INTRODUCTION

Hypertension occurs when there is a pressure exerted by blood on the vessels, thereby causing the systolic or diastolic blood pressure (DBP) to be consistently and abnormally elevated above the normal threshold. Tabassum and Ahmad (2011) defined hypertension as having a systolic blood pressure (SBP) of ≥140 mmHg and a DBP of ≥90 mmHg. Additionally, it is the most important risk factor attributed to coronary heart diseases such as stroke, congestive heart failure, atherosclerosis, infarction, peripheral vascular disease, and overall mortality. There are two main types of hypertension: the first is termed essential hypertension which develops with no evident cause and the second is termed secondary hypertension, which exists due to prior disease conditions such as kidney problem, endocrine disorders, or diabetes (Paxherbal, 2010). The organs that are usually linked to hypertension are the heart, the kidney, vascular...
smooth muscle cell membrane, and the brain (Figure 1). It is important to also note that the four main factors that contribute to the development of high blood pressure in the arteries are the level of contraction of the blood ventricle, elasticity of arterial walls, the volume of blood in the arteries, and the systemic vascular resistance, all of which are constrained or increased when hypertension occurs (Richard, 2016).

Hypertension is a global epidemic health problem with a huge impact and variation in prevalence across all geographical areas. Report by Rajati et al. (2019) gives acclaim to the number of hypertensive patients rising to 1.56 billion worldwide toward 2025. Generally, the burden of hypertension and its ever increasing trends is prevalent across all social class (high, low, or middle-income countries) and enhanced as a result of its disparities in awareness, treatment, and control rates in various regions (Michael, 2016). It is common to have elderly populace with hypertension but report from O’Shea, Griffin, and Fitzgibbon (2017) revealed that more than 40% of people over 25 overtime develop the disease condition. High blood pressure is the most common non-communicable disease in Nigeria and accounts for an approximate range between 25% and 36.6% of emergency medical admissions in urban hospitals in Nigeria (Davies, Catriona, Adewale, Jacqueline, & Felix, 2015). The causative factors for the high rate of hypertension according to Kayima, Wanyenze, Katamba, Leontsini, and Nuwaha (2013) are the major problems of awareness, treatment, and control of the disease which have been low, when compared to developed countries. These developed countries have high levels of awareness where 50%–66% of the patients are conversant with their diagnosis. It is interesting that previous reports stated that low or middle-income countries have almost three times more cases of hypertension than high-income countries (Michael, 2016).

The etiology of hypertension is multifactorial (Dickson & Sigmund, 2006) and there are modifiable and nonmodifiable risk factors that cause the disease (Appel et al., 2003).

1.1 | Modifiable factors

The modifiable factors that contribute to hypertension include obesity or overweight, consumption of unhealthy diets, unhealthy lifestyle habits, negative mental attitude, physical inactivity, and socio-economic conditions (Figure 2). In many developed and a few developing countries, rising affluence has modified the dietary pattern of many, and this is characterized by increased consumption of diets rich in fat, sugar, and calories which affect the flow of blood in the vessels and functions of the heart (Rabia, Nousheen, & Arshad, 2011). This increases the availability of cholesterol and fat that block the walls of the arteries leading to hypertension (Das, Sanyal, & Basu, 2005).

Furthermore, an individual’s mental disposition toward day-to-day activities could predispose to hypertension. Negative mental attitudes to life such as hatred or excessive worry can complicate the severity of hypertension as it causes more stress to the arterial veins (Paxherbal, 2010). The socio-economic state of a region including the level of economic “hardship” and poverty, health care resources, health literacy or awareness are possible be major contributors to hypertension. Lifestyle habit and Physical inactivity are also major contributors to the development of hypertension. For instance, intake of alcohol and smoking affects normal body functioning in hypertensive patients (Andrew et al., 2016). In addition, excessive alcohol consumption and smoking have been shown to reduce absorption and bioavailability of many drugs including anti-depressants and anti-hypertensive drugs in the blood stream.

![Figure 1](image-url)  
**FIGURE 1** Schematic representation of the interplay between the systems and their respective organs when high blood pressure occurs.
Individually living sedentary lifestyles or are obese experience reduction in blood flow and contraction of the heart, hence, predisposing to or worsening the hypertensive condition (Paxherbal, 2010).

1.2 | Nonmodifiable factors

The nonmodifiable factors contributing to hypertension are hereditary/family history, age, gender, ethical or racial differences, coexisting disease condition such as kidney problems or diabetes (Figure 2). To illustrate this, a study by Framingham reported by Kannel (1987), revealed that patients with hypertension and hyperlipidemia also demonstrated particularly high risk of arteriosclerotic diseases. Also, in Japan, globalization has resulted in an increased number of hypertension patients living with hypercholesterolemia (Matsuzawa et al., 2000).

1.2.1 | Management of hypertension

Early treatment of hypertension significantly reduces the chances of complications thereby improving the range of blood pressure.
to a healthier status (Chobanian et al., 2003). Therapeutic means for the treatment of hypertension can be grouped into the Non-pharmacological approach and the Pharmacological approach. Non-pharmacological approach revolves mainly around changes in diet and lifestyle including actions such as "no smoking" habits, weight reduction, and increased physical activity. The use of antihypertensive drugs is a pharmacological approach. Interestingly, studies on dietary modification or intervention, which is a non-pharmacological approach to hypertension management have given encouraging results (Chukwuma, 2018).

### 1.2.2 Pharmaceuticals in hypertension therapy

Pharmaceutical drugs which target certain enzymes, proteins, receptors, and channels are readily available in the market and they include beta-blockers, calcium-channel blockers (CCBs), centrally acting sympatholytic, diuretics, and smooth muscle relaxants among others. These drugs act at specific target sites on the renin–angiotensin–aldosterone system (RAAS) and in other organs related to the regulation of blood pressure. Although they are commonly in use, they are known to have side effects in patients on long-term treatment posing a question of reliability (Ahmadi, Bahmani, Tajeddini, Kopaei, & Naghdí, 2016; Popovi, Mati, Bojovi, Stefanovi, & Vidakovi, 2016).

### 1.2.3 Renin–angiotensin–aldosterone system

The renin–angiotensin system (RAS) (also known as (RAAS)) hormone system increases blood pressure volume, fluid or electrolyte balance, and arterial tone (systemic vascular resistance) causing sodium reabsorption, water reabsorption, and vascular tone in a prolonged manner (Fountain & Sarah, 2019). Juxtaglomerular cells produce prorenin in the afferent arterioles of the kidney when prorenin gets activated to its active form (renin) by these cells, the sympathetic nerve is activated causing a decrease in blood pressure (systemic or renal artery hypotension) and decreased sodium load in the distal tubules of the kidney (Nehme, Zouein, Zayeri, & Zibara, 2019; Ren, Lu, & Danser, 2019). Renin binds to target protein, angiotensinogen found in the liver plasma and cleaves it to angiotensin I, a precursor for angiotensin II in the presence of the enzyme, angiotensin converting enzyme (ACE) found mostly in the vascular endothelium of the lungs and kidneys (Figure 3).

Produced angiotensin II binds to angiotensin II type I (AT) and type II (AT) receptors in the kidney, adrenal cortex, arterioles, and brain. Binding to these receptors leads to a number of physiological changes including vasodilation and relaxation when nitric oxide is generated. When angiotensin II binds to G protein-coupled receptors, it activates secondary messenger cascade causing arteriolar vasoconstriction which subsequently increases total peripheral resistance and an increase in blood pressure (Sztechman, Czarzasta, Cudnoch-Jedrzejewska, Szczepanska-Sadowska, & Zera, 2018). The presence of angiotensin II in the adrenal cortex stimulates the release of steroid hormone, aldosterone, leading to reabsorption of sodium in the salivary gland, sweat gland, and the gut and subsequent potassium excretion at the distal tubule and collecting duct of the nephron, osmotic pressure, extracellular cell fluid/blood volume, and blood pressure (Santos et al., 2019). In the systemic arterioles, the mechanism of action of angiotensin in the brain involves three stages which includes its binding to the hypothalamus causing thirst and increased water intake. Then, the release of antidiuretic hormone (ADH) which increases water reabsorption in the kidney using aquaporin channels in the posterior pituitary. The sensitivity of baroreceptor I (found in the walls of the vessels) decreases leading to an increase in blood pressure, which is the final response in the RAS (Fountain & Sarah, 2019).

### 1.3 Mechanism of action of antihypertensive drugs

Antihypertensive or cardio-inhibitory drugs basically are readily available medications to reverse or treat symptoms or adverse complications of hypertension and they target various organ sites. Importantly, their role is to simply decrease cardiac output, arterial pressure, systemic vascular resistance, thereby decreasing blood pressure and in some instances, the electrical conduction generated in the heart (Richard, 2016). Other routes of action of antihypertensive drugs includes targeting proteins like endothelin 1, dopamine 1, ATP acting K+ channel (acting as smooth muscle relaxant), and nitric oxide release related to the mechanistic pathway causing increased blood pressure (Sinha & Agarwa, 2019).

#### 1.3.1 Centrally acting sympatholytic drugs

Sympatholytic drugs include centrally acting antiadrenergic agents, peripheral sympatholytic drugs (which includes alpha-adrenergic blockers and beta-adrenergic blockers) and ganglionic blockers that acts on the sympathetic ganglia reducing sympathetic outflow (Richard, 2016). Sympathetic drugs that are not converted into active forms for the stimulation of presynaptic α2-receptors in the brain via negative feedback reduces the release of catecholamine, vascular resistance of blood, cardiac output, and subsequently blood pressure incudes clonidine and guanfacine. They are converted to an active product form MethylDopa to yield methylnorepinephrine before activating presynaptic α2-receptors, hence, releasing/decreasing blood pressure subsequently (Figure 4).

#### 1.3.2 Alpha- and beta-blockers/beta-adrenoceptor antagonists

Alpha- and beta-adrenoceptor antagonists are synonymously called beta-adrenergic blocking agents (BABAs) are known peripheral sympatholytic drugs activated by released norepinephrine from sympathetic
adrenergic nerves and they possibly bind to other catecholamine and epinephrine circulating in the blood stream (Richard, 2016). Alpha-blockers or α1-adrenergic receptors blockers increase nitric oxide release causing a reduction in systemic vascular resistance, cardiac contractility, vasodilation, and subsequently lowers blood pressure, examples include Doxazosin and Prazosin (Figure 5).

However, Beta-blockers binds to beta-adrenoceptors in cardiac nodal tissue, the conducting system, and contracting myocytes...
competitively to stimulate alpha-adrenergic receptors (Jáuregui-Garrido & Jáuregui-Lobera, 2012). There are beta₁ (β₁) and beta₂ (β₂) adrenoceptors which at attached to beta-blockers preventing norepinephrine or epinephrine supposed ligands from binding to beta-adrenoceptors at the binding site reducing sympathetic tone or influences on the heart. There are two types of beta-blockers based on the receptors they bind to: nonselective (β₁/β₂) blockers (Labetalol, Carvedilol) and selective (Atenolol, Metoprolol) β₁ blockers (Figure 5).

1.3.3 | Angiotensin-converting (ACE) enzyme inhibitors

During a hypertensive state the enzyme, ACE activates angiotensin I yielding angiotensin II, which is a vasoconstrictor (Fountain & Sarah, 2019). Inhibitors of ACE act by blocking angiotensin II generation, which is a major effector of the RAAS to subsequently produce aldosterone, a vasoconstrictor. ACE inhibitors act by completely binding to angiotensin-converting enzyme and are known as heterogeneous agents with pharmacologic, pharmacokinetic, and therapeutic differences among them (Arjun & Rajiv, 2019). They include Captopril, Quinapril, and Benazepril (Figure 6).

1.3.4 | Angiotensin II receptor blockers (ARBs)

Angiotensin II is a mineral corticoid and a product of the RAAS which binds to angiotensin II receptor (AT1 receptor) releasing aldosterone from the adrenal cortex, which regulates salt and water balance in the body (Richard, 2016). However, the presence of angiotensin II receptor blockers (ARBs) antihypertensive agents blocks the interaction of angiotensin II and angiotensin II receptor specifically. Hence, causing relaxation of smooth muscles and increase in salt and water excretion. Thereby, leading to reduction of plasma volume of sodium and reduction in renal damage and cellular hypertrophy (Jáuregui-Garrido & Jáuregui-Lobera, 2012). Examples of ARBs include Irbesartan, losartan, and valsartan (Figure 6).

1.3.5 | Diuretics

These drugs are prescribed with the aim of removing excess water and salt from the kidney which is from the body’s tissues and blood. They include Loop diuretics, potassium-sparing diuretics, and thiazide diuretics (Arjun & Rajiv, 2019) (Table 1). Loop diuretics drugs acts in the kidney loops by reducing Na⁺ reabsorption by acting on Na⁺/K⁺/2Cl⁻ co-transporter. Therefore, reducing the cardiac volume and blood pressure as such, it is specially used in the therapy of volume-induced hypertension (Brunton, Chabner, & Knollmann, 2011). Thiazide diuretics reduces salt concentration but in a lesser volume than diuretics (Alan, 2019). However, potassium-sparing diuretics acts on Na⁺/K⁺ exchanger mechanism in order to block the action of aldosterone from binding to mineralocorticoid receptor resulting in an increased sodium concentration or reduced sodium reabsorption state at the expense of potassium, which will be excreted slowly (Richard, 2016).

1.3.6 | Vasodilators

Direct muscle relaxants or vasodilators antihypertensive drugs include Hydralazine and Minoxidil apart from others such as D₂ dopamine receptor agonists, calcium channel blockers, potassium channel

---

**Figure 6** Schematic representation of the strategic site of action of angiotensin converting enzyme (ACEIs) inhibitors and angiotensin II receptor blockers (AT1-blockers)
openers, nitric oxide relaxants (gaseous vasodilator) (Richard, 2016). In the smooth muscle, Hydralazine activates guanylyl cyclase leading to a decrease in intracellular calcium concentration in the sarcoplasmic reticulum causing a reduction of the peripheral vascular resistances and low blood pressure (Brunton et al., 2011). Minoxidil stimulates the opening of ATP modulated K⁺ channels in the vascular smooth muscle, membrane stabilization, vasodilation, and smooth muscle relaxation, thereby increasing cardiac output when activated to its active form by the liver (Bennett, 1997). Its side effect includes hirsutism (excess hair growth as a result of excess androgen hormone secretion).

1.3.7 Calcium channel blockers, a vasodilator

Calcium channel blockers binds to α₁-subunit of the L-type calcium channel in muscle cell membranes (Figure 7). They cause the reduction of calcium flux mainly to lower calcium concentration and reduce vascular smooth muscle tension as such, reducing muscle contractility. There are three groups: (a) dihydropyridine derivatives (nifedipine, amlodipine, nicardipine, felodipine, nisoldipine, barnidipine, and isradipine) found in vascular smooth muscle, its effect is not as frequent on the cardiac muscle during arterial vasodilation (Sinha & Agarwa, 2019) while (b) phenylalkylamines (verapamil) and (c) derived from benzodiazipines (diltiazem) not only inhibit L-type Ca²⁺ channels non-selectively on the smooth muscle cells, but also on cardiac cells known as AV nodes (Brunton et al., 2011).

2 FOOD BIOACTIVE COMPOUNDS IN THE MANAGEMENT OF HYPERTENSION

Omega-3 fatty acids possess antihypertensive effects which enables them to regulate inflammatory signaling modulating expression of cytokines and prostaglandins with vasoactive properties, wherein they interact with cyclooxygenase-1 (COX-1) enzyme to moderate
prostaglandin synthesis (Ulu et al., 2014). In addition to its ability to regulate the levels of oxylipins, a vasoconstrictive with inflammatory effects produced by soluble epoxide hydrolase derived from fatty acids. According to Caligiuri, Aukema, Ravandi, Guzman,

and Dibrov, 2014 omega-3 fatty acids can inhibit the activity of soluble epoxide hydrolase, thereby reducing the production of such oxylipins. Food rich in plants oils like flaxseed oil and soybean oil, nuts, and seeds (walnuts, flaxseed), fish and seafood (salmon, tuna, and sardines) are recommended to hypertensive patients by dieticians as compared to diet rich in saturated and trans fat, which contributes to the development of hypertension. Diet rich in fat and low intake of vegetable and fruits like garlic, citrus, and pomegranate juice causes hypertension complications (Asgary, Keshvari, Sahebkar, Hashemi, & Rafieian-Kopaei, 2013).

Garlic is a vegetable with antihypertensive and antioxidant effects as a result of allicin, a sulfur compound that inhibits angiotensin II and promote vasodilation (Ried, Frank, & Stocks, 2013). Fruits which includes citrus fruits, garlic, and pomegranate juice have cardiovascular benefits (Andrew et al., 2016). Typically, oranges and grapefruits citrus fruits have demonstrated antihypertensive properties although at different degree/extent experimentally (Díaz-Juézar, Tenorio-Lopez, Zarco-Olvera, Valle-Mondragón, & Torres-Narváez, 2009). Citrus peels have been reported to be a rich source of bioactive compounds which are beneficial in the management of hypertension (Ademosun, Oboh, Tosin, & Opeyemi, 2018; Oboh & Ademosun, 2012). Other diet in managing hypertension and its complications includes high intake of fiber and potassium in fruits and vegetables, reduction in the quantity of meat and animal products, consumption of low-fat dairy (Drouin-Chartier et al., 2014).

Taking lifestyle and diet as a regulator of this disease condition have been acceptable worldwide with a known guideline for the prevention of hypertension with five non-pharmacological approaches which includes increasing physical activity; limiting alcohol consumption to 2 drinks a day for men and 1 drink a day for women; controlling dietary salt intake at 6 g/day; having a dietary approach to stop hypertension (DASH), that is, a diet rich in fruits, vegetables, and low-fat dairy products and reduced in saturated and total fat and attaining a normal weight, which is a body mass index (BMI) of <25 kg/m² (Appel et al., 1997; Harrington et al., 2013). Apart from these, there are several dietary nutrients that have been reported to act at noticed target sites during the stage of hypertension like the consumption of magnesium, phosphorus, calcium, and fiber irrespective of the fact that their consumption shows some inconsistency in managing hypertension, they still hold promising effects.

The use of herbal medicine as a promising alternative in the treatment of hypertension have been embraced for a while owing to the side-effects that pharmaceutical drugs exhibit (Kiriyama, Honbo, Nishimura, Shibata, & Iga, 2016). Even more common is the use of herbal medicines recently alone and/or with chemical drugs to treat various ailments, also common is the use of herbal medicinal plants which cuts across numerous ailments and is also recommended by natives’ communities for the treatment of hypertension providing a new areas of research (Ahmadi et al., 2016; Oboh et al., 2016; Oboh & Ademosun, 2011; Falzon & Balabanova, 2017; Lee & Hur, 2017; Lin, Yen, Chang, Sun, & Chang, 2017). Ginger contains a chemical compound, 6-gingerol functioning as a novel angiotensin II type1 receptor antagonist reflecting its function and ability to lower blood pressure (Liu et al., 2013). Interestingly, aqueous extract of ginger had been shown to inhibit lipid peroxidation as well as ACE in rat hearts (Akiniyemi, Ademiluyi, & Oboh, 2013). Additionally, bioactive compounds of ginger; 6-gingerol, 6-shogaol, and zingerone have also been shown to decrease blood pressure (Shin et al., 2001). Numerous traditional/folkloric plants have been used as complements to antihypertensive drugs, for instance, Passiflora edulis is capable of inhibiting angiotensin-converting enzyme (ACE), Achillea wilhelmsii blocks receptor operated and voltage dependent calcium channels, Crocus Sativus activates β2-adrenoceptors and Viscum album antagonizes alpha 1-adrenoceptor (Lee & Hur, 2017; Llorens et al., 2015; Mahmoudabady et al., 2014; Poruthukaren, Palatty, Baliga, & Suresh, 2014; Restrepo, Nieto cárdenas, Aristizabal, & Landazuri, 2014).

2.1 Some mechanisms for the antihypertensive action of food bioactive compounds-based therapy

Investigation with phytochemicals in treating various disease conditions are not made without through scientific backings. Folkloric plants with bioactive compounds acts via numerous channels in inhibiting or activating enzyme action related to hypertensive state. To illustrate, Hibiscus sabdariffa (Roselle) at 200 mg dosage administration to stage one and two hypertensive humans reduces Angiotensin 1-converting enzyme (Herrera-Arellano et al., 2007), its vascular relaxant properties includes the ability to increase NO release, block Ca²⁺ channel, and open K⁺ (ATP) channels (Al-Disi, Anwar, & Eid, 2016). The antioxidant prowess of Camellia sinensis (tea plant) was revealed by Newsome et al. (2014) in C57BL/6 mice at a dose of about 1% green tea extract concentration found to increase the level of antioxidant the body system in order to maintain body homeostasis.

Hibiscus sabdariffa (Roselle) and Nigella sativa (Black Cumin; Seed of Blessing) are typical examples of plants that are used for the folkloric treatment of hypertension due to their action as diuretics. Nigella sativa Increases Na⁺, K⁺, and Cl⁻ ion content in the urine at 5 ml · kg⁻¹ · day⁻¹ in SHR (spontaneously hypertensive rats) and the action of Hibiscus sabdariffa in both SHR and healthy men by reducing their uric acid level and plasma Na⁺ content in stage one and two hypertensive states makes it a preferred diuretic (Al Disi et al., 2016). Whereas, the inhibition of pro-inflammatory marker NF-kB and level of VCAM-1 was notable reduced in experimental models rats fed with high fructose treated with Allium sativum (Garlic) (Padiya et al., 2014).

The anti-protective effect of ginger owing to the bioactive compound 6-gingerol, a constituent was reported by Liu et al. (2013) to be an angiotensin II type1 receptor antagonist at an IC₅₀ of 8.17 × 10⁻⁶ M and a concentration as low as 0-50 μM in enzyme human aortic smooth muscle cells. Camellia sinensis Increases HO-1 (Heme-Oxygenase-1) as such its anti-proliferative role here will evidently
cause it to reduce the level of superoxide radicals produced in the body system and vascular blood pressure (Liu, Liu, Kuo, Chong, & Hsieh, 2014). Broadly, the antioxidant roles of plants with bioactive compounds can be found in numerous plant varieties. To illustrate, Ginger also inhibit lipid peroxidation as well as ACE in rat hearts (Akinyemi et al., 2013) while aqueous extract of ginger (0.05 mg/ml) has also been reported to inhibit it was found that ginger not only reduces levels of total cholesterol, LDL, VLDL, and triglycerides, but also inhibit ACE-1 activity (Akinyemi, Ademiluyi, & Oboh, 2014). Coptis chinensis increases antioxidants and reduces NADPH oxidase enzyme activity (Al Disi et al., 2016) and Panax Increases antioxidants levels at 60–120 μM in Hypoxia/Reoxygenation-induced oxidative injury in rat cardiomyocytes model (Doh et al., 2013) whereas, Hibiscus sabdariffa and Salviae miltiorrhiza are involved in the scavenging of reactive oxidant species and subsequently increasing antioxidant (Cho et al., 2013; Frank et al., 2012).

It is only reasonable that individuals with hypertension undergoing treatment with herbal or phytochemical foods should correlate the mechanism of actions of these compounds with their respective drugs to avoid unfavorable alterations in their blood pressure since every herbal plant follows multiple pathways, as this is not only important but relevant as some extreme cases leads to toxicity.

3 | FOOD–DRUG INTERACTION

Just like the any other substances, dietary compounds affect the activities of antihypertensive drugs as they alter the therapeutic efficacy and can lead to possible adverse effect. The term Interaction during metabolism can be defined as any alteration, pharmacokinetics, and/or pharmacodynamics, produced by different substances like other drug treatments, dietary factors, and habits such as drinking and smoking (Jáuregui-Garrido & Jáuregui-Lobera, 2012). Antihypertensive drugs are metabolized by drug metabolizing enzyme (CYP 450) so a correlation or association exists between drugs and other drugs and/or food (Mohammed & Mohammed, 2009). This could be either toxic, serve as inducers or inhibitors to CYP system (Jáuregui-Garrido & Jáuregui-Lobera, 2012). However, regulation of blood pressure while on treatment with medicinal plants/food is and has remained a controversial issue for decades. It is only important that the mechanism of which diet modulates the physiology of hypertension is explored (Patrcia, Nelsy, & Beatriz, 2017). The obvious challenges of using antihypertensive drugs has to do with the side effects that have been observed with some of the drugs. Hence, there is the need for new alternative or complementary therapies, which is the reason why research in this area is needed (Leung et al., 2017). Basically, food–drug interaction has been reported to cause new side effects since they have the ability to prevent a medicine from working the way it should by lowering drug effect or make disease state get worse (Semih & Ahmet, 2014). The interactions between antihypertensive drugs and food relating their mechanism of action and specific target sites to reflect their food/drug association have been reported although with a need for in-depth studies in the future.

3.1 | Interaction between food and diuretics

Loop diuretics (Furosemide) when taken together with food, it decreases the bioavailability of these drugs (with a decrease seen between 16%–45%) while Bumetanide reflect no changes in availability when administered with food (McCrindle, Li kamon wa, Barron, & Prescott, 1996). The decrease in bioavailability of loop diuretics when administered orally with food is affirmed with a single study found used to relate the threshold of the diuretic effectiveness as a result of a decrease in urinary excretion of these drugs after food intake (Bard, Bleske, & Nicklas, 2004). Accordingly, Jáuregui-Garrido et al. (2012) revealed that it is important to increase the bioavailability of hydrochlorothiazide in rats that are protein-calorie malnourished due to a decrease in the gastrointestinal and hepatic metabolism since Hydrochlorothiazide (a thiazide diuretic) have increased bioavailability with food. Hydrochlorothiazide reduces the level of magnesium, folic acid, vitamin B6, zinc, and coenzyme Q10. Hence, advice is designed toward intake of multiple vitamin and 30–90 mg CoQ10 daily replace these nutrients to reprimand this state (Stemen & Ahmet, 2014). In addition, Thiazide diuretics leads to increase in calcium content, it is thus reasonable to avoid intake of calcium supplements (above 400 mg/day) or vitamin D (above 400 IU/day). Likewise, diet rich in potassium like banana and green leafy vegetables (spinach) affect Potassium sparing diuretics resulting in severe hyperkalemia (Wallace, Gerencser, & Surley, 2013) and arrhythmias (Table 2).

3.2 | Interaction between food and alpha- and beta-blockers

The two common α blockers, Prazosin, and Doxazosin metabolism does not seem to have any significant changes based on food availability and there is no possible drug–nutrient interaction for Prazosin in relation to hypertension in humans yet recorded. However, experiment of undernourished animals revealed its ability to reduce SBP when administered at the periventricular nucleus of the hypothalamus (Pérez et al., 2006). The bioavailability of beta-blockers (bevantolol, metoprolol, timolol, and propranolol) administered in sustained release form is not affected when taken at the same time when ingested with food (Jáuregui-Garrido et al., 2012). Carvedilol and metoprolol are commonly prescribed beta-blockers. It should be noted that Carvedilol should be taken with food in order to decrease the chance of over depletion of the blood pressure. The FDA (2013) also suggest this medication should be taken in extended release capsules in the morning with food preferably not chewed, crushed, or divided. Intake of food rich in high protein diet and garlic increases the bioavailability of propanol although no relevant clinical effects have been reported (Asdaq & Inamdar, 2011). Orange juice has Hesperidin present in them which inhibits celiprolol (beta-blocker) when taken, causing a decrease in the absorption of celiprolol in the intestine (Mohammed & Mohammed, 2009) (Table 2).
3.3 Interaction between food and ACE inhibitors

Captopril, an angiotensin converting enzyme inhibitor, taken with food will have decreased clearance and have been reported to have decreased bioavailability and are with clinical effects taken simultaneously with food and antacids according to a review by Sundas et al. (2015) and Prescription states that any food in general should be eaten between one to two hours of drug intake (Everton, Rumão, & Rivelilson, 2010). Although there are no relevant food–drug interactions described in lisinopril, enalapril, Quinapril, and benazepril administered at any time with or without food (Bell, 1993). It is important for patients ingesting vegetables like bananas, oranges, green leafy vegetables with high potassium content to avoid them with ACE inhibitor drugs co-administered with diuretics (water pills) and/or salt substitutes with potassium supplements, or diuretics (FDA, 2013). Specifically, Digoxin have been reported to be affected by high intake of carrot fibers and patients are advised to avoid fiber foods due to activity (Everton et al., 2010). Treatment with other ACE inhibitors and diet rich in potassium or salt substitutes may cause hyperkalemia (Semih & Ahmet, 2014) (Table 2). Ultimately, the absorption of ACE inhibitors (ACEIs) increases when taken on an empty stomach (Stormer, Reistad, & Alexander, 2006).

3.4 Interaction between food and Angiotensin II receptor blockers (ARBs)

Most angiotensin receptor blockers drugs when simultaneously ingested with food do not get their absorption affected. However, propranolol, a beta-1 adrenergic receptor blocker when consumed with milk protein, increases the bioavailability of the drug in the plasma. Owing to this it is recommended to be taken with foods high in protein (Everton et al., 2010). In contrast, Valsartan, losartan, and telmisartan have decreased bioavailability when administered with food tend to have high plasma drug concentration when taken alone (Israili, 2000; Tamargo et al., 2006). Irbesartan seems to be different because it is not affected when ingested with food when administered (Brunner, 1997; Ruilope, 1997). Nevertheless, it is important to note that drugs that acts with similar cytochrome or drug metabolizing enzymes as ARBs when ingested together are prone to interact with each other.

3.5 Interaction between food and calcium blockers

Dihydropyridine calcium channel blockers (Felodipine and Nifedipine) experience changes in their activity based on food intake. Intake of a meal and nifedipine (tablet) decreases the possibility of side effects associated with peak plasma concentration of the drug causing the efficacy of the drug to remain unchanged and its sustained release formulations have enhanced serum levels (Everton et al., 2010). Intake of food and Felodipine in sustained release forms increased gastric retention time as such, taking grape fruit juice results in the toxicity of Felodipine since it is inhibited during its metabolism by the liver, doubling heart rate (Weitschies et al., 2005) (Table 2). Interestingly, grape juice also interacts to cause higher blood levels when taken with anti-anxiety medication Buspar (buspirone) (Semih & Ahmet, 2014). In contrast, Nondihydropyridine diltiazem and verapamil metabolism with dietary grape fruit juice causes no changes to its metabolism, do not affect the metabolism of which are also metabolized by cytochrome enzyme system (Kane & Lipsky, 2000; Sigusch, Henschel, Kraul, Merkel, & Hoffmann, 1994).

<table>
<thead>
<tr>
<th>Antihypertensive drugs</th>
<th>Medication instruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitors</td>
<td>When taken on an empty stomach, its absorption is enhanced. May cause hyperkalemia when taken with diet rich in potassium or salt substitutes</td>
</tr>
<tr>
<td>Alpha-blockers</td>
<td>It is advised to be taken with liquid or food to ensure extreme blood pressure reduction</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>It is advised to be taken on an empty stomach because food, especially meat, increases the drug’s bioactivity and can cause dizziness and low blood pressure</td>
</tr>
<tr>
<td>Antiarrhythmic drugs</td>
<td>The heartbeat becomes irregular when take with caffeine</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Their bioavailability increases with food except with Furosemide (loop diuretics) and are known to increase the risk of potassium deficiency</td>
</tr>
<tr>
<td>Potassium sparing diuretics</td>
<td>It is best to not take diuretics with potassium supplements or salt substitutes, which can cause potassium overload (hyperkalemia)</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Dihydropyridine calcium channel blockers metabolism is altered when food is ingested, Grape fruits causes Felodipine toxicity</td>
</tr>
</tbody>
</table>

**TABLE 2** Illustration of instances wherein pharmaceutical medication are given to antihypertensive patients with consideration linked to food–drug interaction
4 | CONCLUSION

Antihypertensive drugs act at strategic target sites of either the Renin-Angiotensin Aldosterone system or arterial blood pressure system operating using specific mechanism to modulate blood pressure. Although antihypertensive drugs actions are known, there is limited information with regard to the interaction of food and these antihypertensive drugs. The bio-availability of food substances have the tendency to alter drug reactions as seen in changes in the pharmaceutical, pharmacokinetic, and pharmacodynamics properties of drugs after intake of these medication. A brief chemistry was described in this review on the relevance of interaction of food and antihypertensive drugs nevertheless, further research is needed to extensively investigate the interaction between food and specific mechanism of action of individual antihypertensive drugs currently in existence in the market.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

ORCID

Olufunke Florence Ajeigbe https://orcid.org/0000-0002-4277-3859
Ayokunle Olubode Ademosun https://orcid.org/0000-0001-9767-1844

REFERENCES


How to cite this article: Ajeigbe OF, Ademosun AO, Oboh G. Relieving the tension in hypertension: Food–drug interactions and anti-hypertensive mechanisms of food bioactive compounds. J Food Biochem. 2020;00:e13317. https://doi.org/10.1111/jfbc.13317