



An Overview on Role of Nutraceuticals in Lowering Hypertension: A Review Article

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Abstract: Hypertension (HTN) is a global disease, hitting both developed and developing countries. It is a leading cause of significant health issues such as cardiovascular disease, stroke, and heart attack. In recent years, various studies have found links between specific dietary elements and improved HTN. Nutraceuticals are natural dietary components that have therapeutic potential. According to reports, functional foods and nutraceutical ingredients may help patients achieve their therapeutic blood pressure (BP) goals while also lowering cardiovascular risks by modulating oxidative stress, renin-angiotensin system hyperactivity, inflammation, hyperlipidemia, and vascular resistance. We reviewed the biological and pharmaceutical activities of various nutraceuticals like polyphenols and flavonoids, lycopene and tomato, garlic, fibers, vitamin D, Pycnogenol, omega-3-poly unsaturated fatty acid, coenzyme Q10, alpha lipoic acid, flaxseed, amino acid and minerals. This review emphasizes current understanding concerning the effects of common nutraceuticals on blood pressure management.

INTRODUCTION

Hypertension is considered as a global epidemic and a primary risk factor for cardiovascular disorders such as stroke, heart attack, heart failure, and aneurysm. According to the 8th JNC report, hypertension is defined as “an increase in blood pressure with systolic blood pressure greater than 140mmHg and diastolic blood pressure greater than or equal to 90mmHg”. Managing blood pressure is critical for maintaining health and lowering the risk of these dangerous conditions. Hypertension can be caused by excessive salt consumption, a high-fat diet, physical inactivity, genetics, tobacco and alcohol intake and being overweight. Most persons with hypertension do not feel any symptoms and hypertension is also called as silent killer disease. The signs and symptoms include severe headaches, chest pain, dizziness, difficulty in breathing, nausea, blurred vision, confusion epistaxis, abnormal heart beat. The complications include stroke, angina, heart attack, heart failure, kidney failure. The JNC-7 recommends lifestyle changes for all individuals with prehypertension or hypertension. Modifications include weight loss, reduced salt intake, aerobic exercises, minimizing alcohol use, and adopting the dietary approach to stop hypertension (DASH) diet plan. If lifestyle changes are insufficient to achieve desired blood pressure levels, drug therapy may be necessary. First-line treatments for hypertension include diuretics, Angiotensin Converting Enzyme (ACE) inhibitors, Angiotensin Receptor Blockers (ARBs), beta-blockers, and Calcium Channel Blockers (CCBs). Some people will take two or more antihypertensive medication to reach their blood pressure goal. Patients using hypertension drugs might experience dry cough with ACEIs, excessive or frequent urination with diuretics, erectile dysfunction, sleeplessness, depression, ankle oedema, and other side effects. While considering these side effects Nutraceuticals are a viable option for reducing high blood pressure in its early stages, while taking into account potential negative effects of antihypertensive medications. Nutraceutical products are substances that offer physiological benefits or prevent chronic diseases. Nutraceuticals are naturally occurring dietary supplements and have advantages over medicine because they rarely cause side effects.

1. Polyphenols and flavonoids

Polyphenols are the most prevalent secondary metabolites in the plant kingdom, which comprises of molecules of the flavonoid. (Flavones, flavan-3-ols, flavonols, flavanones, anthocyanins and isoflavones) and non-flavonoid family (Phenolic acids and stilbenes). Flavonoids are diverse group of naturally occurring phenolic compounds with anticarcinogenic and cardioprotective properties that can be found in fruits, vegetables, tea, and red wine. Furthermore, a high dietary intake of flavonoids prevents the development or progression of several cardiovascular illnesses, especially hypertension, by exerting cardio-vasculo-protective actions.

Classification

a. Flavonols

Glycosides, specifically quercetin and kaempferol, stand in for them. Quercetin administration was shown to lower systolic blood pressure in Goldblatt (GB) hypertensive rats and it also prevent cardiac and renal hypertrophy, both of which follow hypertension.

Kaempferol (KF) which is a naturally occurring dietary flavonoid. Because of its possible anti-inflammatory and antioxidant properties, kaempferol may have a beneficial effect on the cardiovascular system.

b. Flavones

Numerous research investigations have examined the antihypertensive effects of luteolin and chrysin; never the less there is a dearth of evidence regarding apigenin.

c. Flavanones

Flavanones have the cardioprotective properties include antioxidant, anti-inflammatory, hypolipidemic, and antiatherogenic activities.

d. Anthocyanins (ACN)

Anthocyanins are a large class of water-soluble plant metabolites belonging to the flavonoid family of phenolics, that give many fruit- and vegetable-based food products their vibrant reddish-orange to blue-violet hues. According to epidemiological research, consuming more anthocyanins may reduce the incidence of cardiovascular disease (CVD). Three main mechanisms have been linked, either directly or indirectly, to ACNs and the control of blood pressure.

1. It has been consistently demonstrated that ACNs raise endothelium-derived nitric oxide (NO) via modifying the expression and activity of endothelial nitric oxide synthase.

2. Due to their potent antioxidant properties, ACNs inhibit radical-induced NO conversion and NO oxidative damage, including the process that is triggered by NADPH oxidase.

3. It has been demonstrated that ACNs suppress the synthesis of chemicals that constrict blood vessels, including endothelin-1, thromboxane, and angiotensin II by inhibiting the activity of the angiotensin-converting enzyme (ACE) and by blocking the cyclooxygenase (COX) pathway.

e. Flavanols

Flavanols are antioxidants, which means they scavenge the harmful free radicals which damage cells, contributing to illnesses as cardiovascular disease.

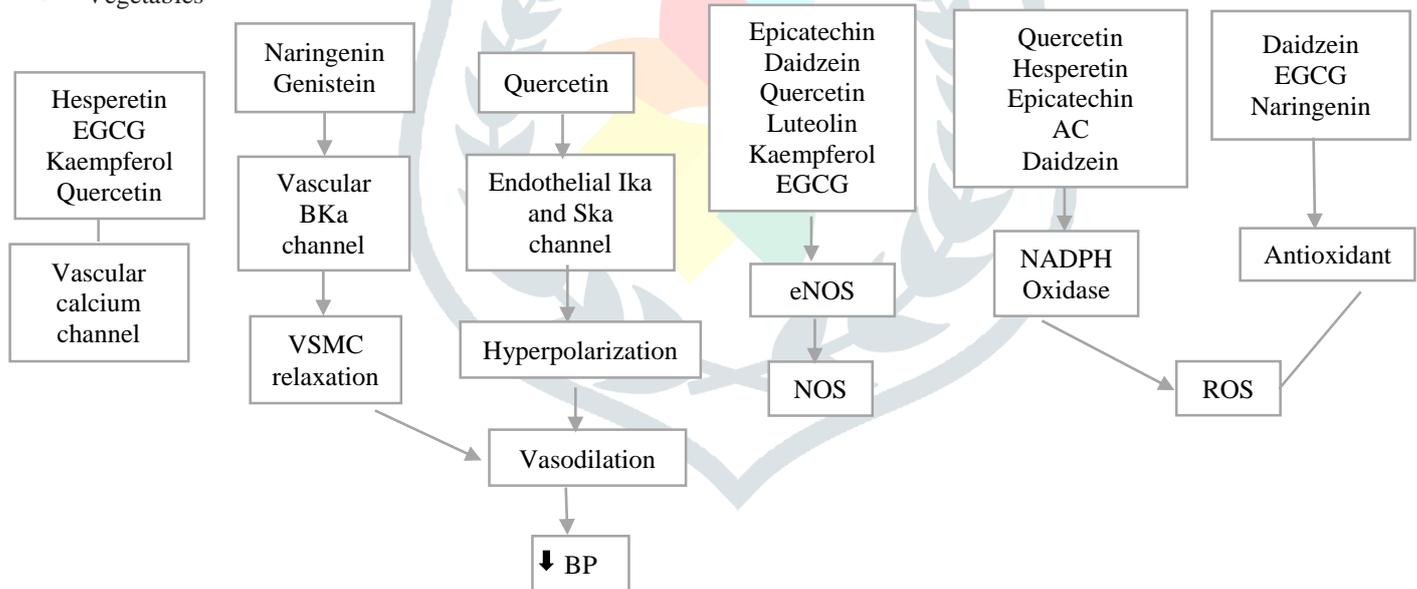
f. Isoflavones

Isoflavones are a class of flavonoid phenolic compounds. They are also referred to as phytoestrogens. Soy isoflavones supplementation may be considered as beneficial tool for blood pressure control and cardiovascular risk reduction in adults in general, including pre hypertensive patients. They have the ability to increase vasodilation by stimulating the endothelium and contributing to the maintenance of vascular homeostasis. Soy isoflavones have also been shown to reduce hypertension by influencing the components of the renin – angiotensin aldosterone pathway.

Genistein and daidzein, in particular, have been demonstrated to increase nitric oxide release in endothelial cells, resulting in vasodilation, reduced vascular resistance and eventually lower blood pressure

Dietary source of flavonoids:

- Berries
- Olives
- Soy and soy products
- Whole grains
- Wine
- Blak tea
- Onions
- Vegetables



Mechanism of action of flavonoids

2. Fibers

Dietary fiber decreases blood pressure by influencing the gut bacteria. A diet rich in fiber causes changes in gut microbiota and are linked to lowered blood pressure (BP) and have a protective role in the development of cardiovascular disease (CVD). The following foods include dietary fiber

- Beans
- Wholegrain cereals
- Cereal products
- Nuts and Fruit
- Vegetables
- Seeds
- Lentils

2. Lycopene and Tomato



Lycopene is a carotenoid found in red fruits and vegetables like papayas, tomatoes, red peppers, watermelon and others. Although lycopene cannot rise HDL cholesterol, research has indicated that it can enhance the LDL, HDL ratio. It has been discovered that lycopene reduces the production of defective HDL via modifying HDL functionality in the direction of anti-atherosclerotic phenotype. Tomato juice had a hypo-triglyceridemic impact, but only in those serum triglyceride levels were already high. Additionally lycopene is crucial in preventing CVs issues such as blood clots brought on by atherosclerotic alterations. Because of its antioxidant properties, lycopene reduces oxidative stress caused by angiotensin 2 and indirectly increases nitric oxide generation in the endothelium, hence having an antihypertensive impact.

3. Garlic



Garlic is the ripe bulb of *Allium sativum* Linn., belonging to the family Liliaceae. The benefits of raw garlic and garlic-based preparations include reducing blood pressure, preventing atherosclerosis, lowering cholesterol, decreasing plasma fibrinogen and inhibits platelet aggregation, enhancing fibrinolytic activity, and promoting cardiovascular health. Garlic reduces the production of vasoconstrictor prostanoids, inhibits the activity of the angiotensin-converting enzyme, increases the concentration and activity of nitric oxide, produces hydrogen sulfide, and reverses arterial remodeling by upregulating growth suppressors. Its pharmacological effect is thought to be attributed to a number of active ingredients, including allicin, which is extracted from alliin (*S*-allyl-cysteine-*S*-oxide) and the enzyme alliinase.

4. Omega-3 Poly Unsaturated Fatty Acid

It is also known as “healthy fats”. They are a class of lipids with a variety of biological functions including supporting heart health. There is an inverse relationship between cardio-vascular mortality or morbidity and the dietary intake of omega-3-PUFA, as they reduce the risk of coronary heart disease. PUFA increases the production of endothelial nitric oxide (NO) and reduce the activity of the ACE, which produces angiotensin II and also suppress the expression of TGF-Beta. As a result, it provides improved vasodilation and vascular compliance in both large and small arteries.

Dietary sources include:

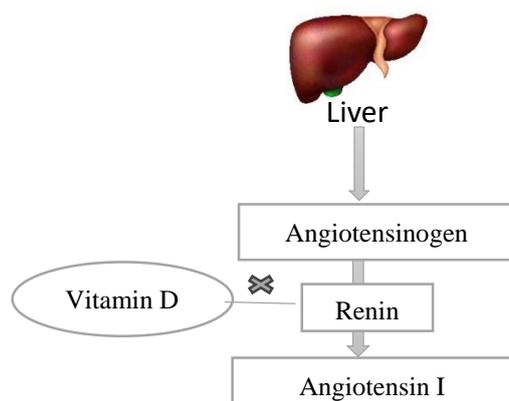
- Certain type of fish
- Ground flaxseed
- Walnuts
- Edamame

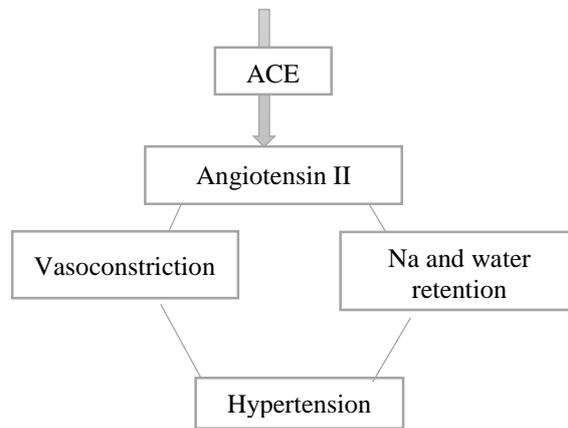
5. Vitamin D

There is an inverse association between vitamin D and hypertension. In addition to its antihypertensive properties, vitamin D also lowers parathyroid hormone and renin levels and has anti-inflammatory, vasculo-protective, and reno-protective effects. The renin-angiotensin-aldosterone system (RAAS) is impacted by vitamin D. Elevation of PTH levels, a sign of insufficient vitamin D, can also lead to hypertension. Vitamin D improves vascular endothelial function, which has a vaso-protective effect, lowers blood pressure, lowers vascular and myocardial remodeling, lowers the risk of left ventricular hypertrophy, slows fibrosis, lowers the risk of atherosclerosis, lowers insulin resistance and inflammation, and boosts immunity. At a normal level of vitamin D, the concentrations of renin and angiotensin II fall, which improves the course of hypertension. Vitamin D can alter blood pressure through a variety of processes, including the renin-angiotensin-aldosterone system (RAAS), the endothelium, and vascular smooth muscle. Damage to vitamin D receptors raised renin activity and circulation angiotensin II levels, resulting in arterial hypertension that can be minimized by inhibiting the RAAS.

Dietary sources include:

- Fatty fish
- Cheeses
- Beef liver
- Eggs





Mechanism of action of Vitamin D

6. Alpha Lipoic acid

It is naturally occurring di-sulfide molecule that is an important cofactor for numerous enzyme complex, including the respiratory enzymes of the mitochondria. Lipoic acid's anti-hypertensive effect appears to be linked to its anti-oxidase properties, since it reduces oxidative stress and increased superoxide anion production.

Dietary sources:

- Yeast extract
- Beetroot
- Spinach
- Tomatoes
- Broccoli
- Rice bran
- Garden peas
- Potatoes

7. Coenzyme Q10 (CoQ10)

It is commonly known as ubiquinone, is a vitamin-like, fat-soluble molecule present in human mitochondria. Coenzyme Q10, a non-prescription dietary supplement, may help reduce blood pressure. The main action of CoQ10 in hypertension is vasodilation, through direct effects on the endothelium and vascular smooth muscle.

- Impact on vascular endothelium.

Although the mechanism of CoQ10's antihypertensive action is unknown, it is likely due to its capacity to promote vasodilation through reduced peripheral resistance in the vasculature.

- Antioxidant properties.

Another suggestion is that CoQ10's antioxidant qualities enable free radicals to be quenched, resulting in the inactivation of endothelium-derived relaxing factor and/or fibrosis of arteriolar smooth muscle.

8. Pycnogenol

Pycnogenol is a standardized pine bark extracted specifically from French maritime pine trees (*Pinus pinaster*) found along France's coastline. Although the exact mechanism is unknown, Pycnogenol's blood pressure lowering effect involves angiotensin converting enzyme (ACE) inhibition, nitric oxide (NO) generation, and the oxidative and anti-inflammatory activities. Pycnogenol stimulates endothelial NO production via the enzyme nitric oxide synthase (NOS) with improved level of perfusion. Pycnogenol demonstrated anti-inflammatory effect to C-reactive protein (CRP), the most well-known inflammatory factor, which is linked to vascular stiffness, high blood pressure and atherosclerosis. Furthermore, NO interacts with platelets and prevents platelet aggregation.

9. Amino acids

Amino acids are organic compounds that combine to form proteins, hence they are also known as protein building blocks. These biomolecules have a variety of biological and chemical roles in the human body and are required for human growth and development.

During pregnancy, amino acids are necessary for fetal growth and development. Imbalanced amino acid consumption during pregnancy may increase the risk of hypertension in adult offspring.

Arginine, homoarginine, and tryptophan in blood arteries have been shown to regulate the development of atherosclerosis. Arginine is a NO substrate that is essential for endothelial-dependent vasodilation in blood vessels. Additionally, some arginine-related amino acids play a role in blood pressure management.

In addition, tryptophan and its metabolites have been demonstrated to cause vasodilation in blood vessels in a dose-dependent manner. Homoarginine is a nonproteinogenic amino acid that is structurally similar to arginine. Homoarginine, like arginine, has been shown to be a substrate in the production of NO.

Taurine is the most abundant sulfur-containing amino acid and is primarily obtained through dietary sources, despite the fact that it may be produced from cysteine. Taurine has antihypertensive properties due to its vasodilator function.

Homoarginine is a nonproteinogenic amino acid that is structurally similar to arginine. Like arginine, it has been shown to be a substrate in the production of NO.

Methionine is an important amino acid; one of its metabolic by products, homocysteine when increased, may stimulate asymmetric dimethylarginine synthesis, decrease endothelial function and raise blood pressure. Like taurine, cysteine is a sulfur-containing amino acid. Cysteine is also known to have a rate-limiting effect on glutathione production. Furthermore, cysteine is a component of glutathione, a key antioxidant molecule in our bodies. Cysteine is thought to have an antihypertensive effect due to its association with glutathione and H₂S signaling in blood pressure regulation. Furthermore, tryptophan and its metabolites have been demonstrated to cause vasodilation in blood vessels in a dose-dependent manner. These findings suggest that some amino acids have organ or tissue-specific effects on blood pressure regulation.

10. Flaxseed



Flaxseed, which is also called "linseed" belonging to the family Linaceae. It is a plant-based food that contains antioxidants, healthful fat and fiber. There are numerous mechanisms that describe the antihypertensive effect of flaxseeds.

1. The main 4 components in flaxseed that are capable for decreasing blood pressure include alpha-linolenic acid (ALA), lignan, fibers and peptides or a synergistic action of all the 4 components. The antihypertensive impact of ALA may be explained by its anti-inflammatory properties. Inflammation has been associated to the development of high blood pressure, and lignan found in flaxseed may have an antihypertensive impact due to its antioxidant function. Flaxseed's high fiber content may also help with blood pressure management. The hydrolysis of flaxseed protein causes hypotension by inhibiting renin and ACE function.
2. Guanylate cyclase activation regulates blood pressure.
3. Antihypertensive efficacy is mediated by the decrease of oxylipins caused by alpha linoleic acid-induced suppression of soluble epoxide hydrolase activity.

11. Minerals

a. Potassium

A potassium-rich diet and elevated blood potassium levels produce endothelium-dependent vasodilation by hyperpolarizing the endothelial cell via sodium pump activation and potassium channel opening. Endothelial hyperpolarization is transmitted to vascular smooth muscle cells, resulting in lower cytosolic calcium levels, which promotes vasodilation. In addition to increased vasodilation, other proposed mechanisms by which potassium can influence BP include natriuresis, alterations in intracellular sodium and tonicity, modulation of baroreceptor sensitivity, reduced vasoconstrictive sensitivity to norepinephrine and angiotensin II, increased serum and urinary kallikrein, increased sodium/potassium ATPase activity, and alteration in DNA synthesis and proliferation in vascular smooth muscle and sympathetic nervous system, improved insulin sensitivity, reduction in cardiac diastolic dysfunction, decrease in vascular neointimal formation, reduction in transforming growth factor (TGF)- β , and decreases in NADPH oxidase, oxidative stress, and inflammation

b. Magnesium

Magnesium is the most abundant divalent intracellular cation in the human body, and it ranks second only to potassium. Magnesium competes with Na⁺ for binding sites on vascular smooth muscle and functions as a direct vasodilator, similar to a calcium channel blocker. Magnesium promotes prostaglandin E (PGE), controls intracellular calcium, sodium, potassium, and pH, boosts nitric oxide, enhances endothelial function, lowers oxidized LDL, thromboxane A₂, and norepinephrine.

CONCLUSION

The management, prevention, and treatment of cardiovascular illnesses, such as hypertension, are determined by lifestyle, genetic factors, and physical activity. Nutritional supplementation may be a useful technique for managing and preventing hypertension and other cardiovascular disorders. Pharmacological therapy of hypertension has severe implications for health, and adverse effects are unpredictable. This review focusses on the non-pharmacological therapy of hypertension employing nutraceuticals that have anti-hypertensive action. Nutraceuticals work not only via antioxidant or anti-inflammatory characteristics, but also through vasodilation, hypolipidemic activity, vasculo-protective and reno-protective effects, as well as suppression of radical-induced nitric oxide conversion. Many nutraceuticals, such as phenolic compounds or polyphenols, lycopene, and flavonoids, are known to have beneficial effects on the cardiovascular system. The consumption and supplementation of nutraceuticals may help control blood pressure when combined with improvements in diet and lifestyle.

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