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An Ethno Botanical Review on Medicinal Plants Used for the Management of Hypertension

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Abstract

Hypertension has become one of the most principal growing health problems in developing countries, and is an important cause of cardiovascular death in the world. It is also called the silent killer as it usually shows no direct symptoms and many people die of the disease without understanding its. Despite their availability and effectiveness, the conventional drugs used for the treatment of hypertension have caused adverse side effects and increased the risks of developing new diseases. Herbal medicines, therefore, are gaining great demand and more importance in the treatment of hypertension because of their wide biological and medicinal activities, higher safety margins and lesser cost. Accordingly this review article mainly focuses on medicinal plants used for the management of hypertension in Ethiopia and provides a list of sixty six anti-hypertensive plants obtained from various sources. Furthermore, the review briefly describes the photochemistry and pharmacological properties of *Moringa stenopetala*, *Thymus serrulatus*, *Thymus schimperi*, *Syzygium guineense* and *Calpurnea aurea*. The purpose of this review is to create baseline data for future pharmacological and phytochemical investigations involving traditional medicinal plants used for treating hypertension and to preserve the traditional knowledge.

Keywords: Hypertension; Medicinal plants; Antihypertensive drugs; Phytochemicals; Efficacy; Safety

Abbreviations:

AU: African Union; HIV: Human Immunodeficiency Virus; CVD: Cardiovascular Disease; DBP: Diastolic Blood Pressure; MABP: Mean Arterial Blood Pressure; SBP: Systolic Blood Pressure; MoH: Ministry of Health; NCD: Non-Communicable Disease; WHO: World Health Organization; mM: Millimolar; SSA: Sub-Saharan African; WBCs: White Blood Cells; KCl: Potassium Chloride; GC: Gas Chromatography; GC-MS: Gas Chromatography Mass Spectrometer; ALT: Alanine Amino Transferase, AST: Aspartate Transaminase; ALP: Alkaline Phosphatase; GGT: Gamma-Glutamyl Transferase; BUN: Blood Urea Nitrogen

Introduction

The world population has encountered growing burdens of Non-Communicable Diseases (NCDs) which result in economic as well as a serious current and long term health problems [1,2]. The prevalence of Cardiovascular Disorders (CVDs) has been increasing across many regions of the world which are experiencing a rapid health transition [3]. CVDs account approximately for one-third of total deaths a year [4]. Several studies indicate that CVDs are responsible for almost 80% of the global burden of diseases in low and middle income countries [5-7] and it is predicted to be the leading cause of mortality and disability by 2020 mainly because of its rise in the future in these countries [5]. Globally, the major risk factors for CVD include tobacco use, high blood pressure, high blood glucose, lipid abnormality, obesity and physical inactivity. In Sub-Saharan Africa (SSA), the leading risk factors were accountable to 54% mortality and 45% of the burden of the disease in 2001 [5,6].

Hypertension is one of the major risk factor for CVD throughout the world [8]. It contributes to myocardial infarction, cerebrovascular accidents, congestive heart failure, peripheral vascular insufficiency, coronary artery disease, stroke and premature mortality [4-11]. Hypertension has been identified as the leading risk factor for mortality and ranked third as a cause of disability-adjusted life years [12]. Hypertension has become a growing common health burden globally because of the rising prevalence of the contributing risk factors such as obesity, physical inactivity and unhealthy diet [13]. The disease affects both sexes and increases as function of age in both sexes [11-15]. Complications of hypertension account for 9.4 million deaths worldwide. Hypertension is responsible for at least 45% for deaths due to heart disease and 51% of deaths due to stroke [6]. Hypertension has been reported to be the fourth contributor to premature death in the developed countries and the seventh in developing countries [16].

The prevalence of hypertension is higher in low and middle income countries than higher income countries. Besides this, the number of people affected also exceeds those of high income countries because of the high proportion of population living in these regions and their weak health system [6]. According to the World Health Organization, about one third of the world's population suffers from hypertension and the incidence has been increasing at a rapid rate due to life style modification [17].

More than a quarter of the world's adult population is hypertensive, this proportion is expected to increase in the coming years and sub-Saharan Africa is no exception to this trend. According to epidemiological projections in 2025, 29.2% of adults worldwide will suffer from hypertension whose three-quarters will live in developing countries. The total number of adults with hypertension in many African countries has been estimated to be over 40% in recent years [6-19]. Population growth, ageing and behavioural risk factors, such as unhealthy diet, harmful use of alcohol, lack of physical activity, excess

weight and exposure to persistent stress are contributing factors for the increasing prevalence of hypertension [6,20]. The prevalence of the disease and its related conditions has been recognized to be increasing in the developing countries [21].

Epidemiological Status of Hypertension in Ethiopia

Ethiopian has been facing the consequences of epidemiologic, demographic, economic and nutrition transitions which favour the chronic diseases epidemic. Some of the major contributing factors for the prevalence of NCDs in Ethiopia include the adoption of Western lifestyle in urban areas particularly a more sedentary way of life, increased cigarette smoking, employment in manufacturing industries, greater stress, and consumption of more refined food and increasing life expectancy in cities [22]. In Ethiopia, there is a lack of reliable CVD mortality and morbidity data which is due to the nature of the diseases and the less attention given to chronic diseases and lack of nationwide survey on chronic diseases [5,22].

Although there was no well documented data on prevalence of hypertension at national level, few studies conducted at different regions of Ethiopia and at the capital city reported an increased prevalence of hypertension [16-24]. One earlier study showed that the prevalence of hypertension in rural villages of Ethiopia was 1.8% [25]. Another study conducted on the rural and semi-urban residents of Butajira also showed that 12.3% of men and 8.2% of women had hypertension [26]. Furthermore, a population based study in Addis Ababa in the year 2006 found that the prevalence of high blood pressure or reported use of anti-hypertensive medication was around 32% males and 29% females [23]. A study has recently indicated that the prevalence of hypertension and diabetes among Ethiopian adults is 14.9% in women and 22% in men [27].

Recent evidences indicate that hypertension and raised blood pressure are increasing partly because of the increase in risk factors including smoking, obesity, and harmful use of alcohol and lack of exercise [28]. Moreover, according to the health and health-related indicators of MoH, hypertension was ranked as the seventh and sixth leading cause of death in the country in 2001 and 2006 respectively [29,30]. Therefore, the need to control hypertension is very crucial as its prevalence and severity has been escalating across the developing countries, including Ethiopia.

Management of hypertension with conventional medicines

A number of synthetic anti-hypertensive drugs have become available in the market through research owing to the rising prevalence and severity of hypertension throughout the world [11,31]. Despite their availability, people who live in many developing countries are forced to frequently recourse to and rely on traditional medicine which mainly uses medicinal plants due to their low socio-economic levels, the high cost and harmful side effects of conventional medicines [19-33].

Treatment of hypertension with anti-hypertensive synthetic drugs are associated with side effects such as dizziness, nausea, stomach problems, impotence, fatigue, insomnia, loss of appetite and many others [34-36]. Moreover, they increase the risk of developing new diseases which worsen the situation and result in suboptimal control of high blood pressure [37]. As a result, many scientific studies suggest different life style changes and use of appropriate herbal medicines in the treatment of high blood pressure due to the various side effects that come with the use of different types of conventional anti-hypertensive drugs [35,36].

The role of herbal medicines in management of hypertension

Traditional medicines had been used to treat various health problems for thousands of years in many parts of the world and are still utilized by the developing countries. The use of herbal medicine has been on the increase in many developing countries [38]. The developed countries have also shown an increased interest and use of herbal drugs due to public dissatisfaction with the cost of prescription drugs and interest in returning in to natural remedies [37,39]. Herbal medicines have significantly played a great role and contributed immensely to the development of cardiovascular research. For the treatment of cardiovascular diseases, herbal medicines have been used in patients with hypertension, congestive heart failure, angina pectoris, atherosclerosis, cerebral insufficiency, and arrhythmia [40].

Up to 90% of Ethiopian population use traditional medicine [41]. This is primarily due to the cultural acceptability of healers and local pharmacopeia, the relatively low cost of traditional medicine and poor access to modern health facilities [38-43]. The use of medicinal plants for the treatment of hypertension is very common among non-industrialized nations due to their easy availability and low cost than novel pharmaceuticals [44]. Numerous drugs from plants such as root of *Solanum sisymbriifolium*, *Cocos nucifera Linn* and *Hibiscus sabdariffa* have also been used in the treatment of hypertension [45].

Herbal medicines have been gaining more importance in the treatment of hypertension in recent years and are in great demand both in the developed and developing countries for primary health care because of their wide biological and medicinal activities ease of availability, higher safety margins and lesser cost [21,31]. With the increasing trend of hypertension prevalence and burden as well as serious adverse side effects, treatment failure, absence of cost effective mono therapeutic anti-hypertensive drugs in use and their serious adverse side effects, herbal plants would have been important and sustainable alternative sources of treatment for high blood pressure [21,46].

Hence, in order to overcome the rising prevalence and severity of hypertension and its associated cardiovascular risk factors, a consolidated scientific investigation should be adopted by the developing countries for the search of novel, safe and effective compounds from plant sources. The current review provides a list of medicinal plants used to treat high blood pressure in Ethiopia. In addition to listing the anti-hypertensive medicinal plants, it also made a brief review on the phytochemistry, pharmacological activities, safety, and toxicity studies of five commonly used antihypertensive plants.

Moringa stenopetala: Family: Moringaceae; Local name: Shiferaw or Haleko

Part used: leaf

Phytochemistry: Phytochemical screening tests performed on the crude aqueous leaf extracts of *Moringa stenopetala* confirm the presence of alkaloids, saponins, polyphenols, flavonoids, coumarins, terpenoids, anthraquinones, tannins, phytosterols and cardiac glycosides and the presence of all the secondary metabolites except saponnins in 70% alcohol fractions [7]. A preliminary phytochemical analysis carried out for butanol fraction of solvent-solvent separate and column chromatographic fractions of *Moringa stenopetala* leaves also

proved the presence of flavonoids, phenolic compounds and phenolic glycosides [47].

Pharmacological properties, antihypertensive activity: The Various parts of the *Moringa stenopetala* are claimed to contain disease preventing chemicals [48]. *Moringa stenopetalais* is traditionally used for the treatment of various ailments such as malaria, hypertension, asthma, diabetes, stomach pain [49]. People with high blood pressure boil the leaves and drink the water to get relief from their ailment [48].

Several scientific studies have also confirmed that the various parts of the plant possess anti-malarial, antileishmenial and anti-fertility [50], hypotensive [40], anti-hypertensive [7], vasodilatory [51], hypoglycemic [52], and anti-diabetic effects [47,53].

A study on antihypertensive and anti-hyperlipidemia effect of *Moringa stenopetala* leaves in experimental rats revealed that the aqueous crude extract and 70% ethanol fraction significantly prevented blood pressure increment in a dose-dependent manner and suppressed increment in cholesterol, glucose and triglycerides. Similarly, the crude aqueous leaf extract of *Moringa stenopetala* caused a significant reduction in SBP, DBP and MABP at doses of 10, 20, 30 and 40 mg/kg in normotensive anaesthetized guinea pigs [40]. In addition, the ethanol and aqueous crude extracts has shown a dose dependent relaxation effect at doses 1.25, 2.5, 5.0 and 10 mg/ml and the greater percent relaxant effect was shown on against (80 mM) potassium chloride and (1 μM) epinephrine pre-contracted isolated whole spirally-cut strips thoracic of guinea pigs [51]. According to Geleta et al. [54], the diuretic activity of hydro-ethanol extract of *Moringa stenopetala* leaves was evaluated in Swiss albino mice. The hydro-ethanol extract of the plant has shown a significant urine output at all doses and significantly increased the excretion of Na^+ and Cl^- at higher doses [54]. These pharmacological activities might be attributed to presence of different phytochemical constituents found in the plant extract, especially glycosides and alkaloids [7,51].

Safety and toxicity: Ghebreselassie et al. evaluated the effects of aqueous leaf extract of *Moringa stenopetala* on blood parameters, and the histopathology of liver and kidney in experimental mice [55]. Sub-chronic toxicity testing of this study revealed that no significant changes in the weight and in the histopathology of liver and kidney were detected in the animals treated with aqueous extract of the plant in comparison with the controls [55]. Whereas, the aqueous and ethanol crude extracts showed a rise in liver function indicators with no effect on kidney function indicators compared with normal control [56]. Similarly, the aqueous leaf extract of *M. stenopetala* caused a significant decrease in body weight of mice treated with 900 mg/kg of dose as compared with the controls. The acute toxic effect of n-butanol fraction of the leaves of *M. stenopetala* in experimental mice was evaluated [57]. The results of this study illustrated that no behavioral, gross pathology and body weight of the experimental mice treated with up to 5000mg/kg doses of the fraction were seen in comparison with the control groups. This suggests the safety of the fraction.

Musa et al. also investigated the biochemical and hematological activity of n-butanol fraction of the leaves of *M. stenopetalain* experimental Rats [49]. The results of this sub chronic toxicity study indicated that n-butanol fraction of the leaves of *M. stenopetala* produced no significant difference on the biochemical and hematological parameters (except blood glucose) of the treated rats from the control groups and laid within the reference range at two doses administration (500 and 1000 mg/kg) of the fraction [49].

Another recent study by Geleta et al. on the acute toxic effect of the n-butanol fraction of the leaves of *M. stenopetala* in experimental mice also suggested that the n-butanol fraction of the leaves of *M. stenopetala* did not cause any mortality up to 5000 mg/kg doses of the fraction [56]. Similarly, no body weight reduction, visible signs of toxicity and gross pathological alteration (colour, size and texture) were observed. Furthermore, the study results showed that the fraction did not produce adverse effects on hematological and biochemical parameters of the blood [56].

The effect of various solvent crude extracts and fractions of *M. stenopetala* on liver and kidney of experimental rats was toxicologically evaluated for sub-acute toxicity study. As compared with the normal control, both the crude extracts and solvent fractions at 250, 500 and 1000 mg/kg doses administration caused to increase ALT, AST, ALP and GGT, but produced no significant rise in the plasma level of BUN and creatinine in the treatment rats. However, repeated oral daily administration has revealed potential damage to the liver in a dose dependent manner but not to the kidney. No signs of toxicity, mortality and gross physical and behavioural changes were observed with close follow up after 4 h, 24 h 14 days of extract administration, at a dose of 5000 mg/kg [56].

Thymus serrulatus: Family: Lamiaceae; Local name: Tossign

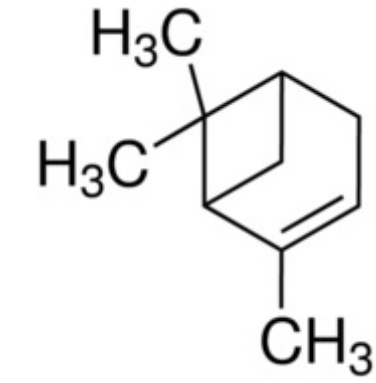
Parts used: leaf

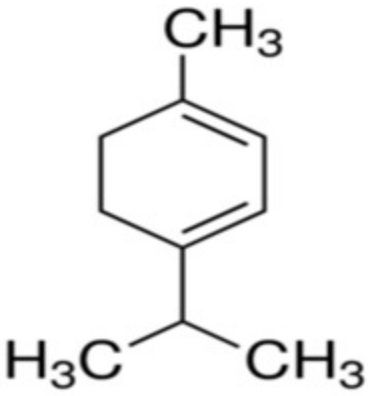
Phytochemistry: Different studies reported that the presence of α-pinene, α-terpinene, γ-terpinene, p-cymene, carvacrol, thymol and linalool as the major constituents of the essential oil of *Thymus serrulatus* using GC-MS analysis [58]. Thymus extract as well as powdered leaves were also found to contain polyphenols, phytosterols, alkaloids, tannins, saponins, and withanoids [59].

Some of the chemical structures for potentially active compounds of thymus species in Ethiopia are shown below:

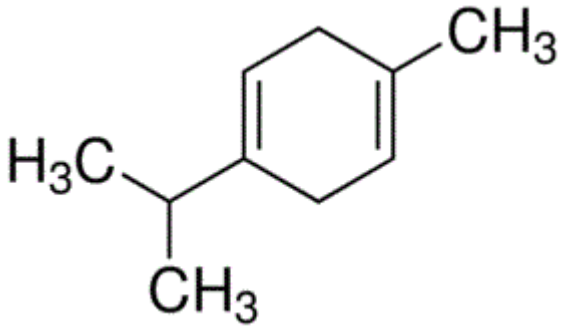
Pharmacological properties, anti-hypertensive activity: *Thymus serrulatus* is used as a spice and as culinary ingredient, food preservative and in aroma industries in Ethiopia. The leaf of this medicinal plant is utilized for the treatment of renal diseases, hypertension and *Taenia captis* [60]. The aqueous and methanol extract of *Thymus serrulatus* showed a significant spasmolytic activity using a charcoal meal test in mice [59]. In addition, the studies reported that the aqueous and methanol extracts of *T. serrulatus* have moderate diuretic activity. Whereas, the n-butanol fraction of aqueous crude extract revealed a comparable diuretic activity to standard drug, hydrochlorthiazide [61,62].

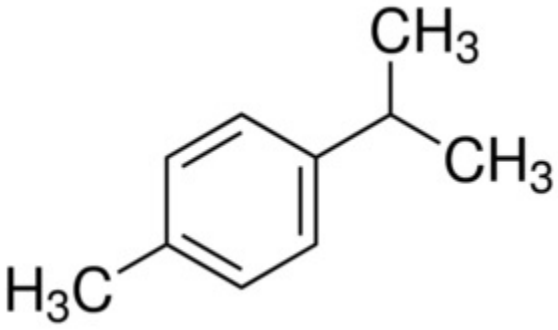
The vasodilator effect of the aqueous leaf extract of *T. serrulatus* on isolated thoracic aorta rings pre contracted with 80 mM KCl solution was investigated. The results of this study revealed that a sequential administration of increasing concentration of the aqueous leaf extract this plant weakened the force of contractions induced with potassium chloride solution on thoracic aorta of Guinea pigs both in intact and removed endothelium. The greater percentage of relaxation was observed in intact endothelium than in denuded endothelium of the guinea pigs thoracic aorta at the same concentration of the extract [60]. This pharmacology activity might be attributed to the phytoconstituents found in the plant extract, majorly by alkaloids and phenols [59-62].



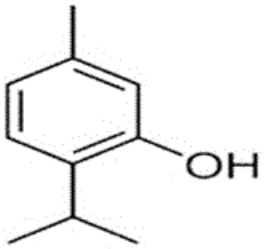


Alpha (α-pinene) Alpha–terpinene (α-terpiene)

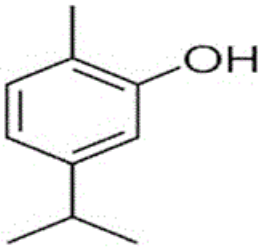




p-cymene γ-terpinene



Thymol



Carvacrol

Safety and toxicity: The toxic effect of the aqueous leaf extract of *T. serrulatus* in experimental mice was investigated. In the acute toxicity study, the experimental mice received the extract up to 10,000 mg doses per kg body weight. Intra-gastric administration of the extract in the mentioned dose caused no sign of morbidity and mortality during the period of the experiment. The experimental mice were given 200 and 600 mg/kg doses of the aqueous leaf extract at one day interval for ninety days in the sub chronic toxicity testing. The study results indicated that no significant changes were observed on the hematological parameters of both female and male mice and biochemical parameters of female mice. However, the plant extract at 200 mg/kg dose significantly increased the quantities of WBCs in experimental groups compared to the control groups. Similarly, the concentration level of BUN per urea was significantly decreased in the female mice by both doses of the plant extract compared to the control groups. The aqueous leaf extract of *T. serrulatus* did not reveal any significant change on the weight of liver and kidneys of male and female mice treated with doses of 200 and 600 mg/kg compared to the control groups. Gross pathologic examinations of internal organs of treated rat and mice also revealed no abnormal changes in texture, shape, size or color of liver and kidney and no sign of necrosis or lesion were observed [63].

Thymus schimperi: Family: Lamiaceae; Common name: Tossign

Parts used: leaf

Phytochemistry: Results of GC and GC–MS analysis revealed the presence of p-cymene, α-terpiene, thymol and carvacrol as the main constituents of the essential oils of *Thymus schimperi* taken from four different regions of Ethiopia. Furthermore, phytochemical tests conducted on the crude extract and powdered plant leaves of *Thymus schimperi* for the major classes of secondary metabolites only confirmed the presence of phenols, tannins and, saponins which are responsible for the diuretic and anti-hypertensive activity of the plant [64,65].

Medicinal properties, antihypertensive activity: *Thymus schimperi*, locally known as 'Tossign', mostly grows at altitude of 2250-4000 masl (afromantane and afro alpine vegetation zones [66]. In traditional medicine, Thymusspecies in Ethiopia are used to treat different illnesses like gonorrhea, cough and liver disease, renal diseases, stomach pain, hypertension, kidney problem and dermal fungi [67]. They have been reported to have anti-helminthic, antibacterial and fungicidal activities [58,68].

The anti-hypertensive effect of the leaves of *Thymus schimperi* has recently been investigated [65]. The oral administration of aqueous extract of *Thymus schimperi* leaves and its essential oil distillate at doses of (250, 500, 750 and 1000 mg/kg) and (1 and 1.5 ml/kg) was respectively evaluated for their diuretic and anti-hypertensive activity against salt–sucrose induced hypertensive rats. The aqueous extract of *Thymus schimperi* leaves for all mentioned doses showed positive diuretic activity at 5 h and the two higher doses significantly increased Na+, K^+ and Cl-content of urine [65]. The pharmacological properties of *Thymus schimperi* might be attributed to presence of various phytochemical constituents in extract such as phenols and saponins [65].

Safety and toxicity: Results of acute toxicity testing showed that no clinical signs of toxicity mortality as well as behavioral changes were observed at the oral limit dose of 5000 mg/kg during the observation period [65]. In addition, acute toxicity study done by Debelo et al. [69] has shown that the extract did not reveal any signs of toxicity; hence the LD50 was suggested to be higher than 10,000 mg/kg.

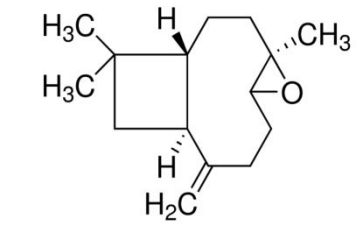
There was no significant change ($p>0.05$) in general body weight and most of evaluated hematological and biochemical parameters after 90 days of sub-chronic treatment at 200 and 600 mg/kg. The kidneys and liver of treatment group appear normal in their texture, shape, size or color compared to the control group in gross and histopathological examination. However, the light microscopic examination reveals that there was localized mononuclear lymphocytic infiltration and mild blood congestion within the hepatic portal and central veins in liver at higher dose (600 mg/kg) [69].

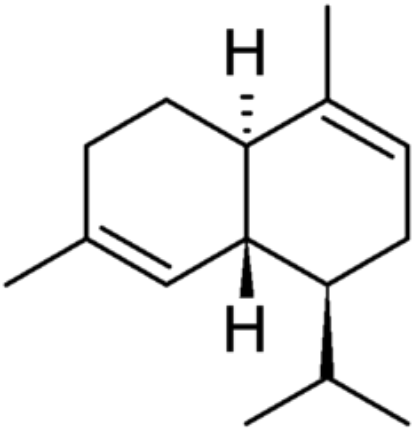
Syzygium guineense: Family: Myrtaceae; Local name: 'Baddeessaa' in Afaan Oromoo and 'Dokma' in Amharic

Parts used: leaf

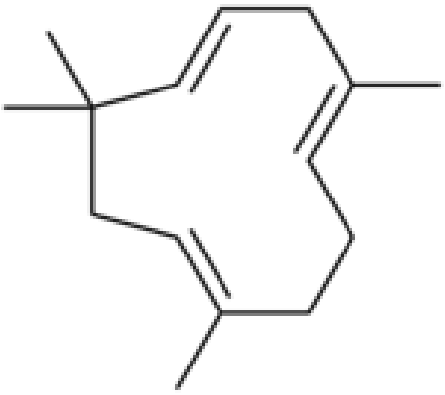
Phytochemistry: Preliminary phytochemical tests for the ethanolic leaf extract of *Syzygium guineense* confirmed the presence of cardiac glycosidic, saponins, flavonoids, tannins and carbohydrates [70]. Two different studies also revealed the presence of caryophylleneoxide (7%), d-cadinene (7.5%), viridiflorol (7.5%), epi-α-cadinol (9.8%), α-cadinol 12.7%), cis-calamenen -10-ol (14%), citronellyl pentanoate (15.2%), β-caryophyllenr (20.1%) and α-humulene (39.5%) in the essential oil of leaves of *Syzygium guineense* [71,72].

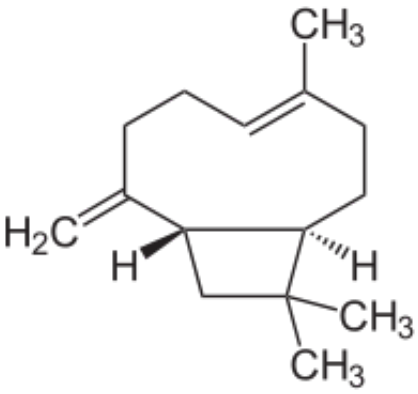
Medicinal properties, antihypertensive activity: *Syzygium guineense*, which belongs to the Family myrtaceae, is available in the altitude range of 2,300-2,700m above sea level. Its bark decoction was used for the treatment of diarrhea and the twigs and roots of this plant were also used for various stomach ailments. Various solvent extracts of different parts of the plant have shown to possess antibacterial and molluscidal activities. Methanol extract of *S. guineense* bark also produced sustained hypotension in anaesthetized rats with greater fall in blood pressure was in diastolic rather than in systolic blood pressure [73].





Caryophylleneoxide d-cadinene





α-humulene β-caryophyllenr

Many morphological parts of *S. guineense* have been traditionally utilized in the management of various ailments in many Ethiopian communities [32]. Several studies reported that various preparations of the parts of this plant have shown to possess anti-diarrheal and anti-dysentery, anti-hypertensive, anti-microbial, anti-malarial, anti-bacterial as well as hypotensive properties [32,74]. The anti-hypertensive effect of the hydro-methanol leaf extract of *S. guineense* at different doses in a 1-kidney 1-clip hypertensive rat model was evaluated for three consecutive days of treatment. The results of this study indicated that the hydro–methanol leaf extract of the plant caused a significant fall in SBP, DBP and MBP with increasing dose. Moreover, the aqueous–methanol leaf extract of *S. guineense* demonstrated a dose-dependent relaxation on the guinea pig isolated aorta pre contracted with 80 mM KCl solutions [32].

Safety and toxicity: The toxic effect of the hydro-methanol leaf extract of *S. guineense* was evaluated in rats. In the acute toxicity testing, group I and II treatment rats were orally given with 2000 and 5000 mg/kg respectively in single administration and the control group received distilled water. The results of this study concluded that the 80% methanol leaf extract of *S. guineense* is safe up to the highest second concentration as no toxicity signs and symptoms as well as mortality were seen in the treated rats in the given concentration levels. In the sub-acute toxicity test, group I and II treatment rats were orally administered respectively with 500 mg/kg and 1500 mg/kg doses of the hydro–methanol leaf extract of *S. guineense*. Results of this test revealed that the hydro-methanol leaf extract showed no significant difference in the hematological parameters as compared with the control groups. No significant difference in the body weight changes was observed at these doses [75].

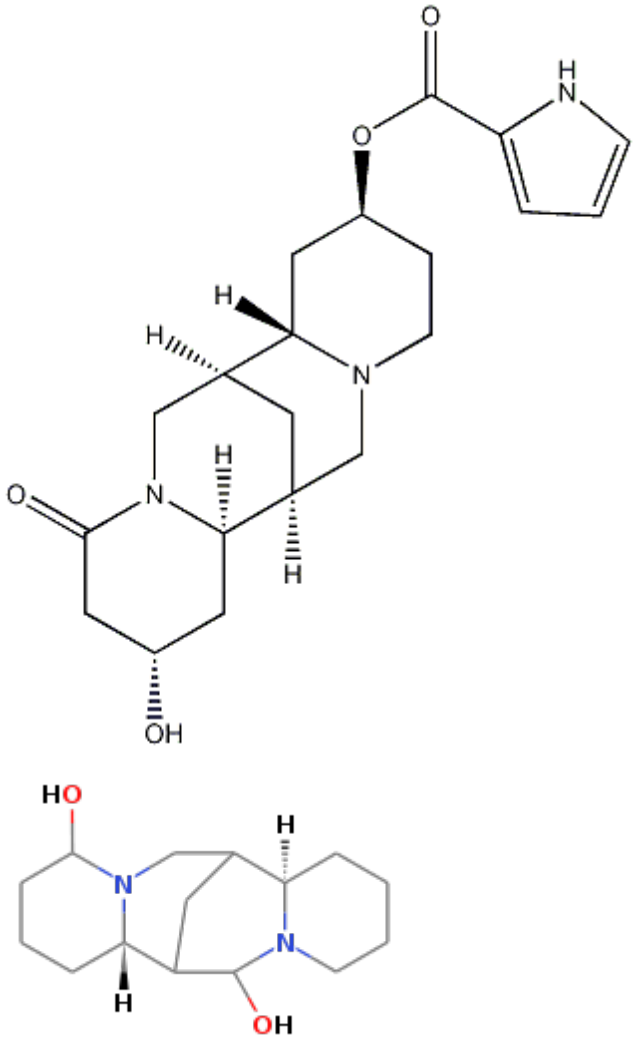
Calpurnea aurea: Family name–Fabaceae; Local name: 'chekata' in Afaan Oromoo and 'digita' in Amharic

Part(s) used: seed

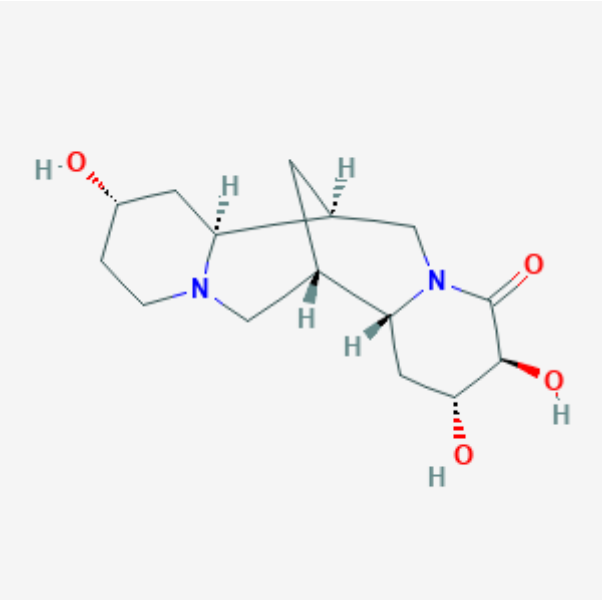
Phytochemistry: The result of preliminary phytochemical screening of powdered leaves of *Calpurnia aurea* showed the presence of several secondary metabolites including alkaloids, cardiac glycosides, flavonoids, phenols, phytosteriods, saponins, terpenoids and tannins using standard qualitative phytochemical screening test procedures [76,77].

Two novel alkaloids 3β,4α,13α-trihydroxylupanine and 3β,4α-dihydroxy 13α–O-(2'–pyrroly l c arbonyl)-lupanine 16 (calpaurine) have been isolated from the leaves of Ethiopian *C. aurea* ssp–aurea. Two minor quinolizidine alkaloids, 4β–hydroxyl-13α-O-(2'-pyrrolylcarbonyl)-lupanine (digittine) and 4β, 13α–dihydroxylupanine have also been detected in the leaves. The main pharmacologically active compound is assumed to be the alkaloid calpurmenin and its 13α-(2'-pyrrolecarboxylic acid) ester. Two novel minor quinolizidine alkaloids 4 beta-hydroxy-13alpha-O-(2'-pyrrolylcarbonyl)-lupanine (digittine) and its amino alcohol, 4 beta, 13alpha-dihydroxylupanine, have been isolated from Ethiopian *C. aurea* ssp. aurea. The structures of these alkaloids were determined by chemical transformation and by means of spectroscopic techniques (UV, IR, CD, MS, (1) H-NMR and (13) C-NMR) including two dimensional NMR [78,79].

Chemical investigations of *C. aurea* have resulted in the isolation of a series of alkaloids, phenolic compounds, flavonoids, flavonols, and proanthocyanidins, which also founds in the genus Calpurnia [78]. Some of the chemical structures of the isolated compounds are clearly depicted below:

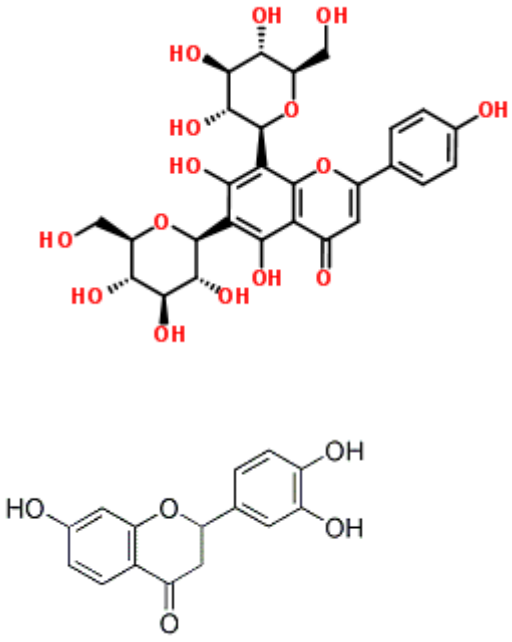


Digittine 4β, 13α–dihydroxylupanine

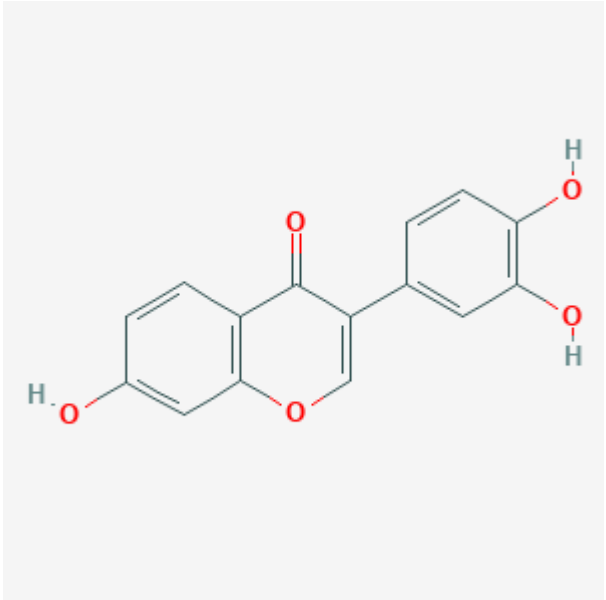


3β, 4α, 13α–trihydroxylupanine

Apart from the quinolizidine alkaloids, the flavonoids vicenin-2 (6,8-di-β-D-glucopyranosyl-5,7,4'-trihydroxyflavone) [A], butin (7,3', 4'trihydroxyflavanone) [B] and 3'-hydroxydaidzein (7,3',4'-trihydroxyisoflavone) [C] were isolated from the seeds of *C. aurea*, in keeping with flavonoids being the other major class of compounds consistently found in the Fabaceae [6].



[A] [B]



[C]

Pharmacological properties: In Ethiopia, traditionally, the leaves of *C. aurea* are used for the treatment of syphilis, malaria, rabies, diabetes, hypertension, diarrhoea, leishmaniasis, trachoma, elephantiasis, fungal diseases and different swellings, stomach-ache, bowel, and bladder disorders [77,79]. Its seed powder mixed with honey is also used to treat giardia and amoebiasis [80]. The roots of *C. aurea* is claimed to show activity against amoebiasis and giardiasis; the leaf in combination with the seed is utilized for treatment of diarrhea, rabies and diabetes; and the seed is used for treatment of hypertension [81].

Efficacy data: The 80% methanolic extract of the seeds of *C. aurea* have been tested for their *in vivo* and *ex vivo* antihypertensive activity. The crude extract caused a marked decrease in SBP, DBP and MABP at the doses of 15, 30 and 45 mg/kg in normotensive anaesthetized. The BP went down dose dependently and significantly in renal hypertensive rats, induced by renal ischemia. The extract produced 15.4%, 26.9%, 33.2% reduction in SBP at the respective doses of 15, 30 and 45 mg/kg. The extract also caused a dose-dependent relaxation of guinea pig aorta pre-contracted with KCl (80 mM), at a concentration of 5-250 mg/ml, with a maximum relaxation of 92.1 ± 0.72% ($p<0.001$) achieved at 250 mg/ml concentration [13].

Safety data: There is a rather contradicting data on the safety of the hydro alcoholic leaf extract of *C. aurea*. An acute toxicity study on the 80% methanolic leaf extract conducted by Birhanu et al. [82] at a limit dose of 2000 mg/kg showed that the plant failed to display any signs of mortality and morbidity for up to 14 days [82]. In contrast, a previous study uncovered that the limit test dose of 2000 mg/kg orally administered sequentially to female mice caused mortality in all test animals. Consequently, the dose was tapered to 300 mg/kg at which the extract didn't show any visible signs of acute toxicity as well as mortality [76].

Methodology

Various types of documents such as books, published research articles and theses were thoroughly explored to collect valuable information regarding the medicinal plants used for the treatment of

hypertension. The references of identified articles and hand searched journals on ethno botany, herbal medicine such as the journal of ethno pharmacology were also searched. Various web sites including Google scholar and pub med have also been searched for the collection of data using important related key words such as Ethno botanical survey, Ethiopian herbal medicine, antihypertensive plants, etc. Using the sources and tools, the scientific, family and local names of each plant species together with the parts used, method of preparation as well as other medicinal benefits of the identified plants were clearly described and presented in a Table 1.

S No.	Scientific Name	Local Name	Part(s) Used	Method of Preparation	Medicinal Use(s)	References
1	*Premna schimperi* [Lamiaceae]{Engl} [lamiaceae]	Chocho (Am) Uregessa (SH)	Leaf	Not Specified	Hypertension, hemorrhoids, wound, inflammation of skin	[83]
2	Cymbopogon citrates [Poaceae]	Tej-sar (Am)	Whole part	Not Specified	Hypertension, abortifacient, bronchitis, cold, fever, malaria, hemorrhoids, tooth ache	[84-87]
3	*Thalictrum rhyme*	Sirebizu (Am)	Root	The root is ground, blended with honey and taken for seven-days orally.	Flu, hypertension, abdominal wounds or Stomach ache, unknown diseases	[86]
4	Aloe spp. [Asphodelaceae]	Eret (Am)	Gel latex	Not Specified	Rheumatic pain, hemorrhoid, hypertension, Emollient, purgative, anti-helminthes, anti-fungal, antiseptic and cosmetic, for fever, spleen and liver troubles, anti-diabetic etc..	[86-89].
5	*Allium cepa* L. [Amaryllidaceae]	Key shinkurt (Am)	Bulb (fresh) seed/ Root and leaf	The seed is crushed, immersed in little water for 1 day, then filtered using a clean cloth and is drunk before food.	Asthma, Malaria, Blotting hypertension	[90-92].
6	Botanically unidentified	Bekurelomi(Am)	Fruit and leaf	The juice is drunk most frequently.	Cholesterol, liver, bile pancreas problems, cancer, Hypertension, obesity	[86]
7	*Carica papaya* L. [Caricaceae]	Papaya (Am)	Seeds	The seed is ground, blended with honey and taken with empty stomach.	Gastric, constipation, malaria hypertension, Amoebic diseases, abdominal colic	[86]
8	*Allium sativa* L. [Alliliaceae]	Nech shinkurt (Am)	Bulb	The bulb is frequently eaten with food	Hypertension, snake bit, abdominal pain, antibacterial, insecticidal, cholesterol diarrheal, diabetes, cancer, anti-microbial, antifungal, anti-asthma, anti-malarial	[86-97]
9	*Ajugainte grifolia* [Lamiaceae]	Armagusa (Am) Harmagusa[O]	Leaf	The leaf is boiled with butter, filtered and taken orally	Stomach diseases, hypertension, Cholesterol, asthma, bad spirit, addiction problems, diabetes	[86-99]
10	*Merendra bengalensis* (Roxb.) Benth. [Lamiaceae]	Mesaguh (T)	Leaf	The leaf is crushed, filtered and the filtrate is taken orally	Ascariasis, hypertension	[100]
11	*Berasama abtyssinica* Fresen [Melianthaceae]	Azamir (Am) dobi warabechaa (O)	Leaf (fresh) and root	The leaf is boiled with water and the filtrate is mixed with teff powder and eaten with yoghurt. Alternatively, the root is crushed, mixed with honey and eaten.	Ascarisis, kitgn cancer, hypertension, pest control (parasitic)	[86,101]
12	*Hibiscus sabdariffa* [Malvaceae]	Kedkedie(Am)	Flower	Not Specified	To increase and decrease blood pressure depending on concentration.	[86,102]

13	*Moringa stenopetala* [Moringaceae]	Shiferaw (Am) Shifera (Sd) Kelanqi (Ha)	Dried leaf	The dried leaf is prepared as a tea and taken orally orthe fresh leaf is boiled with Allium cepa and Capsicum annuum, oil is added and taken orally	Hypertension, diabetes, kidney infection, malaria, hypoglycemic, anti-leis menial, ant-fertility, anti-hyperglycemic anti-cancer, anti-asthmatic, antioxidant.	[47-105]
14	*Achyranthes aspera* L. [Amaranthaceae]	Telenji (Am)	Root and tip shoot	The root is sniffed through the nostrils	Stabling pain, Cutaneous leishmaniasis, urine retention, hypertension, kintarot, wound	[86]
15	Botanically unidentified	Yedemie (Am) Etse-demawit (G)	Root and leaf	Not Specified	Hypertension	[86]
16	*Lupines termis Forssk* [Leguminosae]/Fabaceae]	Gibto (Am)	Seed	Seeds are soaked with water for 5 days, after discarding the water the decanted seeds arethen eaten.	Cleans blood, pneumonia, bowl and hypertension related problems, Giardiasis	[86-107]
17	Spinacia oleracea[Amaranthaceae]	Kel (Am)	Leaf	Eat frequently.	Hypertension, obesity	[10,86]
18	*Hordeum vulgare* L. [Poaceae]	Gebs (Am)	Leaf	Germinated barley and Sorghum are baked in bread, broken up and fermented together with malt starter, brewed and distilled.	Hypertension	[86,108]
19	*Trigonellafoenumgraecum* L. [Fabaceae]	Abish (Am)	Seeds	Not Specified	Cholesterol, hypertension, stomachache, antispasmodic, powder used for wound dressing	[86,108]
20	*Dovyalisabyssinica* (A. rich) Warb [Flacourtiaceae]	Yehabeshaquo shm (Am)	Root and stem tuber	Root and stem tuber are smashed, mixed and drunk with alcohol	Ascariasis, hypertension, bleeding gum,	[109]
21	*Tamarindusindica* L. [Fabaceae]	Humer(T) roka(Am)	Fruit	Not Specified	Abdominal problems, hypertension, Spleenomegally	[110]
22	*Ferula communis* L. [Apiaceae]	Enslal(Am)	Leaf	Not Specified	Hypertension, urination problems, kidney problems	[109]
23	*Rumex abyssinicus* [Polygonaceae]	Mekemeko (Am)	Root	The root is crushed into powder, mixed with bulbs of garlic. The mixture is boiledwith water and taken with milk	Hypertension, asthma, liver problems, wound, common cold, cancer, colorectal, stomach ache, inflammation and painful conditions	[107-116]
24	*Thymes serrulatus* [Lamiaceae]	Tosghn(Am)	Leaf and flower	Fresh leaves are soaked with hot water andthe filtrate taken orally.	Blood pressure, general pain syndrome, influenza, abdominal pain, ascariasis, intestinal parasites, renal disease	[32-118]
25	*Thymus schimperi* [Lamiaceae]	Tosghn(Am)	Leaf, flower and root	The leaves are dried, powdered, and mixed with the	Blood pressure, general pain syndrome, influenza, abdominal pain, intestinal parasites, gastritis,	[63-120]

				seed powder and eaten. The root is dried, powdered, and drink consumed with tea	cough, anti-oxidant, antifungal and antimicrobial activities	
26	*Syzygium guineense* [Myrtaceae]	Dokma(Am)	Leaf	Not Specified	Malaria, skin rash, itching, diarrheal, gastro-intestinal upsets, hypertension, anti-inflammatory, analgesic and immunological activities	[32]
27	*Balanites aegyptiaca* (L) [Del Balanitaceae]	Dhumuko (Hm)	Bark	Inside of the bark is peeled off, infusion is made with water, filtered and drunk	Hypertension	[103]
28	*Cadaba farinosa* Forssk Capparidaceae	Dhela (Hm)	Root	Roots are chopped, boiled with meat soup and drunk	Hypertension, malaria	[103]
29	*Euphorbia* sp. Euphorbaceae	Kera (Hm)	Bark	Fresh bark is chopped, infusion is made, mixed with honey and drunk	Hypertension	[103]
30	*Leucaena leucocephala* (Lam) De Wit Fabaceae	Lalomb Aka (Hm)	Stem	Different parts of the plants are mixed, crushed, macerated/ infused in water, filtered, mix with honey and milk and then drunk	Hypertension, intestinal parasites, irregular menstruation, loss of appetite	[103]
31	*Meliaazedarch* L. [Meliaceae]	Mimi-zaf(Am) or Fayo (O)	Leaf	Leaves are pounded and the juice is taken orally	Hypertension, prevent irregularity of menstrual cycle diarrhea of human	[121]
32	*Catha edulis* (Vahl) Endl. [Celastraceae]	Chat (Am)	Fresh leaf	Fresh leaves are chewed	Hypertension, asthma	[122]
33	*Citrus aurantiifolia* (Christm.) [Swingle][Rutaceae]	Tutto Lemon (Am)	Fruit	The whole fruit and fruit juice are taken	Hypertension, Skin cutting, Cough, stomachache, body odor, tetanus, wound, constipation	[104-122]
34	*Rumex nepalensis* Spreng. Polygonaceae	Tullet (Am)	Fresh leaf	Fresh leaves are boiled and drunk.	Quaquchia, Hypertension, Amoebic dysentery and Hemorrhoid	[122]
35	*Citrus aurantium* [Rutaceae]	Komtatie (Am) Qomxaaxxee (O)	Flower fruit	The juice is drunk once a day.	Hypertension	[114,123]
36	*Citrus limon* (L.) Burm. F [Rutaceae]	Lomi (Am)	Fresh juice	Fresh juice is mixed with tomato and given orally	Amoebiasis, Hypertension	[124,125]
37	*Calpurnea aurea* (Alt.) Benth [Fabaceae]	Digita (Am) Cekkatta(Sd) Cheka (O)	Seeds	The seeds are crushed and sniffed through the nostrils	Hypertension, jaundice impotence diarrhea, rabies, amoebiasis and giardiasis, diabetes, woundhealing, trachoma, malaria, syphilis, fungal diseases	[13,126]
38	*Crinum abyssinicum* (Hochst) ex A. Rich [Amaryllidaceae]	Yejib shinkurt (Am)	Shoot tip (fresh)	The liquid from the shoot tip is squeezed, mixed with water, and drunk	Hypertension, diabetes	[104]

39	*Foeniculum vulgare* Miller. [Lauraceae]	Wallaago Ensilal(Am)	Fresh leaves	Squeezed and drank 1 glass cup/ Boiled and drank	Hypertension, diabetes, gonorrhea, Kidney Problem, stomachache	[68,104]
40	*Persea americana* Mill) [lauraceae]	Avocado(Am) Abukato (Sd)	Dried fruit	Crushed, powdered, mixed with coffee and drank	Hypertension, diarrhea	[104,127]
41	*Ajuga intergrifolia* [Lamiaceae]	Armagusa (O)	Leaf	Not Specified	Anti-hypotensive, elephantiasis, Breastmassage	[128]
42	*Rosa abtyssinica* [Rosaceae]	Kega (Am)	Fruit	Powdered fruits are, mixed with water and drunk	Hypertension	[129]
43	*Menthax piperata* L. [Lamiaceae]	Nana (O)	Leaf	The juice of squeezed leaf is drunk	Common colds, hypertension	[87-130]
44	*Ocimum lamiifolium* [Labiatae]	Damakase(Am)	Leaf	Fresh leaves are pounded and juice is prepared. Then, taken orally, three times a day for three days.	Hypertension	[130]
45	*Hagenia abyssinica* (Bruce) J. F. Gmel., [Rosaceae]	Kosso (Am)	Fresh flower and fruit	Fresh flower and fruit are boiled with little water and mixed with alcohol given orally	Tape worm, hypertension	[79-131]
46	*Dioscorea praehensilis* Benth [Dioscoreaceae]	Wacino (O)	Bulb	Bulbs are boiled and eaten	Tonsillitis, hyper tension	[68]
47	*Leucas martinicensis* (Jacq.)R.B. [Lamiaceae]	Raas Kimir (Am)	Leaf	Crushed leaves are, squeezed and half a coffeecup of the liquid is drunk	hypertension, malaria	[68]
48	*Salvia tiliifolia* Vahl, [Lamiaceae]	Aqorarach (Am)	Fresh leaf	Fresh leaf juice is mixed with little water and given orally	Hypertension, tonsillitis, febrile illness	[125]
49	*Psidium guava* [myrtaceae]	Zeytun (Am)	Leaf	Not Specified	Hypertension	[132]
50	*Datura stramonium* L. [Solonaceae]	Asangra (O)	Root	The root is decocted overnight and mixed with rancid butter	Asthma, hypertension, diabetes mellitus, toothache	[99]
51	*Centarium pulchellum* [Gentianaceae]	Lesser (En)	Root	The root is boiled in water and taken orally	Gastric, abdominal pain, hypertension, diabetes, elimination of stones from kidney and urethra	[133]
52	*Dorstenia barnimiana* Schwienf) [Moraceae]	Work bemeda (Am)	Root	Not Specified	Blood pressure, Hepatitis donkey's wart, cancer, rabies, syphilis, weight loss, diarrhea and fever	[86,134]
53	*Impomea* sp. [Convolvulaceae]	Fiatsut (Am)	Leaf	Not Specified	Babies' sickness, hypertension, cancer	[86]
54	*Vernonia amygdalina* [Asteraceae]	Grawa (Am)	Leaf	Not Specified	stimulates the digestive system and helps in reduction of fever, to treat	[135]

					hiccups and kidney disease, as a remedy against high blood pressure	
55	*Asparagus aethiopicus*[Asparagaceae]	Yeset-kest (Am)	Root	Not Specified	Taenicidal, hypertension	[131]
56	*Artemisisa absinthium* L. [Asteraceae]	Aguffa/ natra (O)	Leaf	Not Specified	hypertension, cough, febrile, malaria, dandruff	[92]
57	*Acanthospermum hispidum*[Asteraceae]	Harmaagussa(O)	Leaf	Leaves are crushed, boiled and one tea cup is drunk within 12 h interval for a week.	Hypertension	[136]
58	*Croton macrostachys* Hochest. ex. A. Rich [Euphorbiaceae]	Bisana (Am)	Root	Not Specified	Treats cancer, diabetes, hypertension, dysentery, fever, hypercholesterolemia, malaria, inflammation, ulcer, pain, infectious diseases	[88]
59	*Salvadoroa persica* L. [Salvadoraceae]	Kerja (Ha)	Root/stem	Root or stem is chewed and juice is kept in mouse	Abdominal colic, malaria, blood pressure, gum bleeding	[103]
60	*Stevia rebaudiana* Bertoni [Asteraceae]	Not specified	Leaf	Not Specified	Antihypertensive, antimicrobial, anti-obesity and antioxidant activities	[88]
61	*Meriandra dianthera* [Lamiaceae]	Mesaguh (T)	Leaf	Not Specified	Hypertension and diarrhea	[137]
62	*Otostegia integrifolia* Benth [Lamiaceae]	Chendog (T)	Leaf	Leaves are boiled in water and a cup of solution is taken every morning until recovery	Hypertension	[137]
63	*Zingiber officinale* Rosc. [Zingiberaceae]	Gengible (T)	Rhizome	The rhizome is chewed	Hypertension	[137]
64	*Schinus molle* L [Anacardiaceae]	Tselim berbere (T)	Stem	The stem is chewed	Hypertension	[137]
65	*Crepis rueppellii* Sch. Bip [Asteraceae]	Yemidir gusmt [Am]	Root	Root is boiled in water and taken as tea at bed time	Hypertension, dysentery with blood	[138]
66	*Satureja punctata* Benth. Briq [Lamiaceae]	Lomishet (Am)	Leaf	Leaves are cooked and the extract is taken orally	Treatment of liver diseases, hypertension, diabetes and other disorders	[139]

Table 1: List of medicinal plants used for management of hypertension.

Am: Amharigna, O: Afaan Oromoo, T: Tigrigna, Sd: Sidamigna, G: Geez, S: Somaligna, Ha: Hammerigna.

Conclusion

The prevalence of hypertension and the use of herbal medicines have been shown to increase all over the world, particularly across the developing countries. More than 80% of people who live in the developing countries rely on herbal medicines for their health care needs. The medicinal plants reported in this study are anti-hypertensive herbal agents that have been studied scientifically as well as used in Ethiopian traditional medicine. In the present review, a total of sixty six medicinal plants have been identified and recorded for their use in management of hypertension. Though most of these medicinal plants are widely utilized in different parts of the country, only safety and efficacy information of some of them such as *Moringa stenopetala*, *Thymus serrulatus*, *Thymus schimperi*, *Syzygium guineense* and *Calupurinea aurea* were scientifically tested in animals. Thus, it is relevant for recent and future researchers in the field to conduct the safety and efficacy study of the remaining traditional claimed medicinal plants and generate the information to protect the public health.

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