory activity on the thoracic aorta of Guinea pigs [146].

The Genus Ajuga

The plants in the genus *Ajuga* are evergreen, clump-forming, rhizomatous, annual or perennial herbaceous flowering species in the mint family, *Lamiaceae*. There are at least 301 species of the genus *Ajuga* with many variations: *Ajuga* is one of the 266 genera of the family *Lamiaceae*. *Ajuga integrifolia,* mostly known under the name *Ajuga bracteosa,* is a herb often lying on the ground and rooting at the nodes, covered with soft hairs, stems growing up to 40 cm high. Its leaves are oblanceolate and coarsely toothed. Its flowers are small, pale blue, white, or pale violet found in small clusters in the leaf axils [147,148]. It is found at an altitude of 1500 to 3200 m above sea level [147-149]. In Ethiopia it grows in different regions including Bale, Gojam, Gondar, Harerge, Kefa, Shoa, Sidamo, Tigray and Wollo [149,150]. Andarge et al. [151], also reported that *Ajuga integrifolia* has been found abundantly (plenty) in Dawuro Zone, SNNPR, Ethiopia. *Ajuga integrifolia* Buch.-Ham. (Syn: *Ajuga remota*; *Ajuga bracteosa*) is known by common names: 'Armagussa', 'Etse Libawit', 'Medhanit' (in Amharic). *Ajuga integrifolia* is widely used in traditional medicine for treating; It can also be used for veterinary purposes [134,152]. A decoction of the leaves of the herb is used in traditional medicine for a number of diseases including diarrhea, stomach disorders, evil eye, retained placenta, ascariasis, malaria, swollen legs, hypertension, jaundice and wounds, diabetes, fever, and malaria [153,154].

Hagenia abyssinica

Rosaceae, in the order Rosals, is a large family containing more than 100 genera and 2,000 species of herbs, shrubs, and trees of economic value, both for food (e.g., fruit trees including plums, apples, pears, loquats, blackberries and strawberries) and as ornamentals (e.g., flowers of the genus *Rosa*) . This family is represented on all continents except Antarctica [155,156]. *Hagenia abyssinica* (Bruce) J. F. Gmel is commonly known as Kosso in Ethiopia belongs to a monotypic genus in the family Rosaceae. It is a deciduous tree with distinct male and female trees, both of which are endowed with colourful flowers. The tree attains heights of up to 20 m, with a short trunks and thick branches. The flowers are greenish or white, turning reddish to maturity in female flowers. In Ethiopia, *H. abyssinica* was once abundant in the semi-humid mountain woodlands with the altitudinal range of between 2,450 and 3,250 m. The traditional healer claims that kosso are also useful in the treatment of fever/cough, intestinal worms (tape worm), stomachache, diarrhea, healing of wounds, typhoid, bronchitis, epilepsy, livestock disease (thin/skinny body), evil eyes, hepatitis, sexually transmitted diseases (STDs), throat disease, problems related to bile cancer (mixed with other plants),

dermatology, and malaria [157-160]. The female flowers of Kosso have long been used to expel tapeworms, a widespread infestation among Ethiopians due to the age-long practice of eating raw beef by a large sector of the population [161]. It is used in the treatment of syphilis together with powdered bark of *Albizzia anthelmintica* and against scrophulous tumours and cough. Women also use the bark of *H. abyssinica* during childbirth to prevent blood clotting and use to treat skin diseases. The seeds and the resin are toxic and are used as a fish poison. Decoction of the roots is used as a laxative. Oil of the seed is used against ear inflammations. The soup of leaves for headaches; inhaling smoke from burning leaves or drinking the leaf sap is said to relieve the pains of a woman in labour; chewing the root, bark or wood relieves toothache. The juice of flowers and leaves is used for hypertension and diabetes mellitus [157,158]. Besides being a source of medicine, *Hagenia abyssinica* has been utilized for various other purposes such as construction, furniture, fuel wood, and soil fertility management. As a result of its enormous significance, *H. abyssinica* is one of the endangered tree species in the country due to over exploitation [162].

CONCLUSION

Traditional medicine is commonly regarded as an indigenous, unorthodox, alternative or folk and largely orally transmitted practice used by communities with different cultures. If any evidence of activity is observed, the extract is fractioned, and the active compound is isolated and identified. Besides their use in fighting various ailments, medicinal plants are used as export commodities, which generate considerable income. From a pathophysiological perspective, it is obvious that HTN is not purely an increase of blood pressure values, but rather a sophisticated web of neurohormonal and haemodynamic interactions. Depending on the underlying causes of the condition, HTN is categorized as primary (essential) and secondary. HTN is the most important public health problem in the world as well as imposes severe economic burdens. HTN is common and readily detectable; many standard antihypertensive drugs are used to manage blood pressure levels in hypertensive patients. However, the frequent side effects that comes with the use of these synthetic antihypertensive drugs. These antihypertensive drugs also increase the risk of developing new diseases. Clinically, various antihypertensive drugs have been also used to manage HTN and to alleviate symptoms. Therefore, newer antihypertensive agents are needed to expand therapeutic options, increase treatment efficacy, decrease side effects, and enhance patient adherence. It is estimated that 70 – 80% of people worldwide rely chiefly on traditional, largely herbal medicines to meet their primary healthcare needs. Modern studies on traditional medicinal plants in Ethiopia started in 1973. Nowadays, the rate of bioassay-guided fractionation has been significantly enhanced by the development of precision instruments. Despite the success of research to produce medicinal plants over the past few decades, future efforts face many challenges. Many scientific studies suggest different life style changes such as stress reduction, proper diet, regular exercise, limited salt intake, smoking cessation, limited alcohol intake, and the use of appropriate herbal medicines in the management of HTN. The *Rumex* species, *cymbopogon citratus*, *cymbopogon citratus* stapf, calpurnia aurea, thymus species, genus ajuga, hagenia abyssinica are common medicinal plants used for the management of hypertension in Arsi zone of Ethiopia.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

ETHICAL APPROVAL

Ethical approval was obtained from Arsi University Ethical Review Committee (No.CoHS/CS/005/2018/2019).

COMPETING INTERESTS

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

AUTHORS' CONTRIBUTIONS

LM had participated in the design of the study, data analyses, and manuscript preparation; and the authors could have read and approved the final manuscript.

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RIGHTS AND PERMISSIONS

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