



# Role Of Nutraceuticals In Clinical Manifestation And Control Of Hypertension

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**Abstract:** Cardiovascular Disease (CVD) is a major adjustable risk factor linked to Hypertension, which is the primary cause of death globally. Although antihypertensive medications are available, blood pressure management remains inadequate in many demographics. This review examines the significance of dietary methods and nutraceuticals in hypertension management, highlighting their potential as complementary treatments. Nutritional strategies include reducing sodium intake, and increasing magnesium, vitamin C, calcium, garlic, L-arginine, omega-3 fatty acids, and beetroot consumption, among others. These elements function through various mechanisms, such as improving endothelial function, diminishing oxidative stress, and regulating vascular tone. Key findings underscore the blood pressure-lowering impacts of limiting sodium intake and increasing potassium intake, which effectively regulate electrolytes and enhance vascular health. Polyphenols and Omega-3 fatty acids present in tea, cocoa and fish, help alleviate vascular inflammation and rigidity. Nutrients such as magnesium and L-arginine boost nitric oxide levels, facilitating vasodilation. Emerging research supports the beneficial effects of flavonoids, garlic, and beetroot in enhancing endothelial function and lowering blood pressure. This review also highlights the potential benefits of combining dietary elements with antihypertensive drugs to improve blood pressure management. However, further long-term safety and efficacy studies on nutraceuticals are required to establish standard guidelines. The integration of these dietary approaches with lifestyle changes presents a promising method for hypertension management, especially in individuals with mild to moderate cardiovascular disease risk. The evidence supports incorporating dietary interventions into clinical practice to improve patient outcomes and lessen the global burden of hypertension.

**Key Words:** - Hypertension, Inflammation, Nutraceuticals, Antioxidants, Diet.

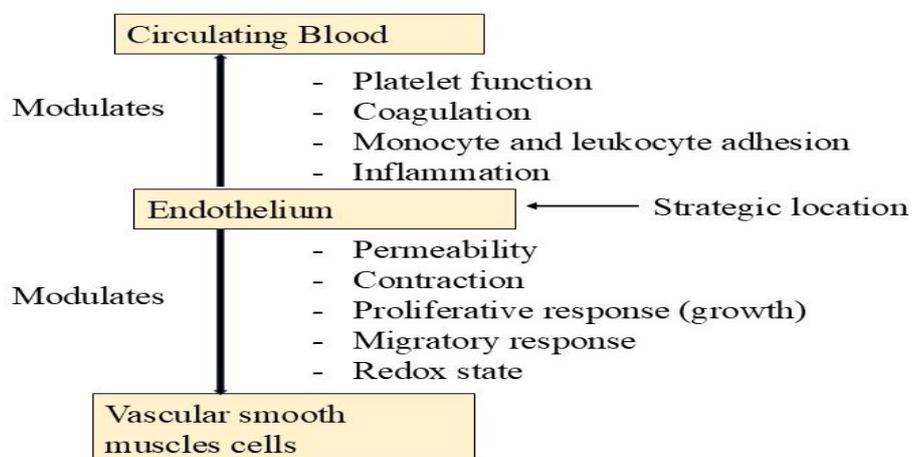
## I. INTRODUCTION

Cardiovascular diseases (CVD) represent the primary cause of death globally, accounting for 31% of fatalities as of 2012 [1]. Specifically, ischemic heart disease (IHD) and atherosclerosis are responsible for 38% of male deaths and 42% of female deaths under 75 in Europe, making them the top causes of premature mortality [2]. Estimates indicate that the global economic impact of CVD was \$906 billion in 2015 and is anticipated to rise by 22% by 2030 [3]. In affluent countries, CVDs are also the primary reason for disability. It is estimated that the growing burden of these diseases may lead to an increase in disability-adjusted life years (DALYs) lost from 85 million in 1990 to approximately 150 million by 2020, representing a major contributor to productivity loss as a result of psychological challenges [4]. Multiple risk factors play a role in the development of CVD. Historically, these have been categorized as modifiable factors, which can be altered through lifestyle changes or pharmaceutical treatments (like medications for hypertension, smoking, diabetes, and high cholesterol), and non-modifiable factors (such as family history, gender and age) [5]. Essential hypertension, which is a modifiable risk factor, is notably the most common in the general community, with occurrence rates in Western countries, including Italy, varying from 25% to 45%. Despite the presence of effective and well-tolerated antihypertensive treatments, hypertension is a

significant contributor to cardiovascular disease (CVD) across various CV risk profiles, especially in the elderly population (specific to those over 65 Year). In this context, numerous studies have shown that individuals with hypertension often present additional metabolic and cardiovascular risk factors primarily hypercholesterolemia, hypertriglyceridemia, metabolic syndrome and diabetes. These factors additionally elevate each individual's risk of experiencing hypertension-related complications such as congestive heart failure, cardiovascular death, end-stage renal disease, acute kidney injury, stroke. In clinical practice, the complex challenge of achieving the recommended treatment goals for blood pressure and cholesterol levels is often connected to the coexisting conditions of dyslipidemia and hypertension. A range of interventions, both medicinal and lifestyle-based, have been proposed to enhance the relatively low rates of hypertension management [6, 7]. Among these intervention, a dieting abundant in food and nutraceuticals has demonstrated beneficial core in wangle and controlling hypertension [ 8 ]. This consensus written document will systematically represent and psychoanalyze the data presently available to endorse the employment of nutrients and nutraceuticals for individuals with high spirits blood pressure who have different CVD hazard profiles.

## 2. Epidemiology

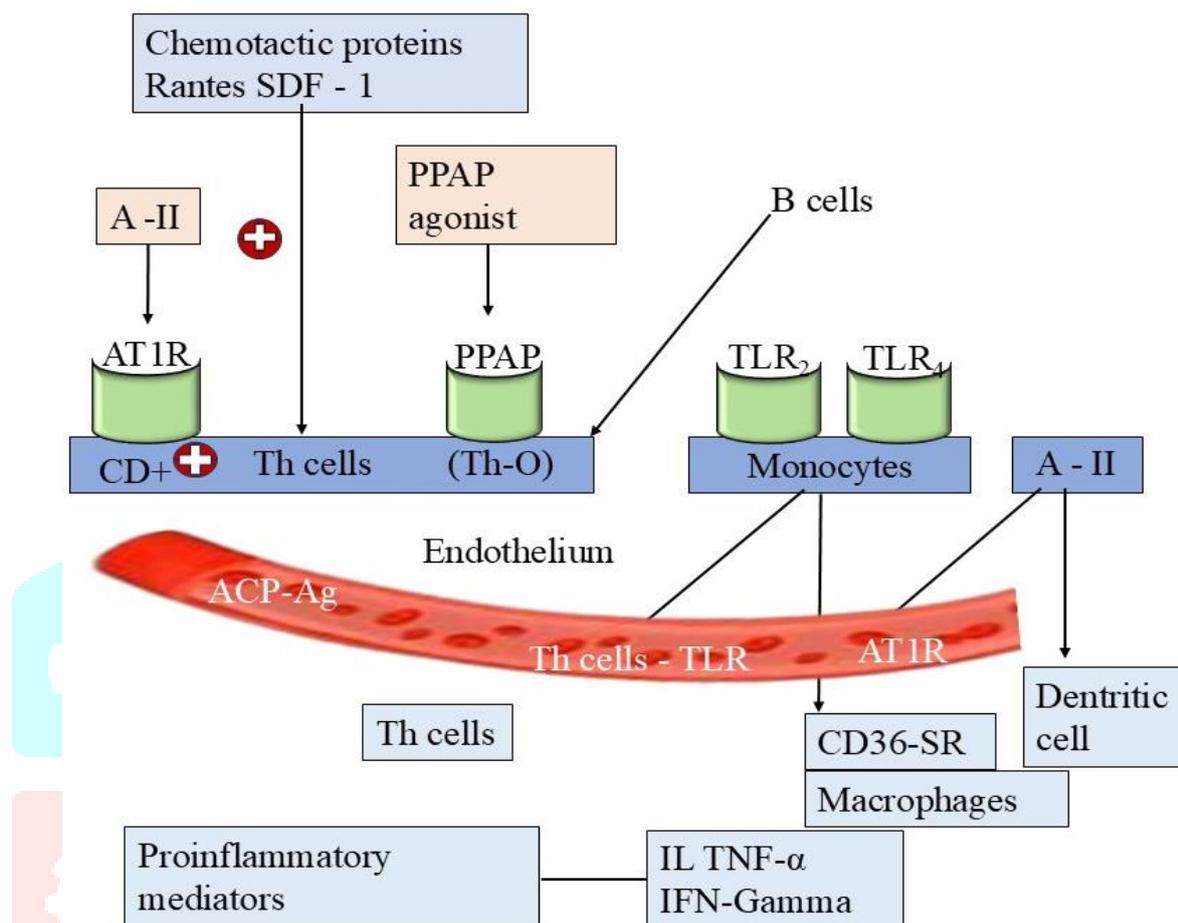
Epidemiology emphasises the causal role that nutrition intake and diet play in hypertension. The modern diet, which includes produce, replaced the Palaeolithic diet and led to an increase in diseases associated with malnutrition. Hypertension, atherosclerosis, and coronary heart disease, Kidney disease, Cerebral Cardiovascular events (ACCA), MI, and congestive heart failure (CHF), type 2 diabetes (T2DM) and diabetes type 2 metabolic syndrome (MS), obesity, and among these illness contrasts and compares with nutritional intake of Palaeolithic and modern diets that are linked to blood pressure control[9,10]. People now follow an unhealthy and unnatural diet as a result of their development from an agrarian, hunter-gatherer society to an agricultural, refrigerated society. Because 99.9% of human genetic material is shared, overall dietary changes have affected us more than our genes can compensate for. Our dietary, vitamin, and mineral consumption differs significantly from that of our Palaeolithic ancestors [11]. The greater risk of hypertension and cardiovascular diseases is due to the effects of the presented mechanisms that were the result of the metabolic dysregulation or oxidative stress that was caused by the possible interactions of macronutrients and micronutrients and oxidative stress from ROS and RNS with the formation of the free radicals and the subsequent activation of T and B cells related to auto-inflammation and the inflammation of vasculature (as shown in Figure\_1). In this sense, the immune response itself it include in the pathogenesis of hypertension and the magnitude of oxidative stress by the accumulation of RNS and ROS also other types of inflammation that involve T and B lymphocytes, cytokines, and adhesion molecules. Lowering of nitric oxide, Increases in endothelin, angiotensin II and bioavailability Initiate the heart failure, hypertension, and vascular dysfunction in conjunction with endothelial activation. Nutritionally related diseases have skyrocketed as a result of poor nutrition, obesity, and sedentary lifestyles.



**Figure\_1.** The Role of the vascular endothelium to maintain vascular homeostasis and health particularly, the high intake of  $\text{Na}^+/\text{K}^+$  Ratio of contemporary diet, along with the relatively low intake of omega-3 PUFA, rise in omega-6 PUFA, trans fatty acids, and saturated fat have been linked to hypertension, MI, CVA, CHF, CHD and renal disease [11–19].

### 3. Pathophysiology

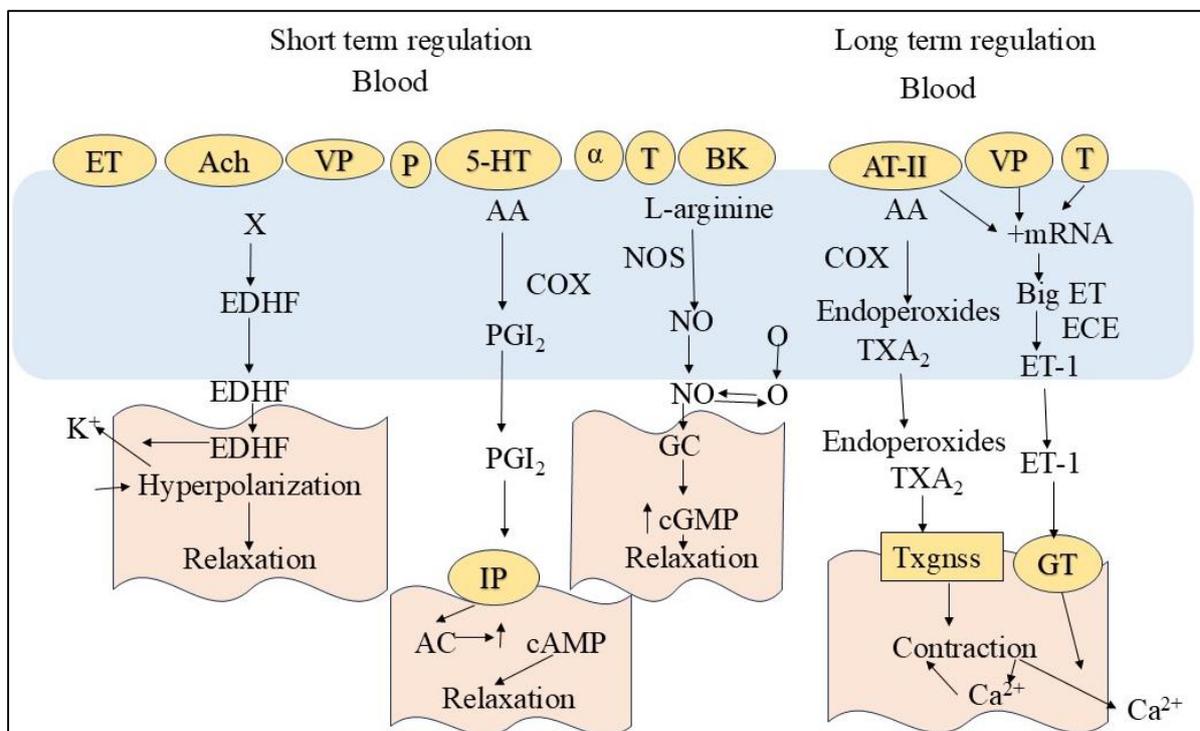
The development and maintenance of hypertension and cardiovascular TOD are largely influenced by vascular biology. Oxidative stress (RNS and ROS), inflammation (increased expression of CAMs, redox-sensitive pro-inflammatory genes, and autoimmune vascular dysfunction (T cells and B cells) and migration, infiltration of circulating cells, and recruitment), are the main functional and pathophysiological causes of vascular disease[9,20-22].



**Figure 2.** Immunated Vascular Dysfunction.

Stimulation of angiotensin receptors and toll-like receptors and direct stimulation of T cells on the on the endothelium, along with immune system, endothelium, and vascular smooth muscle cells, causes inflammation and oxidative stress (as shown in Figure\_2).

These three have a close relationship with one another and create the lethal combination that not only causes the hypertension, cardiac dysfunction, vascular smooth muscle, atherosclerosis, vascular disease, but cardiovascular disease as well. Simulating time-based distortion on vasculature, the experimental surreptitious combination of a defined genetic material's effect on the genome and the exposure to other cascades of intentionally atherogenesis produced an example of the biological system. The Western diet is characterized by its lack of fibre, high in processed products, high in refined sugars, and saturated fats. What was first meant to provide vascular defence against endothelial insults turns into a maladaptive vascular response[9,21-23].

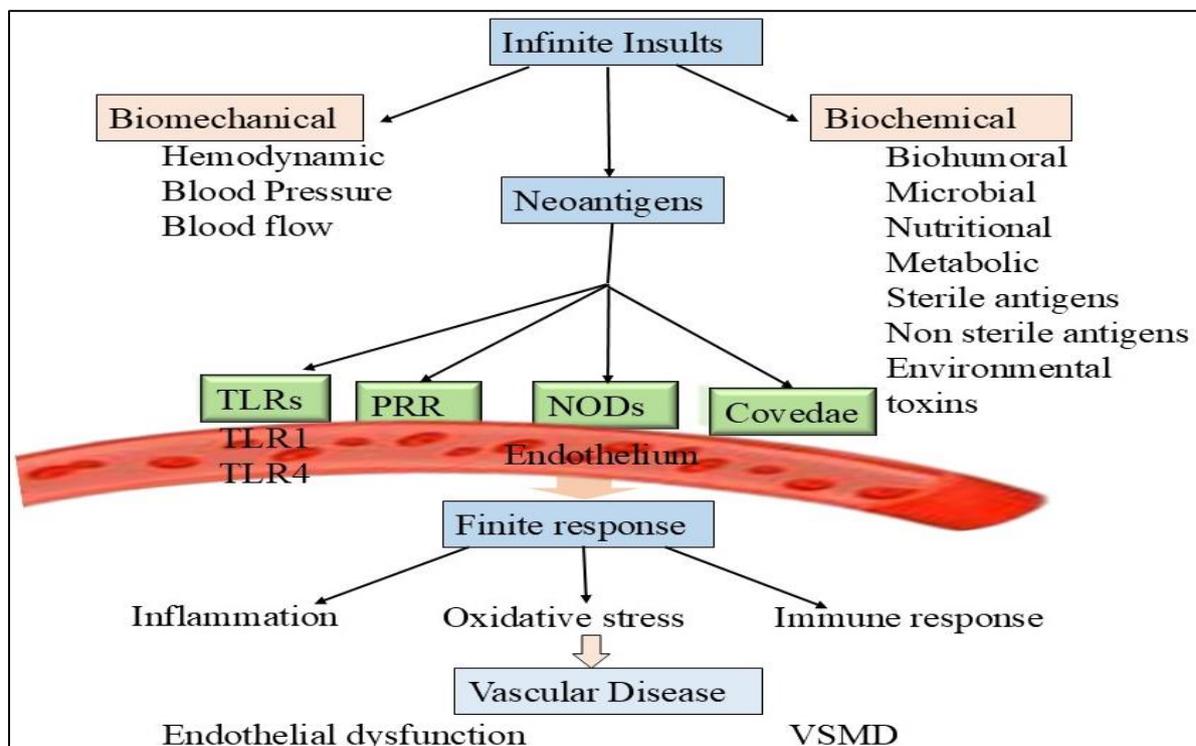


**Figure\_3.** Endothelium dependent responses

Excessive activation of the AT1R produces the superoxide anion which not only deactivates nitric oxide, but also produces another level of downstream radical oxygen species and radical nitrogen species, thus increasing the oxidative stress of the vessels. NOS: Nitric oxide synthase; AA: Arachidonic acid (as shown in Figure\_3).

Hypertension known as Vasculopathy is characterised by ED, decreased distensibility, vascular inflammation, structural re-modelling, increased arterial stiffness and elasticity loss[21]. These insults known percentages that other non-mechanic causes of diseases like metabolic, endocrine, nutritional, toxic, infectious, and other aetiologies. Emboli Blocking and stenosis in arteries are some forms of biomechanical insults[9].

Both poisons and organisms lower or raise blood pressure and are secondary causes of hypertension besides the ascertained ones [24–28]. BP and CVD are also elevated by a number of toxins, including iron, mercury, lead, cadmium, arsenic, polychlorinated biphenyls, and cadmium [24, 25]. Many microorganisms have been linked to CHD and hypertension [18]. Hypertension is a clinical manifestation of impaired microvascular structure and function caused by all of these insults. The degree of blood pressure may not be a reliable indicator of the impairment and microvascular involvement in hypertension. Inward eutrophic re-modelling of the small resistance arteries is an abnormal microvasculature seen in hypertensive patients. This reconfiguring results in a lower maximal organ perfusion, increased media to lumen ratio and a reduced flow reserve, higher vascular resistance, which are particularly noticeable in the heart when the coronary flow reserve gets lower, and so.



**Figure 4.** Infinite insults with three finite vascular responses

The biomechanical insults such as hypertension will make pattern recognition receptors (PRR) come alive, and caveolae take part, thus leading to making the endothelial, oxidative stress, immune dysfunction, vascular inflammation, vascular and cardiac smooth muscle dysfunction (VSMD) and vascular and cardiac smooth muscle endothelial dysfunction. TLR: Toll-like receptors (as shown in Figure 4).

In normotensive offspring of hypertensive parents, the microvascular injury undergoes significant functional than structural alternation before the blood pressure elevates. This is marked by symptoms such as diastolic dysfunction, impaired vasodilation, ED, increased septal and posterior wall thickness, LV hypertrophy and increased LV mass index. Hence, those pathways at the cellular level which underlie the disturbances in function of vessels represent endothelial dysfunction and may be reliable markers of early life programming and imprinting, are also strongly affected by vascular aging [20–23].

#### 4. Treatment

Some natural substances that occur in food, antioxidants, minerals, and vitamins, are quite same to a certain group of antihypertensive drugs. The antihypertensive effect becomes more potent and natural supplements help in this way either synergistically or additively when combined with other nutrients. The degree of the nutritional is lower than that of the antihypertensive medicine yet still it is the mix of them that brings the achievement of the intended therapeutic effect. Carvedilol, Clonidine, Furosemide, Hydralazine, Nifedipine, Prazosin, Ramipril, Telmisartan, and Aliskiren are the major classes of drugs used for the treatment of hypertension.

**Enhancing Lifestyle to Lower Blood Pressure: Potential and Constraints** Modifying one's lifestyle is a crucial component of any plan to better control blood pressure. Therefore, they are the first action that a hypertensive patient needs to be elevated to take in order to achieve blood pressure normal and lower their personal overall cardiovascular risk. There has to be a clear and distinct emphasis on the need for the implementation of community-wide education programs, as well as the building of infrastructure and the introduction of legislation for medical professionals to be able to advise healthy lifestyle and talk about its viability. Research has also revealed a lot of the potential use of the DASH and Mediterranean diets on blood pressure, but there are many studies in which researchers have gone a little further in exploring the use of dietary supplements and nutraceuticals on lowering blood pressure [29].

## 5. Dietary methods for treating hypertension

### 5.1. Sodium

In America on average, a person eats 5000 milligrams of sodium per day, although some areas in the country consume as much as 15,000-20,000 milligrams [30]. However, it is highly possible that the daily minimum need of sodium is about 500 milligrams. Research from observational, controlled, and epidemiologic studies shows that consuming more  $\text{Na}^+$  is linked to elevated blood pressure. In hypertensive patients, particularly those who are sensitive to salt, a decrease in  $\text{Na}^+$  intake will result in a significant reduction in blood pressure, ranging from 4–6/2–3 mmHg, depending on the severity of  $\text{Na}^+$  restriction. An increased glomerular filtration rate and a decreased renal plasma flow are what lead to the development of renal insufficiency, microalbuminuria, proteinuria, glomerular injury, and a decrease in renal plasma flow. Besides that, a recent study found that  $\text{Na}^+$  lowers arterial compliance regardless of changes in blood pressure. The response of the cardiovascular, renal, cerebrovascular, and blood pressure systems to the diet salt intake varies enormously in people with the salt sensitive phenotype, the key feature of which is a >10% increase in mean arterial pressure upon salt loading. For instance, salt-sensitive patients are more prone to the cardiovascular incidence in comparison to salt-tolerant patients even in the absence of high blood pressure. The evidence is strong in favor of the idea that reducing salt intake in the diet protects the kidney, heart, brain, and vasculature against damage that can both be related to unrelated to the slight drop in blood pressure. Besides blood pressure control and treatment, the equilibrium of  $\text{Na}^+$  with other nutrients is also of utmost importance for the decrease of the risk of both cardiovascular and cerebrovascular accidents [33-39].

### 5.2. Calcium

Population studies show a correlation between calcium and hypertension, the effects of giving patients calcium supplements on their blood pressure have not always been consistent in clinical trials. Resnick has provided an explanation for the varied reactions to calcium supplementation. The "ionic hypothesis" explains why hypertension, heart disease, and related functional, structural, and metabolic problems occur [40-42].

### 5.3. Zinc

In observational thinks about, low serum zinc levels are related with raised lipoprotein a (LP-alfa), 2-hour postprandial plasma affront levels, affront resistance, and hypertension in expansion to CHD, Sort 2 diabetes, and hyperlipidemia. In comparison to 60 hypertensive control subjects, evaluated the  $\text{Zn}^{2+}$  status in 60 hypertensive subjects. Blood weight and serum  $\text{Zn}^{2+}$  were found to be conversely related. Moreover, BP and  $\text{Zn}^{2+}$ -dependent enzyme-lysyl oxidase movement appeared converse relationship. Through actuated protein-1 (AP-1) and NF-kB zinc dioxide ( $\text{Zn}^{2+}$ ) represses translation and quality expression.  $\text{Zn}^{2+}$ 's antihypertensive impacts may be clarified by these as well as impacts on affront resistance, film particle trade, the renin-angiotensin-aldosterone framework, and the thoughtful apprehensive framework [43, 44]. The prescribed everyday of zinc is 15–30 mg [45].

### 5.4. L-arginine

eNOS converts l-arginine into NO which has widespread impacts in the cardiovascular system, like elevating cyclic GMP levels in vascular smooth muscle, improving erectile dysfunction, and decreasing blood pressure and vascular tone[45, 46]. The metabolism and activity of zymogens like Asymmetric dimethylarginine, which triggers endothelial NO, is observed in increased levels in the serum of people suffering from hypertension, hyperlipidemia and atherosclerosis. In people who have hypertension or normal level of blood pressure, both parenteral and oral forms of l-arginine resulted in decrease in the blood pressure level, so it can be said to have an antihypertensive action. Intake of 10 g of arginine daily resulted in significant decrease of blood pressure by 6.2/6.8 mmHg. In subjects who have high level of normal blood pressure and suffering from hypertension, there are considerable and statistically provable decrease in blood pressure, and metabolic effect after taking l-arginine, which can be compared to dietary approaches to Stop hypertension (DASH)-I a dieting scheme. This reduction on blood pressure was noted after increasing the dose from 5 to 10 grams daily whether l-arginine was taken as supplementation product or in the form of absolutely natural food.

Although many L-arginine doses appear safe, there is a dearth of research which has investigated such dosages in the long-term in humans, and others who have a tendency towards atherosclerosis, MI, CHD or poor endothelial function may be more prone to a pro-oxidative effect[46, 47].

### 5.5. L-Carnitine

L-carnitine, which is a nitrogenous component of muscle, is used by mammals specifically for the oxidation of fatty acids. In the limited human studies on the effect of L-carnitine, no changes have been recorded in blood pressure levels. L-carnitine may be useful in the treatment of patients suffering from essential hypertension, hyperlipidemia, Type 2 diabetes mellitus with cardiac arrhythmias, hypertension, ischemic heart syndromes and congestive heart failure[45, 48].

### 5.6. Fibre

Clinical studies on the efficacy of different types of fibre to hypertension have produced inconsistent outcomes. There is research linking soluble fibre consumption such as guava, guar gum, oat bran and psyllium with decreased blood pressure and a reduction in hypertension -third cognition of diabetic hypertensive patients. Mixed fibre intake of 40 to 50 g/d corresponds with the average blood pressure drop between 7.5/5.5 mmHg. There have been positive changes in renal sodium loss, insulin sensitivity, and endothelial function, and SNS activity[9, 49-52].

### 5.7. Magnesium

Overweight or obesity individuals consuming more than 500 mg to 1000 mg of magnesium have been found linked with lower blood pressure in majority of the clinical trials. However, the effect magnesium provides is not comparable with sodium and potassium. It has also been noted across several epidemiology studies that higher the intake of magnesium, the lower is the blood pressure. Conducted research looking at 60 individuals which were hypertensive showed a 24 hour coverage of blood pressure as well as blood pressure readings at work and home showed a significant decrease with magnesium supplements. Although not many studies were able to establish a connection between reduced blood pressure from magnesium and hypertensive medications, some did show a decrease of 5.6/2.8 mmHg. There is some research suggesting the sodium deficiency coupled with high potassium and magnesium causes a greater reduction in blood pressure. Also more intake of magnesium supplements can result in higher effectiveness of blood pressure medications. Total body magnesium is an indicator where the levels of magnesium in RBC are used with those of serum and urine. Depending on the research, it is suggested to take around 500-1000 mg of magnesium supplements[53-57].

The use of magnesium formulations chelated by amino acids has been demonstrated to improve absorption in addition to reducing the number of diarrheal episodes within the population. There is a need of taurine supplementation of about 1000-2000 mg/d to facilitate the enhancement of magnesium's anti-hypertensive effects. In cases where there are medicinal therapies leading to retention of magnesium or with patients who have established renal failure, magnesium supplementation should not be taken or should be taken with caution[55].

### 5.8. Protein

Research from observational and epidemiological studies consistently indicates a connection between a high-protein diet and a reduction in blood pressure and the occurrence of elevated blood pressure. The type of protein consumed plays a crucial role in its effect on blood pressure; plant-based proteins, especially almond protein, are more beneficial compared to animal proteins. In the Inter-Salt Study, which included over 10,000 participants, those who consumed 30% more protein than the average (81 g vs. 44 g per day) experienced a decline in blood pressure by 3.0/2.5 mmHg. However, lean or wild animal proteins that are richer in essential omega-3 fatty acids and lower in saturated fats may reduce the risk of coronary heart disease, blood pressure, and cholesterol levels[58, 61]. The protein composition was 20% soy, 20% pea, 30% milk and 30% egg protein isolate[62]. Daily protein intake from all food sources should ideally fall within the range of 1.0 to 1.5 g per kg of body weight, depending on factors like age, kidney function, physical activity level, and other variables[9, 51, 52]. In several studies, soy protein has been found to reduce blood pressure in patients with hypertension[63-72]. In a study involving Chinese women who consumed 25 g or more of soy protein daily over three years, the intake of soy protein was considerably and conversely associated with both systolic and diastolic blood pressure, with the association becoming stronger with age. This resulted in a decrease of 1.9 to 4.9 mmHg in systolic blood pressure and a drop of 0.9 to 2.2 mmHg in diastolic blood pressure[64].

### 5.9. Omega-3 fatty acids

In observational studies, epidemiological research, and forward-looking clinical trials, omega-3 fatty acids found in fish oil, flax, flax seeds, flax oil, cold water fish, and nuts have demonstrated the ability to reduce blood pressure. These findings are supported by a connection to specific concurrent diseases associated with hypertension and a dose-dependent effect on hypertension [73–83]. For those with high blood pressure, consuming cold water fish three times weekly can be as efficient as taking high-dose fish oil for lowering blood pressure. Additionally, the protein content in fish may contribute antihypertensive effects [9, 73]. With a polyunsaturated to saturated fat ratio exceeding 1.5 to 2.0, the ideal ratio of omega-6 fatty acids to omega-3 fatty acids falls between 1:1 and 1:4 [10].

### 5.10. Vitamin C

One notable hydrophilic electron donor is vitamin C. At regular physiological levels, it functions as an antioxidant; however, at higher doses, such as those achieved through intravenous administration, it exerts pro-oxidative effects on various enzymes by donating electrons. Vitamin C has been shown to enhance erectile dysfunction, promote diuresis, and replenish vitamin E at typical physiological doses. There is an inverse relationship in humans between plasma ascorbate concentration and dietary vitamin C intake with diastolic blood pressure (DBP), systolic blood pressure (SBP), and heart rate. A review of available clinical trials indicates that consuming 250 mg of vitamin C twice daily can reduce diastolic blood pressure by 2-4 mmHg and systolic blood pressure by 5-7 mmHg over an eight-week period [84-98].

### 5.11. Garlic

Clinical research employing suitable types, dosages, and well-absorbed long-lasting garlic products has demonstrated reliable decreases in blood pressure in hypertensive patients, averaging a reduction of 8.4/7.3 mmHg[99, 100]. The efficacy of different garlic products in reducing blood pressure varies due to differences in their processing methods[9]. Moreover, the effects of aged, fresh, and long-lasting garlic preparations vary, just as the effects from cultivated garlic (*Allium sativum*), wild garlic, or bear garlic (*Allium ursinum*) differ [51, 52]. People with poorly controlled hypertension who are currently taking antihypertensive medications can still benefit from garlic's ability to lower blood pressure[99-101].

### 5.12. Quercetin

Apples, berries, and onions contain quercetin, a flavonol antioxidant that aids in lowering blood pressure in those with high blood pressure. Nonetheless, the blood pressure-reducing effects of quercetin seem not to stem from alterations in vascular response, hsCRP, ACE activity, tumor necrosis factor alpha, ET-1, NO, or flow-mediated dilation (FMD). Given that quercetin blocks CYP 3A4, it is recommended that patients taking medications metabolized by this cytochrome system exercise caution when using quercetin. In a study involving 12 men with high blood pressure who received 1095 mg oral dose of quercetin, the average blood pressure, diastolic blood pressure (DBP), and systolic blood pressure (SBP) were reduced by 5 mmHg, 3 mmHg, and 7 mmHg, respectively [102-104].

### 5.13. Tea

In clinical studies and meta-analyses involving humans, both green tea and black tea, along with their active ingredient extracts, have demonstrated a reduction in blood pressure. In a randomized, double-blind, placebo-controlled trial lasting three months with 379 participants with hypertension, a daily dose of 370 mg of green tea extract (GTE) led to a notable reduction of 4/4 mmHg in blood pressure. According to a meta-analysis, consuming two to six cups of black or green tea each day for durations between four to twenty-four weeks significantly lowered blood pressure. Black tea led to a decrease in systolic blood pressure (SBP) by 1.1 mmHg and diastolic blood pressure (DBP) by 1.4 mmHg, whereas green tea caused a decline of SBP by 2.1 mmHg and DBP by 2.0 mmHg. Ongoing 24-hour ambulatory blood pressure monitoring (ABPM) demonstrated an overall decline of 3.6 mmHg in SBP, showing a decrease of 3.61 mmHg during the day and a 3.9 mmHg reduction at night. The DBP stayed the same. A meta-analysis involving 10 studies with 834 participants showed that after three months, the mix of green and black tea lowered blood pressure by 2.36/1.77 mmHg.

#### 5.14. Flavonoids

Resveratrol and Pomegranate Flavonoids, which encompass isoflavones, flavonols, and flavones, are potent agents that neutralize free radicals and possess antihypertensive properties, promote vascular relaxation, and help prevent atherosclerosis. In studies where resveratrol was administered to humans through 250 mL servings of either regular or de-alcoholized red wine, the results showed a decrease in the augmentation index, improved arterial compliance, and a reduction in central arterial pressure. The aortic augmentation index saw a reduction of 10.5% with regular red wine and 6.1% with de-alcoholized red wine. De-alcoholized red wine led to a 7.4 mmHg decrease in CRP, whereas regular red wine resulted in a 5.4 mmHg reduction. Along with improving flow-mediated vasodilation in a dose-dependent way, resveratrol also helps endothelial dysfunction, inhibits the uncoupling of endothelial nitric oxide synthase (eNOS), and mitigates the effects of angiotensin II. The recommended daily amount of trans-resveratrol is 250 mg. Pomegranate (*Punica granatum*) has been shown to reduce blood pressure, enhance endothelial function, diminish carotid intima-media thickness (IMT), and lower serum angiotensin converting enzyme (ACE) activity by 36%. A meta-analysis involving eight randomized controlled trials demonstrated notable decreases in SBP (4.96 mmHg;  $P < 0.001$ ) and DBP ( $P = 0.021$ ) following the intake of 6 oz of pomegranate juice [117-131]. Along with improving flow-mediated vasodilation in a dose-dependent way, resveratrol also helps endothelial dysfunction, inhibits the uncoupling of endothelial nitric oxide synthase (eNOS), and mitigates the effects of angiotensin II. The recommended daily amount of trans-resveratrol is 250 mg. Pomegranate (*Punica granatum*) has been shown to reduce blood pressure, enhance endothelial function, diminish carotid intima-media thickness (IMT), and lower serum angiotensin converting enzyme (ACE) activity by 36%. A meta-analysis involving eight randomized controlled trials demonstrated notable decreases in SBP (4.96 mmHg;  $P < 0.001$ ) and DBP ( $P = 0.021$ ) following the intake of 6 oz of pomegranate juice [117-131].

#### 5.15. Cocoa

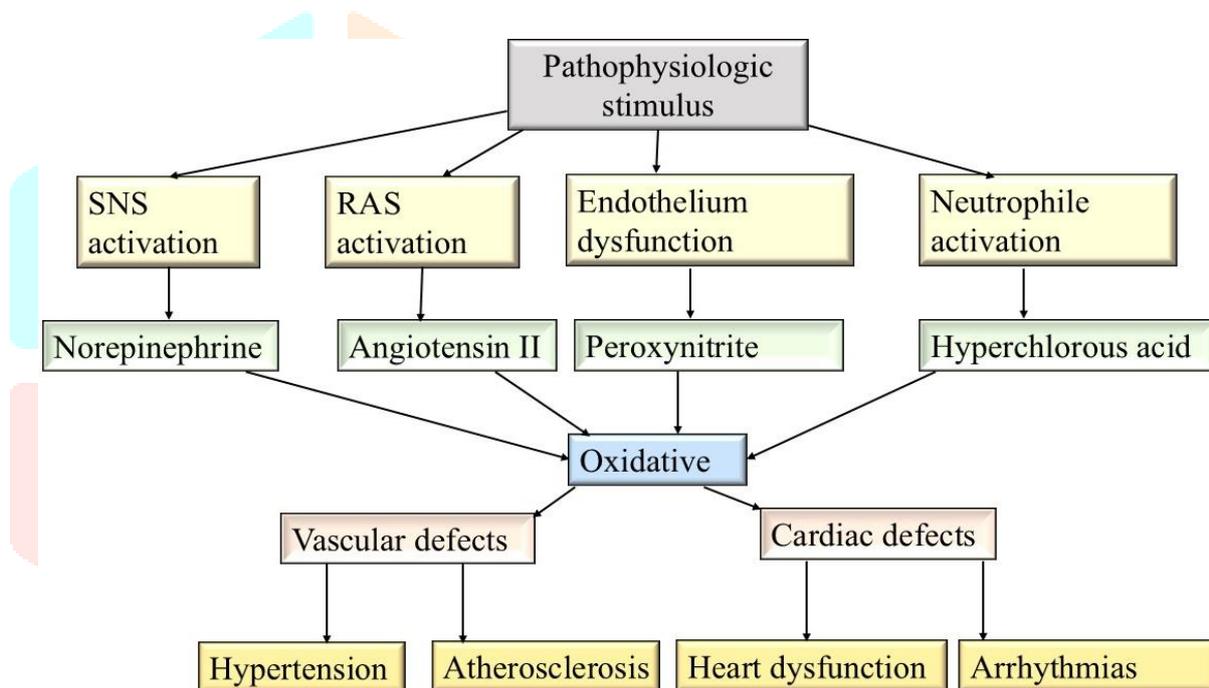
Numerous meta-analyses and prospective clinical trials have indicated that ingesting 100g of dark chocolate or 30mg of cocoa rich in polyphenols can significantly reduce blood pressure [128–151]. A meta-analysis involving 173 hypertensive individuals treated with cocoa for a duration of two weeks revealed a reduction in blood pressure of 4.7/2.8mmHg ( $P = 0.002$  to  $0.006$ ) [140]. In the active intervention cohort, which included fifteen participants who consumed 100g of dark chocolate containing 500mg of polyphenols over a fifteen-day period, there was a decrease of 6.4mmHg in SBP ( $P = 1080$ mg flavanols;  $M = 545.5$ mg) for daily intake ranging from 3.6 to 105.0g of cocoa products [118]. Cocoa has been found to enhance endothelial function, insulin resistance, and nitric oxide (NO) production in both patients with and without hyperglycemia [141,147–150].

#### 5.16. Grape seeds extract

Clinical research and meta-analyses have shown that grape seed extract (GSE) can significantly lower blood pressure. A meta-analysis involving nine randomized trials that used various doses and amounts of resveratrol found that GSE led to a significant decrease in systolic blood pressure (SBP) by 1.54 mmHg ( $P < 0.02$ ), although it did not affect diastolic blood pressure (DBP). An intake of 300 mg of GSE daily for one month resulted in a meaningful reduction of 11/8 mmHg ( $P < 0.05$ ) in blood pressure. In a 2016 meta-analysis reviewing 16 clinical trials with 810 participants, GSE produced a significant decrease of 6/3 mmHg ( $P < 0.001$ ), particularly in younger individuals as well as those suffering from metabolic syndrome or obesity. In one study involving thirty-six middle-aged adults with pre-hypertension, a 12-week parallel randomized, double-blinded, placebo-controlled trial was conducted. Participants ingested a juice with either a placebo or 300 mg of GSE daily (150 mg two times a day) for six weeks, then underwent a two-week placebo run-in and a four-week follow-up with no beverage. The findings indicated that SBP reduced by 5.6% ( $P = 0.012$ ) and DBP reduced by 4.7% ( $P = 0.049$ ) due to GSE consumption. After halting the GSE drink for four weeks, blood pressure values reverted to normal. The impact was more evident in people with elevated initial blood pressure [128–131, 152–156].

### 5.17. Beetroots

A diet high in fruits and vegetables is likely to have a variety of health benefits, but some food groups, like green leafy vegetables, may offer the best defence against ischemic stroke and cardiovascular disease [157]. Of these, Beetroot (*Beta vulgaris*), may be the vegetable that accumulates nitrates the highest. A growing body of observed indicates that inorganic nitrate consumption can result in the biosynthesis of Nitric oxide in vivo. One study that looked at healthy volunteers found lower DBP after consuming 0.1 mmol kg/body wt of sodium nitrate daily, and it suggested beetroot juice as a potential source [158]. Nitrate will proceed according to a different route than the body's normal course, which involves the NO synthase pathway converting L-arginine to Nitric oxide. Instead, oral cavity commensal Gramme negative bacteria transform ingested nitrate to nitrite, which is then absorbed in the stomach [159]. Vasodilatation results from its ultimate reduction to NO in the erythrocytes and vessel wall. Additionally, betalains color compounds containing nitrogen that are uncommon in edible plants are abundant in beetroot. Generally speaking, betalains can be classified as either red/purple beta-cyanins, which give red beetroot its colour, or yellow/orange beta-xanthins, which give yellow beetroot its colour. By donating electrons, betalains can function as antioxidants and may be involved in the prevention of diseases linked to oxidative stress, hypertension, and cardiovascular disorders [160](as shown in Figure\_5).



Figure\_5. Pathophysiological stimulus of Beetroots

**Table\_1.** Dietary Components and their Role in Hypertension Control

Sr. No.	Nutrient/Dietary Component	Source	Daily Dose	Mechanism of Action
1.	Sodium	Processed foods	≤ 2,300 mg/day (recommended)	Reduces fluid retention and blood pressure by modulating renal function and reducing vascular resistance.
2.	Calcium	Dairy, leafy greens	1,000–1,500 mg	Stabilizes blood vessel tone and improves endothelial function.
3.	Magnesium	Nuts, seeds, greens	500–1,000 mg	Relaxes blood vessels and reduces oxidative stress and inflammation.
4.	Zinc	Meat, seafood, beans	15–30 mg	Modulates renin-angiotensin-aldosterone system and reduces insulin resistance.
5.	L-Arginine	Meat, nuts, seeds	6–10 g	Precursor to nitric oxide, enhances vasodilation and lowers vascular resistance.
6.	Omega-3 Fatty Acids	Fish, flaxseed, nuts	1–4 g (EPA/DHA)	Reduces vascular inflammation, lowers blood pressure, and improves endothelial function.
7.	Vitamin C	Citrus fruits, peppers	250–500 mg twice daily	Antioxidant, enhances nitric oxide availability, and reduces vascular stiffness.
8.	Garlic	Garlic cloves, extracts	600–1,200 mg of aged extract	Reduces systolic and diastolic blood pressure through vascular relaxation.
9.	Beetroot	Beet juice, beet powder	250 mL (juice) or equivalent	Provides nitrates, converted to nitric oxide, improving

				vasodilation and lowering blood pressure.
10.	Quercetin	Apples, berries, onions	~1,000 mg	Antioxidant effect reduces vascular oxidative stress and enhances endothelial health.
11.	Green/Black Tea	Tea leaves	2–6 cups	Polyphenols reduce oxidative stress and improve vascular function.
12.	Flavonoids	Red wine, cocoa	Moderate servings	Improves endothelial function and reduces vascular stiffness.

**6. Clinical considerations**

Taking prescription drugs in addition to food and nutrients It has been demonstrated that a number of carefully chosen combinations of nutraceutical supplements and anti-hypertensive medications can lower blood pressure more effectively than the medication alone:

- Sesame with beta blockers, diuretics, and nifedipine.
- Pycnogenol with ACEI and CCB.
- Lycopene with ACEI, CCB, and diuretics.
- ALA with ACEI or acetyl-L Carnitine.
- Vitamin C with CCBs.
- NAC with arginine.
- Garlic with ACEI, diuretics, and beta blockers.
- Coenzyme Q10 with ACEI and CCB.
- Taurine with magnesium.
- Potassium with all anti-hypertensive agents.
- Magnesium with all anti-hypertensive agents.

**Figure 6.** Nutraceutical supplements and anti-hypertensive medications

Many anti-hypertensive drugs have the potential to deplete essential nutrients, which may impair their effectiveness in lowering blood pressure, or lead to additional metabolic side effects that can manifest in lab tests or as clinical symptoms. Diuretics can elevate levels of homocysteine, calcium, and creatinine; decrease sodium, vitamin B6, magnesium, potassium, phosphorus, chloride, zinc, folate, iodine, and coenzyme Q10; and increase serum glucose due to inducing insulin resistance. Beta blockers can lower levels of coenzyme Q10. Angiotensin receptor blockers (ARBs) and ACE inhibitors (ACEI) can deplete zinc. The primary causes and persistence of target organ damage (TOD) cardiovascular disease (CVD), and hypertension, are rooted in vascular biology, encompassing endothelial function and vascular smooth muscle dysfunction (VSMD). The impact on cardiovascular health and hypertension—whether positive or negative—is mainly influenced by the interactions between nutrients and genes, as well as epigenetics. Nutrition and dietary choices can play a crucial role in preventing, managing, and treating hypertension via various vascular biology pathways. The onset and progression of cardiovascular disease and hypertension

are linked to autoimmune dysfunction, inflammation, and oxidative stress. Research indicates that there is a role for the targeted use of vitamin, mineral, and antioxidant nutraceutical supplements in treating hypertension. These supplements should complement other lifestyle changes and optimal nutrition through food sources. Clinical practice can systematically and effectively incorporate a holistic approach involving diet, nutrition, physical activity, smoking cessation, weight management, and the moderation of caffeine and alcohol consumption, among other lifestyle strategies.

## 7. Conclusion

Nutraceuticals appear to be beneficial in managing individuals who are pre-hypertensive or have reached stage 1 hypertension, especially when paired with improved dietary and lifestyle habits. In addition to various dietary supplements (such as alpha-lipoic acid, soluble fibers, hawthorn extracts, pomegranate juice, sesame, vitamin B6, among others) that have shown antihypertensive effects in isolated studies, several well-executed trials support the efficacy of L-arginine, potassium, cocoa, flavonoids, vitamin C, coenzyme Q10, beetroot juice, controlled-release melatonin, and aged garlic extract. However, there is still insufficient information concerning the long-term safety of many of these products. Additional clinical research is required to determine which active nutraceuticals provide the optimal cost-benefit ratio and the minimal risk-benefit ratio for broader use among the general population facing substantial cardiovascular risk. To improve long-term compliance with dietary management of hypertension, it might be most beneficial to incorporate a variety of these products into the daily diet on a rotation.

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