

## REVIEW

# A review of some common African spices with antihypertensive potential

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## Abstract

Hypertension is the most common non-communicable disease, with about 1.28 billion hypertensive people worldwide. It is more prevalent in men than women and more common in the elderly. Hereditary, age, obesity, lifestyle, diet, alcohol, and chronic metabolic diseases are the major risk factors of hypertension. Treating hypertension is a complex process as there are several mechanisms responsible for its pathogenesis; hence, a combination of several drugs is used for managing hypertension. Drugs used in managing hypertension are expensive and often come with associated side effects; thus, there is need for alternative means of managing this life-threatening disease. These drugs do not achieve the recommended blood pressure target in most people; more so majority of people with hypertension do not follow the treatment regimen religiously. Some Africans have been reported to become normotensive as a result of dietary consumption of spices. Several spices have been used over the years in Africa to manage hypertension. The aim of this review is to evaluate the ethno-medicinal use, bioactive phytochemical composition, bioactive compounds present, and pharmacological applications of spices commonly used in Africa for managing hypertension. Most of the plants used contained polyphenols, flavonoids, tannins, anthraquinone, flavonoids, cardiac glycosides, and saponins. Dietary supplementation of *Xylopiya aethiopica* and other spices in diet have been proven to significantly reduced plasma angiotensin-I-converting enzyme (ACE) than simvastatin (the reference drug). Toxicological, histological, and hematological evaluation revealed that acute and chronic consumption of most of these spices are safe. Studies have also revealed that some of the spices can be used as alternative therapy alongside usual antihypertensive medications.

**Practical implication:** The prevalent rate of hypertension is on the increase in both the developed and developing countries. People often skip medication due to their busy schedule and anti-hypertensive potential side effects; however, this is not the case with food/spices as most people consumed them daily. Deliberate, right combinations and consistent incorporation of spices with proven anti-hypertensive potential into our diet may be of great benefit in normalizing blood pressure and mitigate other complications on the heart and vital organs.

**KEYWORDS**

ACE, hypertension, medication, spices, supplement

## 1 | INTRODUCTION

Hypertension or elevated blood pressure means the persistent force of blood against the artery wall leading to increase in blood pressure. According to World Health Organisation (WHO, 2021), blood pressure on two different days with both days exceeding 140/90 mmHg is classified as hypertension. The first (higher) number is the systolic, which is the blood pressure when the heart contracts, while the second (lower number) is the diastolic, which is the blood pressure when the heart relaxes (Ondimu et al., 2019). It is usually measured using upper arm cuff; however wrist devices are used for obese persons with extreme size of the arm (Nerenberg et al., 2018). According to WHO (2021), it is the leading cause of death globally. About 1.28 billion people have hypertension as of 2015 with 75% of them from low- and middle-income countries. 25% men, 20% women, 7% pregnant women, 2% children and adolescent of world population have hypertension; hence it is of serious public health concern (Hoffman, 2020; Nerenberg et al., 2018). It is estimated that 1.56 billion or 31% of the world population will be hypertensive by 2025 (Obarisiagbon et al., 2018). Males are at higher risk of developing hypertension than women, especially for women at that are yet to reach menopause (WHO, 2021). It is a silent killer, because it develops over many years with large number of people unaware of its symptoms (Sharma et al., 2019). It is a chronic and age-related disorder which often progresses to cardiovascular and renal complications (Dai et al., 2021). It is dangerous as it puts the heart under stress of extra work. The best way to detect hypertension is to have blood pressure checked regularly. Several risk factors like hereditary, ethnicity, age, obesity, sedentary lifestyle, use of tobacco, high sodium intake, consumption of diet high in saturated fat and cholesterol, stress, pregnancy, alcohol, certain chronic conditions like diabetes, kidney diseases and sleep apnea (Vedanthan et al., 2019). It is a risk factor for diseases like heart attack, stroke, hypertensive retinopathies induced blindness, aneurysm, angina, kidney failure, dementia (Huang et al., 2017). Common symptoms associated with hypertension include chest pain (angina), muscle tremors, vision changes, irregular heart rhythms, headaches, nose bleeds, fatigue, buzzing in the ears. Primary hypertension has no identifiable cause; hence it is tagged essential hypertension. It is the most common form of hypertension as it accounts for about 85% hypertension cases. It is caused by an interaction between genetic and environmental factors. Secondary hypertension is caused by conditions that affect kidney, heart and endocrine systems. It can also be due to pregnancy. Most times people with secondary hypertension don't respond to anti-hypertension medications because the underlying factors needs to be treated first in order to control secondary hypertension (Lin & Eacker, 2020).

There are several mechanisms through which antihypertensive drugs regulate blood pressure. Based on mechanism of action,

antihypertensive drugs are classified as alpha blockers, alpha-beta blockers, beta blockers, aldosterone antagonist, renin inhibitors, diuretics, calcium channel blocker, angiotensin converting enzyme (ACE) inhibitors, angiotensin (II) receptor blocker, vasodilator and central acting agents (Laurent, 2017). Alpha blockers reduce the effect of substances narrowing blood vessels, relaxes muscles tones of the vascular walls (Aalkjaer et al., 2021). Alpha-beta blocker reduces impulse to blood vessels consequently slowing down heartbeat and the amount of flowing through the vessels (Julian et al., 2021). Beta blockers reduce the heart workload by dilating it, thereby making it to beat slowly with a lesser force (Aksentijević & Shattock, 2021). Aldosterone antagonist prevents salts and fluid retention (Agarwal et al., 2021; Ferreira, 2021). Renin inhibitors slow down renin production (renin initiates reaction that increases blood pressure) (Ferreira et al., 2018). Diuretics eliminate excess sodium and water from the body. They are commonly used in combination with other antihypertensive therapies (Moser et al., 2020). Calcium channel blocker prevents stronger and harder contraction. They relax and widen narrowed blood vessels (Minesh & Chakraborty, 2021). Angiotensin converting enzyme (ACE) inhibitors help blood vessels to relax and open up, consequently lowering the blood pressure (Ahmad et al., 2019). Angiotensin (II) receptor blocker prevents angiotensin from binding to its receptor, thereby preventing blood vessels from being constricted (Moore et al., 2021). Vasodilators prevent muscles in the arterial walls from tightening and narrowing the arteries (Akalu & Belsti, 2020). Central acting agents induce CNS regulation of heart rate and narrowing of blood vessels (Laurent, 2017).

Most of these drugs exert their antihypertensive effect by serving as competitive inhibitors of ACE. Less than 25% of people diagnosed with hypertension attained their recommended blood pressure target by taking drugs (WHO, 2021). However, the use of these drugs is limited due to financial constraints and side effects. This has necessitated the search for safer and lower-cost naturally-occurring alternatives. Studies have shown that food rich in antioxidants have the potential to lower the risk of cardiovascular diseases (Arise et al., 2021). Several spices have been reported to be rich in antioxidants and by extension have demonstrated antihypertensive and cardio protective potentials in both primary and secondary hypertension (Ciumărnean et al., 2020). Angiotensin converting enzyme inhibitor compounds isolated from spices include chlorogenic acid, hydroxycinnamic acid, gingerol, capsaicin, curcumin, eugenol, gallic acid, vanillic acid, rutin, apigenin, epicatechin, linalool,  $\beta$ -ocimene,  $\alpha$ -farnesenerutin, quercetin, ellagic acid, paradol, pellucidin A, peperomia, and  $\beta$ -phellandrene (Adefegha et al., 2018; Ahmad et al., 2019; Ranilla et al., 2010). Hence, the research provides comprehensive list and mechanism of action of spices commonly used in Africa with proven anti-hypertensive effect (Figure 1).

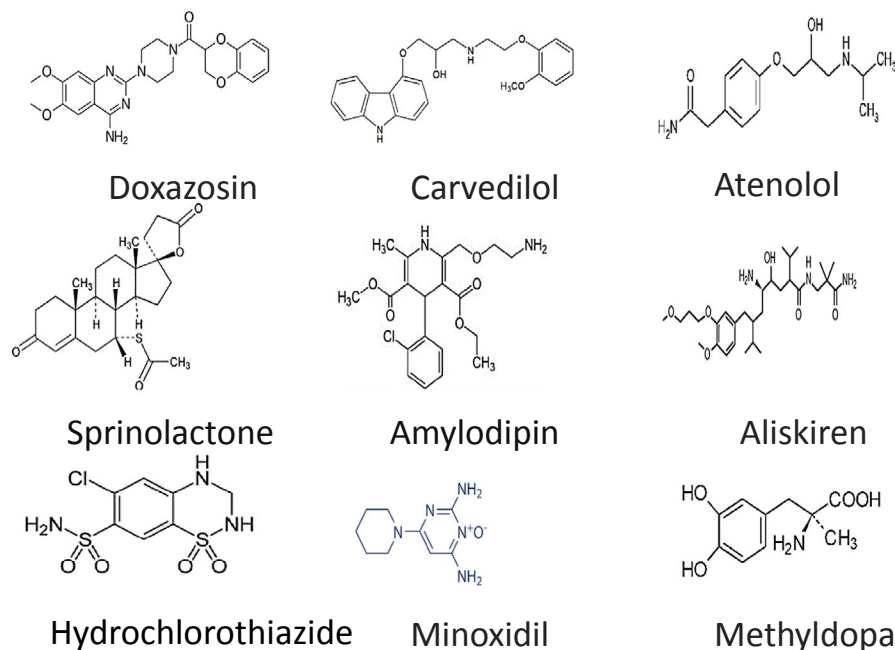


FIGURE 1 Structures of some drugs used for managing hypertension

## 1.1 | Spices with antihypertensive potentials

### 1.1.1 | *Xylopi aethiopica*

*Xylopi aethiopica* is called negro pepper or Ethiopian pepper or African pepper or Guinea pepper. It is a member of Annonaceae family and is commonly found in Central, West and South Africa. In traditional medicine, it is used for treating bronchitis, asthma, pharyngeal infections, arthritis, rheumatism, diarrhea, dysentery; stomach disorder and menstrual disorder (Erhirhie & Moke, 2014). It has been proven to have antimicrobial (Asekun & Adeniyi, 2004), anticancer (Adaramoye et al., 2011), analgesic (Woode et al., 2012), antioxidant, hypolipidemia (Nwozo et al., 2011), antisickling (Uwakwe, 2013), antihelminthic (Suleiman et al., 2005), anti-arthritis (Obiri et al., 2014), antidiabetic (Mohammed et al., 2016), antidepressant (Biney et al., 2016), and anti-inflammatory (Obiri & Osafo, 2013). Phytochemical screening revealed that *Xylopi aethiopica* contained alkaloids, proanthocyanidins, tannins, anthraquinone, flavonoids, cardiac glycosides and saponins (Aguoru et al., 2016; Gbadamosi & Kalejaye, 2017). The major compounds in *Xylopi aethiopica* are  $\beta$ -pinene, 1,8-cineol, linalool,  $\beta$ -ocimene,  $\alpha$ -farnesene,  $\alpha$ -terpineol, terpinene-4-ol, rutin, quercetin, ellagic acid, paradol, bisabolene, myrtenol, and  $\beta$ -phellandrene (Adefegha et al., 2018).

Somova et al. (2001) reported that hexane extract of 20 mg/kg *Xylopi aethiopica* exhibited antihypertensive and diuretic activity. They observed significant difference in the systolic blood pressure and heart rate. They administered compounds isolated from *Xylopi aethiopica* (xylopic acid and kaurenoic acids) on rats and observed significant normotensive activity. Their investigation revealed that these compounds work by blocking calcium channels. They further show that the compounds have coronary vasodilating activity which

is comparable to verapamil (standard calcium channel blocker) and diuretic effect comparable to chlorothiazide (a reference diuretic drugs). They proposed that reabsorption of  $\text{Na}^+$  and  $\text{K}^+$  is inhibited in the early segment of distal tubule by these compounds. Their investigation revealed that the crude hexane extract of *Xylopi aethiopica* has low toxicity with  $\text{LC}_{50}$  of 0.3 ng/mL. Adefegha et al. (2018) reported antihypertensive effect of *Xylopi aethiopica* dietary supplement, their investigation revealed that 4% *Xylopi aethiopica* in diet significantly reduced ACE than simvastatin (the reference drug). Onyebuagu et al. (2013) reported that dietary *Xylopi aethiopica* significantly dose dependently increases serum concentrations of  $\text{Ca}^{2+}$ ,  $\text{HCO}_3^-$ ,  $\text{PO}_4^{3-}$ ,  $\text{Cu}^{2+}$ ,  $\text{Zn}^{2+}$  and  $\text{Mn}^{2+}$ ; while concentrations of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$  and  $\text{Mg}^{2+}$  were not significantly altered. They inferred that increase in  $\text{Ca}^{2+}$  concentration will help to decrease blood pressure by preventing accumulation of  $\text{Cl}^-$  and  $\text{Na}^+$  in the serum.

### 1.1.2 | *Peperomia pellucida*

*Peperomia pellucida* also known as pepper elder or shiny bush is a member of Piperaceae family. It is a native of Africa, Asia South and Central America. It is widely distributed in Madagascar, Somalia, Eritrea, Angola, Zambia, Zimbabwe and other Africa countries (Kartika et al., 2016). It is usually found during the rainy season and with succulent stem. It is used ethnobotanically for treating cough, sores, boil, fracture, conjunctivitis, asthma, hypertension, urinary infection, gastro-intestinal disorder, kidney disease. Also, its pharmacological potential has been reported as anticancer, antibacterial, anti-inflammatory, analgesic, hypotensive, antidiabetic, fibrinolytic, antisickling and antidiarrhea (Adhitia et al., 2017). Phytochemical screening revealed that *Peperomia pellucida* contains glycosides,

anthraquinones, terpenoids and tannins (Saputri et al., 2015). Major compounds isolated from *Peperomia pellucida* are quercetin, pellucidin A, peperomia A,B,C and E, 2,3,5-trimethoxy-9-(12,14,15-trimethoxybenzyl)-1H-indene (Ahmad, 2019).

Saputri et al. (2015) reported strong inhibitory activities of *Peperomia pellucida* on ACE with  $IC_{50}$  value of 7.17  $\mu\text{g/mL}$ . Their investigation revealed that the inhibitory effect of *Peperomia pellucida* was more potent than captopril (the reference drug used as positive control). Adhitia et al. (2017) reported the ability of ethanol extract of *Peperomia pellucida* to inhibit ACE, an enzyme which activity is linked to hypertension. Their investigation revealed that subjecting the extract to about 10 kGy cobalt-60 radiation did not significantly affect its ability to inhibit ACE. Nwokocha et al. (2012) reported that aqueous *Peperomia pellucida* reduced heart rate, systolic, diastolic and mean arterial pressure of rat in a dose dependent manner. Their investigation revealed quercetin, pellucidin A and peperomia A, B, C from *Peperomia pellucida* inhibits angiotensin converting enzyme (ACE) and relaxes blood vessels through nitric oxide dependent mechanism.

They also reported mild inhibition of human cytochrome  $P_{450}$  enzymes by *Peperomia pellucida*, they proposed the use *Peperomia pellucida* as alternative and complementary medicine which might be beneficial as it may not interfere with drugs used in first line treatment of hypertension. Ahmad (2016) isolated quercetin from *Peperomia pellucida* and reported its ability to inhibit ACE, consequently preventing the formation of angiotensin II and development of high blood pressure. Ahmad (2019) also reported the isolation and ACE inhibitory activity 2,3,5-trimethoxy-9-(12,14,15-trimethoxybenzyl)-1H-indene and pellucidin A from *Peperomia pellucida* with  $IC_{50}$  values of 27.95 and 4.4  $\mu\text{g/mL}$  respectively. Their investigation revealed that activity 2,3,5-trimethoxy-9-(12,14,15-trimethoxybenzyl)-1H-indene exhibited stronger ACE inhibitory activity than activity 2,3,5-trimethoxy-9-(12,14,15-trimethoxybenzyl)-1H-indene and pellucidin A. Also, Ahmad et al. (2019) reported the ability of phenolic compounds from *Peperomia pellucida* to inhibit ACE based on in silico studies.

### 1.1.3 | *Ocimum gratissimum*

*Ocimum gratissimum* is also known as sweet, scented basil or scent leaf or Africa basil, it is a member of the Labitae family. It is indigenous to West Africa. It is called "effirin" in Yoruba, "Daidoya" in Hausa and "Ahuji" in Igbo. It has culinary use and is commonly applied to food and soupt to enhance their aroma and flavor. It is rich in polyphenol, terpenoids, tannins, saponins, steroids and flavonoids (Ganguly et al., 2021). It used ethnobotanically for treating hepatitis, headache, stomach upset, fever, cold, fungi infection, diuresis, diarrhea, pneumonia, liver disease (Onyebuchi & Kavaz, 2020). Pharmacologically it has been proven to possess anticonvulsant, anti-arthritis, hypoglycemic, antimicrobial, ovicidal, analgesic, anti-inflammatory and immunostimulatory activities (Irondi et al., 2016). Analysis using HPLC revealed the presence of gallic acid, catechin,

chlorogenic acid, caffeic acid, ellagic acid, epicatechin, quercitrin, quercetin, rutin, kaempferol and luteolin were isolated in *Ocimum gratissimum* leaf (Irondi et al., 2016). Essential oil of *Ocimum gratissimum* contains eugenol, thymol, citral, geraniol and linalool (Bhavani et al., 2019). Shaw et al. (2017) reported the ability of aqueous extract of whole plants of *Ocimum gratissimum* to inhibit ACE with  $IC_{50}$  of 56.3  $\mu\text{g/mL}$ . They isolated rutin (a phenolic compound responsible for the hypotensive activity). 500 mg/kg of was fed to rat and it significantly reduce ACE in this rat when compared to spontaneously hypertensive rats that were not treated (negative control). Their investigation revealed that aqueous extract of *Ocimum gratissimum* had no adverse effect based on liver function test for a period of 8 weeks. They also reported the ability of *Ocimum gratissimum* to inhibit ACE and pancreatic lipase; hence they proposed that it could be used for managing obesity related hypertension. Onyema-Iloh et al. (2018) reported that 200 mg/kg and 400 mg/kg exhibited hypotensive potential of methanolic extract of *Ocimum gratissimum* in NaCl induced hypertensive rat. The extract also exhibited nephroprotective activity. They reported that the extract was able to compete favorably with 30 mg/kg lisinopril (the reference drug) in reducing elevated serum sodium level in hypertensive rat and competed favorable than the reference drug in restoring serum potassium level in hypertensive rat. It also performed better than the reference drug in reducing serum levels of chloride, bicarbonate, urea and creatinine. Interaminense et al. (2005) reported dose dependent hypotensive and bradycardic activities of essential oil of *Ocimum gratissimum* leaves intravenously administer to hypertensive rats. Their investigation revealed that eugenol was responsible for this normotensive activity and results obtained suggested that the extract and the compound isolated acted by relaxing vascular smooth muscles of the rats.

### 1.1.4 | *Allium sativum*

*Allium sativum* is also known as garlic, it is one of the oldest plants cultivated by humans (Ekşi, 2020); it belongs to the Amaryllidaceae family. It is often used as spice due to its aromatic nature. Ethnobotanically, it is used for treating headache, worm, heart disease, tumor, bites, diabetes, renal disorder, intestinal disorder, lung disorder (El-Saber Batiha et al., 2020). It has been reported for anti-cancer, antioxidant, hepatoprotective, hypolipidemic, anti-inflammatory, antithrombotic, antihypertensive, antimicrobial, and cardioprotective activity (Nasir et al., 2020). It is rich in saponins, phenolics and flavonoids. The major compound in garlic is S-allyl cysteine sulfoxide (SACS), thiosulfinates (allicin), alliin, ajoenes, quercetin, and vinylidithiins (Shouk et al., 2014).

Asdaq and Inamdar (2010) reported the ability of 250 mg fresh garlic homogenate (FGH) to lower blood pressure and inhibit angiotensin-I converting enzyme (ACE) in fructose-induced hypertensive rat. Their investigation revealed that co-administration of low dose of captopril (standard anti-hypertensive drug) and FGH produced a remarkable additive blood pressure lowering and ACE inhibitory

activity than those of SACS or captopril and SACS. This enhanced activity by the FSH suggests that there are other bioactive compounds present in it aside SACS that are responsible for its normotensive effect. Asdaq and Inamdar (2011) also reported that 250 mg/kg garlic homogenate complemented the protective effect of hydrochlorothiazide (standard drug) in managing fructose induced hypertension and isoproterenol induced myocardial damage in albino rats. Their investigations revealed that garlic homogenate alone or when combined with hydrochlorothiazide restore blood pressure, body weight, cholesterol and histopathological changes in treated rats. Mukherjee et al. (2009) reported that both freshly crushed garlic and processed garlic possess cardioprotection potential, however, the freshly crushed garlic showed superior performance. Han et al. (2011) reported antihypertensive activity of processed garlic in spontaneous hypertensive rats (SHR) and on human subjects in a dose dependent manner. Their investigation revealed significant reduction of diastolic blood pressure within two weeks of administering 500 mg of processed garlic in humans, while it took 8 weeks to lower the systolic blood pressure by 8.05 mmHg. Daily dose of 30 mg/kg significantly lower blood pressure in SHR. McMahon and Vargas (1993) reported antihypertensive potential of allicin, their investigation revealed that 2,400 mg of allicin from garlic significantly lower diastolic blood pressure within 5–14 hr of administration. Suetsuna (1998) reported that dipeptide derived from garlic inhibits angiotensin I converting enzyme (ACE). They reported that 200 mg/kg of the dipeptide significantly lowered blood pressure in spontaneously hypertensive rats than 10 mg/kg captopril (the standard drug). Garlic works by relaxing the vascular muscles through NO production, inhibiting angiotensin converting enzyme (Hadrache-Jarraya et al., 2021).

### 1.1.5 | *Zingiber officinale*

Ginger is scientifically known as *Zingiber officinale*. It is a member of the Zingiberaceae family. It originated from Asia, but is currently also grown and eaten in Africa (Dissanayake et al., 2020). The rhizome is used as spice due to its aromatic nature. It is used in traditional medicine for treating nausea, vomiting, constipation, diarrhea, anorexia (Langner et al., 1998). Pharmacologically it has been proven to possess anti-inflammatory, diuretics, hypotensive (Sanghal et al., 2012), hepatoprotective (Yassin et al., 2010), analgesic (Jia et al., 2011), antioxidant (Stoilova et al., 2007), antithrombotic, antipyretic (Ghayur & Gilani, 2005; White, 2007). Phytochemical screening revealed the presence of saponins, polyphenols, cardiac glycosides, flavonoids, alkaloids and reducing sugars (Osabor et al., 2015). The major compound is gingerol, shogaol, zingerone, and paradol (Dissanayake et al., 2020).

Ranilla et al. (2010) reported ACE inhibitory activity of 0.5–2.5 mg/kg of ginger extract, with 2.5 mg has the most effective. Also, Mccue et al. (2005) reported ACE inhibitory activity of ginger, their comparative assessment of common America and Asia food and spices revealed that ginger is the most potent ACE inhibitor

investigated. Mohan et al. (2007) reported anti-hypertensive potential of petroleum ether extract (PE) and toluene fraction (TF) of ginger rhizome in hypertensive rats. Their investigation revealed that 50 mg/kg PE and 10 mg/kg TF exhibited significant hypotensive effect within 2–4 weeks in deoxycorticosterone acetate (DOCA) induced hypertensive rats and 5 weeks in fructose induced hypertensive rats, they proposed that ginger rhizome exhibited this effect by possibly stimulating muscarinic receptors and also by blocking calcium ion channels. Sanghal et al. (2012) reported protective role of ginger against systolic high blood pressure in rats that were fed high fat diet, their investigation revealed that rats fed on high fat diet developed elevated blood pressure, whereas those that were fed high fat diet as well as 500 mg/kg of ginger did not develop high blood pressure. Talaei et al. (2018) reported that 1g of ginger significantly lower blood pressure of patient with type II diabetic, while the blood pressure of those placed on placebo did not reduce. Ghayur and Gilani (2005) reported blood pressure lowering activity by crude extract of ginger rhizome in a dose dependent manner (0.3–3 mg/kg) in rats and guinea pig. Their investigation revealed that the mechanism of the hypotensive nature of the extract was a result of blocking calcium ion channels. Sompinit et al. (2020) reported anti-hypertensive activity of peptides from crude hydrolysate of ginger. Their investigation revealed that VTYM peptide from ginger had  $IC_{50}$  of  $16.4 \pm 0.4 \mu\text{mol/L}$  on ACE inhibition.

### 1.1.6 | *Parkia biglobosa*

African locust beans also known as nere is botanically known as *Parkia biglobosa*, it's a deciduous perennial plant commonly found in the savannah region of West Africa. It is a legume that is a member of the Fabaceae family. In Nigeria, it is known as iru in Yoruba, origili in Igbo, and dorowa in Hausa (Airadion & Ogbuagu, 2020). It is highly nutritious and its' commonly used as spice for stew, vegetables and soup. The dehulled seed contains about 42% protein, 24% lipids, 20% carbohydrate, 9% fiber, and about 462 kcal/100 g (Hassan & Umar, 2004). Phytochemical screening shows that it contains polyterpenes, polyphenols flavonoids, catechictannins, saponin, and sterols (Kassi et al., 2018). Oil from of *Parkia biglobosa* seed have been reported to contain arachidic, stearic, palmitic, behenic, and linoleic acids (Balogun et al., 2018).

It is used in traditional medicine for treating jaundice, pneumonia, wounds, eye infection, hypertension, diabetes, diarrhea, leprosy, chicken pox, measles, tooth decay, hernia, hemorrhoids, osteopathies, mumps, microbial infection and many other diseases (Kassi et al., 2018). Pharmacologically, it has been reported to possess hypoglycemic (Okaiyeto et al., 2021), anti-oxidants (Sunmonu and Lewu, 2019), antibacterial (Abioye et al., 2013), antihypertensive, hypolipidemia (Ayo-Lawal et al., 2012) and anti-inflammatory activities (Ukwuani & Ahmad, 2015).

Airadion and Ogbuagu (2020) reported antihypertensive activity of *Parkia biglobosa* in egg-yolk induced hypertension in rats. Their investigation revealed that rats administered with 400 mg/kg



of *Parkia biglobosa* extract did not develop hypertension and there was no significant difference between their blood pressure and the control (group on normal diet) throughout the 21 days study period, while those that did not receive the extract but were fed egg yolk formulated diet developed significant increase in blood pressure.

Ognatan et al. (2011) reported antihypertensive potential of *Parkia biglobosa* in human subjects, they enrolled 100 people of both sexes, each within the age bracket of 40–50 years from a region in Togo, West Africa that are known for high consumption of fermented *Parkia biglobosa* and another 100 people within the same age group from a non-consuming region. Their investigation revealed significant decreased in systolic and diastolic blood pressure and heart rate ( $p < .01$ ) in the consuming group compared non-consumers. They also reported that the consuming group had significant lower HDL and triglycerides, but significantly higher HDL ( $p < .01$ ) and magnesium ion when compared to the non-consuming group. Ouédraogo et al. (2012) reported vasorelaxant activity of roasted and fermented seeds of *Parkia biglobosa* in a concentration dependent manner in aorta pre-contracted by phenylephrine. Their investigation revealed that 10 mg/mL of *Parkia biglobosa* seed totally restored contraction induced by phenylephrine. They proposed that *Parkia biglobosa* seed exhibited vasorelaxant activity by its effect on smooth muscles and through production of prostaglandins in the endothelium.

### 1.1.7 | Curcuma longa

Turmeric is scientifically known as *Curcuma longa*, it belongs to the ginger family, *Zingiberaceae*. It is a yellow rhizome that grows mostly in Asia and Africa (Adaramoye et al., 2009), it is usually processed into powder known as curry, which is often used as spice, flavoring and coloring agents in food and stew (Ahmed et al., 2020). Phytochemical screening revealed that it contains sesquiterpenes, polyphenols, saponins, cardiac glycosides, alkaloids, flavonoids and tannin (Sawant & Godghate, 2013). Curcumin, zingiberene, cineol, borneol, curcuminoids,  $\alpha$ -turmerone, phellandrene, and sabinene are the major compounds isolated from turmeric (Lee, 2006; Yue et al., 2010). Ethnobotanically it is used for treating ulcer, fever, wound skin disease, cough, palpitation, eczema and arthritis (Rahmat et al., 2021). Pharmacologically it has being demonstrated to have antimicrobial, antioxidants, anti-inflammatory, cardioprotective, hepatoprotective, hypoglycemic, antihemolytic, antiulcer, neuroprotective and anticancer activities (Adaramoye et al., 2009; Lan et al., 2018; Yue et al., 2010). Lekshmi et al. (2014) reported that water, methanolic, and ethylacetate extracts were more potent in inhibiting ACE than captopril (reference drug). All the three extracts had  $IC_{50}$  that were significantly lower than captopril, hence confirming their superiority. Lan et al. (2018) reported that curcumin reported of 100 mg/kg of curcumin delay stroke in spontaneous hypertensive rats, they proposed that was able to decrease the production of reactive oxygen species and improve the functioning

of vascular endothelium by relaxing carotid artery. Adaramoye et al. (2009) reported that methanolic extract of turmeric displayed hypotensive, bradycardic and vasodilation effect in rats. Their investigation revealed that 20 mg/kg intravenous administration of turmeric extract caused about 27% reduction in blood pressure and 19.3% bradycardia. Their findings revealed that methanolic extract of turmeric inhibited extracellular  $Ca^{2+}$  influx and/or inhibition of intracellular  $Ca^{2+}$  mobilization by blocking calcium channels. Li et al. (2016) reported that demethoxycurcumin (a compound isolated from turmeric) inhibited production of nitric oxide and prevented endothelium dysfunction in wistar rat. Their investigation revealed that 10 mg/kg of demethoxycurcumin reduced blood pressure by about 26 mm Hg in rats.

### 1.1.8 | Cuminum cyminum

Cumin is scientifically known as *Cuminum cyminum*. It belongs to the Apiaceae family. It is a herbaceous plant that is a native to Egypt and has been cultivated in the Mediterranean region and other parts of the world. It has a strong flavor and aroma (Fatima et al., 2018). Ethnobotanically, it is used for treating jaundice, dyspepsia and diarrhea, gastro-intestinal disorder, headache, rheumatism, and kidney stone. Pharmacologically it has been proven to have anti-microbial, antidiabetic, anticancer, antioxidant, anti-inflammatory, analgesic, hypotensive, hypolipidemia, bronchodilatory, antio-osteoporotic, anti-amyloidogenic, and immunomodulatory activities (Al-Snafi, 2016; Boskabady et al., 2005; Fatima et al., 2018; Johri, 2011). Phytochemical screening revealed that it contained alkaloid, flavonoid, glycoside, resin, saponin, tannin, anthraquinone, coumarin and steroid (Prajapati et al., 2019). Cuminaldehyde, oleoresin, thymol, pinene, hellandren, carvone, cymene and terpinene are the major compounds found in cumin (Al-Rubaye et al., 2017). Kalaivani et al. (2013) reported that 200 mg/kg of aqueous extract of curcumin administered for 9 weeks reduces systolic blood pressure and increases arterial endothelial nitric oxide in renal hypertensive rats. They observed that the extract induces the production of nitric oxide synthase (iNOS), Bcl-2, TRX1, and TRXR1 and represses the expression of Bax, TNF- $\alpha$ , and IL-6. Their investigation revealed that curcumin seed can enhance endothelium function, reduce inflammation and oxidative stress in hypertensive rats. Ranilla et al. (2010) reported low in vitro inhibition of ACE by curcumin, this may mean that the mechanism of the blood pressure regulation might not be by inhibiting ACE. Gurunath (2006) reported that 300 mg/kg of alcoholic extract of cumin significantly lower systolic blood pressure from 178 to 161 mmHg in male Sprague Dawley hypertensive rats.

### 1.1.9 | Thyme vulgaris

Thyme scientifically known as *Thyme vulgaris*, it is a member of the *Lamiaceae* family. It is usually used as spice commonly added to stew, meat, salad and food to enhance their aroma and flavor. It is a native of Egypt and is commonly cultivated in the Mediterranean region

(Alu'datt et al., 2018). It is used as expectorant, antimicrobial, sedative, antirheumatic, antihypertensive, antidepressant, memory enhancer and cold reliever in traditional medicine (Porte & Godoy, 2008). Pharmacologically, it has been shown to possess anticancer, anti-inflammatory, antimicrobial, antioxidant, immunostimulant, growth

enhancing and antispasmodic activities (Mustafa et al., 2020; Salehi et al., 2018). Phytochemical screening reveals that thyme contains alkaloids, flavonoids, resins, saponins, glycosides, tannins and unsaturated sterols and triterpenes (Shaban et al., 2015). Gallic acid, caffeic acid, rosmarinic acid, eugenol, ursolic acid, thymol, carvacrol,

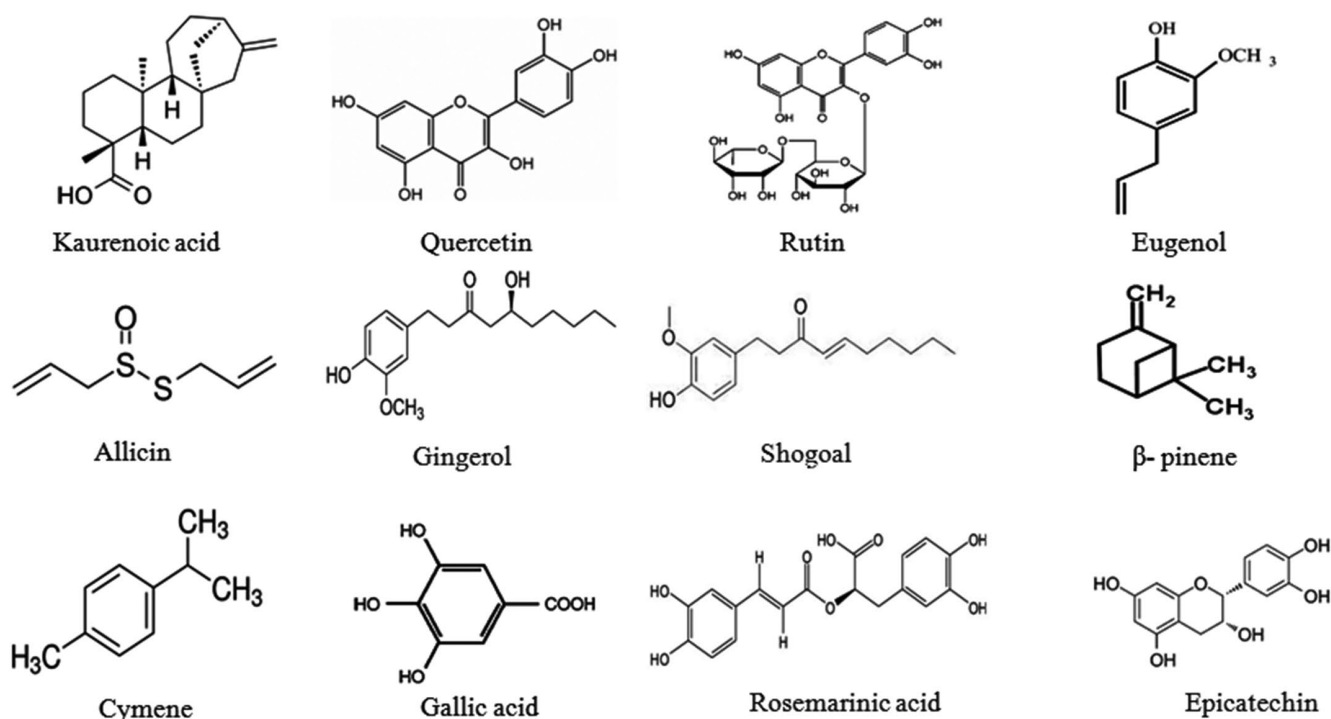


FIGURE 2 Structures of compounds isolated from spices with anti-hypertensive activity

TABLE 1 Major compounds isolated from spices with antihypertensive activity

Compounds	Mechanism	References
Kaurenoic acid	Vasorelaxant by activating NO synthase, blocks extracellular influx of $\text{Ca}^{2+}$ . It activates $\text{NO}^-$ -cGMP pathway and opens $\text{K}^+$ channels	Tirapelli et al. (2004)
Quercetin	Modulation in cell signaling and gene expression; regulation of renin-angiotensin system; increase in endothelial nitric oxide synthase activity	Serbanet al. (2016)
Pellucidin A	ACE inhibition	Ahmad (2019)
Rutin	Endothelium-dependent vasorelaxation ACE inhibition	Ushida et al. (2008) Goud & Nvl (2019)
Eugenol	Activates endothelial cell TRPV 4 channels and dilates mesenteric arteries	Peixoto-Neves et al. (2015)
Allicin	Vasorelaxant activity induced by $\text{H}_2\text{S}$ production through both endothelium dependent and independent pathways	Cui et al. (2020)
Gingerol	Vasodilation and NO production	Ghareib et al. (2015)
Shogaol	Prevents atherosclerosis and endothelial dysfunction	Hong et al. (2013)
Zingerone	Vasorelaxant through $\text{NO}^-$ and guanylate cyclase stimulation	Ghareib et al. (2016)
$\beta$ - pinene	Endothelium-independent vasorelaxation caused by the inhibition of the $\text{Ca}^{2+}$ influx	Moreira et al. (2016)
Cymene	Vasodilator through the participation of potassium channels	Silva et al. (2015)
Terpinene	Relaxation of vascular smooth muscle	Lahlou et al. (2003)
Gallic acid	ACE inhibition and vasorelaxant	Kang et al. (2015)
Rosemarinic acid	ACE inhibition	Ferreira et al. (2018)
Epicatechin	$\text{NO}^-$ mediated vasorelaxation	Galleano et al. (2013)

luteolin, syringic acid, epicatechin, and apigenin are the major compounds present in thyme (Alu'datt et al., 2018). Oil from thyme is one of the most source essential oil in the world.

Kensara et al. (2013) reported that 100 mg/kg aqueous extract of thyme administered to hypertensive rats for 8 weeks reverses hypertension induced elevated serum levels of creatine, creatinine and cholesterol. More so, the coarse, protuberant, and wrinkled surface of aorta endothelium caused by hypertension was ameliorated by the extract. Also, debris and red blood cell cells covering the lumen of the aorta in hypertensive rats disappeared following the administration of *Thyme vulgaris*. Their investigation using electron microscope further revealed that increased aortic extracellular matrix leading to dispersion of cell nuclei in hypertensive-rats disappeared following administration of thyme. Systolic blood pressure of the treatment group ( $138 \pm 3.12$  mmHg) reduced significantly when compared to the untreated group ( $186 \pm 2.53$  mmHg). Mihailovic-Stanojevic et al. (2013) reported that 100 mg of injected wild thyme reduces both systolic and diastolic blood pressure and total peripheral resistance in spontaneously hypertensive rats. Low prevalence rate of hypertension in the Mediterranean region has been linked to their consumption of thyme. Shimada and Inagaki (2014) reported that 10 mg/mL of ethanolic extract of thyme exhibited 36% ACE inhibitory potential. They also reported that ursolic acid, apigenin, and rosmarinic acid isolated from thyme demonstrated ACE inhibitory activities with  $IC_{50}$  of 3.05, 2.93, and 1.67 mM, respectively. Haroun et al. (2002) reported that supplementing 2%–10% of rat feed with thyme display no toxic effect on them during a 6-week study. Acute toxicity test by Shaban et al. (2015) revealed that oral dosage of alcoholic extract of thyme up to 7000 mg/kg body exhibited no toxic effect in mice. Figure 2 shows some common African food spices with antihypertensive activity, while Table 1 and Figure 2 show some of the compounds isolated from spices with antihypertensive activity.

## 1.2 | Future research

This review will bring about the much-needed awareness on the benefits of spices in managing hypertension and also spur further research on drug candidates from compounds obtained from spices.

## 2 | CONCLUSIONS

This study shows that *Xylopi aethiopica* and *Peperomia pellucida* possess significant antihypertensive activity and extremely low toxicity than the reference drugs. The major bioactive compounds isolated from these spices were kaurenoic acid, quercetin, pellucidin A, rutin, allucin, gingerol,  $\beta$ -pinene, terpinene, gallic acid and epicatechin. These compounds normalize blood pressure and prevent other complications of high blood pressure through vasorelaxant and ACE inhibitory activity.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## AUTHOR CONTRIBUTIONS

**Raphael Idowu Adeoye:** Conceptualization; Writing-original draft; Writing-review & editing. **Enoch Joel:** Writing-original draft. **Adedoyin Iggunnu:** Writing-review & editing. **Rotimi Olusanya Arise:** Writing-review & editing. **Sylvia Malomo:** Supervision.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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