CLINICAL SIGNIFICANCE OF NUTRACEUTICALS IN HYPERTENSION: PERSPECTIVES FROM INDIAN RESEARCH

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Abstract

Hypertension is a major global health challenge and a leading risk factor for cardiovascular disease, stroke, and renal complications. Despite effective pharmacological treatment, inadequate blood-pressure control and treatment-related limitations have increased interest in complementary approaches. Nutraceuticals, including medicinal plants, vitamins, minerals, fatty acids, polyphenols, probiotics, and functional foods, have demonstrated potential antihypertensive effects through modulation of nitric oxide availability, endothelial function, oxidative stress, inflammation, the renin-angiotensin-aldosterone system, and renal sodium balance. This review focuses on the clinical significance of nutraceuticals in hypertension, with particular emphasis on Indian research and traditional resources such as garlic, amla, moringa, turmeric, fenugreek, and millet-based foods. Available evidence, mechanisms of action, safety, standardization, and potential integration with conventional therapy are discussed. Although several nutraceuticals show promising blood-pressure-lowering effects, variations in dosage, formulation, bioavailability, and clinical study quality remain important limitations. Further standardized, large-scale clinical trials are required to establish their long-term efficacy and safety. Nutraceuticals may therefore serve as useful adjuncts to conventional hypertension management when supported by appropriate clinical evidence.

Keywords: *Hypertension; Nutraceuticals; Cardiovascular health; Medicinal plants; Functional foods; Indian research*

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1. Introduction

Hypertension is a major modifiable risk factor for cardiovascular disease, stroke, heart failure, and chronic kidney disease. Globally, approximately 1.28 billion adults aged 30-79 years were living with hypertension in 2019, of whom nearly 46% were unaware of their condition and only about 21% had their blood pressure controlled (Zhou et al., 2021). The continuing gap between hypertension prevalence and effective control has increased interest in complementary approaches, including nutraceutical interventions. The increasing prevalence is associated with ageing populations, sedentary lifestyles, obesity, unhealthy dietary patterns, and other metabolic risk factors. Effective long-term blood-pressure control therefore remains an important component of cardiovascular disease prevention (World Health Organization, 2023).

2.1 Overview of Hypertension

Hypertension is a chronic cardiovascular condition influenced by vascular, renal, neurohormonal, metabolic, and environmental factors. Endothelial dysfunction, oxidative stress, activation of the renin-angiotensin-aldosterone system, sympathetic overactivity, and impaired vascular relaxation contribute to its development and progression (Unger et al., 2020). Persistent elevation of blood pressure increases the risk of cardiovascular disease, cerebrovascular events, renal impairment, and premature mortality (World Health Organization, 2023). Hypertension may remain clinically silent for many years, allowing progressive target-organ damage to occur before diagnosis. Early identification and sustained blood-pressure control are therefore essential for reducing long-term complications (Unger et al., 2020).

2.2 Global and Indian Burden of Hypertension

The number of adults with hypertension increased from approximately 650 million in 1990 to 1.28 billion in 2019, with nearly two-thirds of affected individuals residing in low- and middle-income countries (Zhou et al., 2021). India carries a substantial proportion of this burden, with an estimated 220 million adults living with hypertension and only approximately 12% achieving blood-pressure control (World Health Organization, 2023). A nationally representative Indian analysis reported that more than one in four adults had hypertension, while substantial gaps existed in diagnosis, treatment, and control (Geldsetzer et al., 2023). These findings emphasize the need for accessible and sustainable approaches to hypertension prevention and management. The Indian burden is further complicated by the increasing coexistence of hypertension with diabetes, obesity, dyslipidemia, and other

cardiometabolic disorders. Improving awareness, screening, treatment adherence, and lifestyle practices is therefore essential for reducing the overall cardiovascular burden (Geldsetzer et al., 2023).

2.3 Current Therapeutic Approaches and Limitations

Current management of hypertension combines lifestyle modification with pharmacological therapy, including angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium-channel blockers, and diuretics (Unger et al., 2020). Although these therapies effectively reduce cardiovascular risk, inadequate adherence, adverse effects, polypharmacy, and insufficient blood-pressure control remain important challenges. Consequently, complementary interventions that can support conventional therapy have received increasing scientific attention (Cicero et al., 2015). Lifestyle measures such as dietary modification, weight management, regular physical activity, and reduction of sodium intake remain fundamental components of treatment. However, many patients require long-term combination pharmacotherapy, creating a need for safe and evidence-based complementary strategies (Unger et al., 2020).

2.4 Emergence of Nutraceuticals in Cardiovascular Health

Nutraceuticals comprise food-derived bioactive compounds and supplements that may provide physiological benefits beyond basic nutrition. Several nutraceuticals, including omega-3 fatty acids, garlic, potassium, magnesium, L-arginine, cocoa flavonoids, beetroot-derived nitrates, and coenzyme Q10, have been investigated for their potential antihypertensive effects (Cicero et al., 2015; Borghi and Cicero, 2017). Their proposed actions include improvement of endothelial function and nitric oxide availability, antioxidant and anti-inflammatory effects, modulation of vascular tone, and influence on neurohormonal pathways (Sirtori et al., 2015). However, variations in dosage, formulation, study duration, and product standardization continue to limit direct comparison of clinical findings. Some nutraceuticals may also provide additional cardiometabolic benefits, including improvements in lipid profiles, oxidative balance, and vascular function.(Borghi and Cicero, 2017).

2.5 Rationale and Scope of the Review

The substantial burden of hypertension and the relatively low rate of blood-pressure control in India provide a strong rationale for evaluating complementary nutritional approaches. India's diverse dietary resources, medicinal plants, traditional food practices, and growing nutraceutical research base offer considerable opportunities for developing evidence-based

interventions. However, traditional use and experimental findings alone cannot establish clinical efficacy. There is a particular need to evaluate whether findings obtained from laboratory and animal studies translate into meaningful reductions in blood pressure and cardiovascular risk in human populations. Standardization of nutraceutical preparations, appropriate dosing, assessment of safety, and well-designed clinical trials are therefore important for their successful clinical translation.

Therefore, this review evaluates the clinical significance of nutraceuticals in hypertension, with particular emphasis on Indian research. It discusses their major mechanisms of action, clinical evidence, safety considerations, potential role as adjuncts to conventional antihypertensive therapy, and limitations of existing evidence, while identifying future research priorities for their clinical translation. Special emphasis is placed on Indian clinical and translational research to assess the applicability of nutraceutical interventions within the country's dietary, healthcare, and regulatory context. The review also highlights existing evidence gaps that may guide future randomized controlled trials and standardized nutraceutical development

3. Nutraceuticals: Concept and Classification

Nutraceuticals represent a broad group of food-derived products or biologically active components that provide health benefits beyond basic nutritional requirements. The term *nutraceutical* was introduced by DeFelice to describe products derived from food sources that may contribute to disease prevention or health promotion (DeFelice, 1995). Unlike conventional pharmaceuticals, nutraceuticals are generally associated with dietary sources and may contain vitamins, minerals, phytochemicals, fatty acids, amino acids, peptides, probiotics, or other bioactive constituents. Their increasing importance in cardiovascular research is related to their potential ability to influence multiple physiological pathways involved in disease development (Kalra, 2003).

In hypertension, nutraceuticals have attracted considerable attention because several food-derived bioactive compounds may improve endothelial function, enhance nitric oxide availability, reduce oxidative stress and inflammation, and modulate vascular tone and the renin-angiotensin system. Evidence from clinical studies suggests that selected nutraceuticals may produce modest reductions in blood pressure, particularly when used alongside appropriate dietary and lifestyle interventions (Cicero et al., 2015; Borghi and Cicero, 2017). However, differences in composition, dose, bioavailability, formulation, and quality among commercial products can influence their clinical effectiveness.

3.1 Nutraceuticals

The concept of nutraceuticals combines the principles of nutrition and pharmacological activity, recognizing that certain foods and their constituents can exert biological effects relevant to disease prevention and health maintenance. Nutraceuticals may be consumed as part of the normal diet or administered in concentrated forms such as capsules, tablets, powders, extracts, beverages, and functional foods. Their proposed health benefits are generally associated with specific bioactive constituents rather than their nutritional value alone (DeFelice, 1995).

The nutraceutical concept has expanded considerably with advances in nutritional biochemistry and molecular research. Bioactive compounds such as polyphenols, flavonoids, carotenoids, omega-3 fatty acids, dietary nitrates, peptides, and probiotics have been investigated for their potential effects on cardiovascular and metabolic health (Nasri et al., 2014). In hypertension, these compounds may act through several complementary mechanisms, making them potential candidates for adjunctive cardiovascular-risk management.

3.2 Functional Foods and Nutraceuticals

Functional foods are foods that provide physiological benefits beyond their basic nutritional contribution, whereas nutraceuticals are commonly presented in more concentrated or formulated forms. Examples of functional foods include oats, fruits, vegetables, fermented foods, garlic, green tea, and foods rich in omega-3 fatty acids. Nutraceutical products may contain isolated or concentrated constituents derived from these food sources (Granato et al., 2020).

The distinction between functional foods and nutraceuticals is not always consistent across countries because regulatory definitions differ. Nevertheless, both categories are relevant to hypertension because dietary patterns and specific bioactive components can influence blood-pressure regulation.

3.3 Classification of Nutraceuticals

Nutraceuticals can be classified according to their source, chemical composition, biological activity, or intended health benefit. For the purpose of hypertension research, classification according to the major bioactive component provides a practical framework for understanding their mechanisms and clinical applications.

3.3.1 Vitamins

Vitamins such as vitamin C, vitamin D, and vitamin E have been investigated for their potential cardiovascular effects. Their proposed roles include antioxidant protection, modulation of endothelial function, and regulation of inflammatory processes. However, supplementation should be differentiated from correction of nutritional deficiency, and evidence for routine vitamin supplementation specifically for blood-pressure reduction remains variable (Cicero et al., 2015).

3.3.2 Minerals

Minerals, particularly potassium, magnesium, and calcium, are important for vascular function and blood-pressure regulation. Increased dietary potassium intake may promote sodium excretion and reduce vascular resistance, while magnesium contributes to vascular relaxation and cellular electrolyte balance. Dietary mineral interventions may therefore be particularly relevant in populations with inadequate intake (Aburto et al., 2013; Rosanoff et al., 2021).

3.3.3 Polyphenols and Flavonoids

Polyphenols constitute a large group of plant-derived compounds found in fruits, vegetables, tea, cocoa, grapes, and several medicinal plants. Flavonoids, a major subclass of polyphenols, have demonstrated antioxidant, anti-inflammatory, and endothelial-protective properties. Their potential antihypertensive effects have been associated with improved nitric oxide bioavailability and reduced oxidative stress (Cicero et al., 2015).

3.3.4 Omega-3 Fatty Acids

Omega-3 polyunsaturated fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are important nutraceuticals investigated in cardiovascular health. They may influence vascular function, inflammation, lipid metabolism, and blood pressure. Clinical evidence indicates that adequate omega-3 intake may provide modest cardiovascular benefits, although the response can vary according to dose and patient characteristics (Miller et al., 2014).

3.3.5 Amino Acids and Bioactive Peptides

Amino acids such as L-arginine and L-citrulline are investigated for their involvement in nitric oxide synthesis and vascular relaxation. Food-derived bioactive peptides may also

exhibit angiotensin-converting enzyme inhibitory activity, providing a potential nutritional approach to blood-pressure regulation (Cicero et al., 2015).

3.3.6 Dietary Fibers

Soluble dietary fibers, including β-glucan and other fermentable fibers, may contribute to cardiovascular health through effects on lipid metabolism, glucose regulation, intestinal fermentation, and gut microbiota. Increased dietary fiber consumption has been associated with modest improvements in cardiovascular risk factors, including blood pressure (Anderson et al., 2009).

3.3.7 Herbal and Plant-Based Nutraceuticals

Plant-based nutraceuticals constitute an important category because they provide complex mixtures of bioactive phytochemicals. Garlic, turmeric, green tea, grape-derived products, beetroot, amla, fenugreek, and moringa are examples of plant-derived resources investigated for cardiovascular benefits. Their effects may involve antioxidant, anti-inflammatory, vasodilatory, ACE-inhibitory, and endothelial-protective mechanisms. However, differences in plant variety, extraction methods, standardization, and active-constituent concentration can substantially influence clinical outcomes.

3.3.8 Probiotics and Prebiotics

Probiotics are live microorganisms that may provide health benefits when consumed in adequate quantities, whereas prebiotics are substrates selectively utilized by beneficial microorganisms. Interest in these nutraceuticals has increased because the gut-vascular axis and gut microbiota may influence blood-pressure regulation through metabolites, immune signaling, and vascular mechanisms. Preliminary clinical evidence suggests potential blood-pressure benefits, although further well-designed trials are required to establish their therapeutic significance.

3.3.9 Coenzyme Q10 and Other Emerging Nutraceuticals

Coenzyme Q10, dietary nitrates, phytosterols, carotenoids, and other bioactive compounds have also been investigated for cardiovascular applications. Coenzyme Q10 may influence mitochondrial function and oxidative stress, whereas dietary nitrates can increase nitric oxide availability and promote vasodilation. These emerging nutraceuticals warrant further clinical evaluation to determine their appropriate dosage, target populations, and long-term safety.

3.4 Classification Based on Source

From a source-based perspective, nutraceuticals may be broadly categorized into plant-derived, animal-derived, microbial-derived, marine-derived, and synthetic or semi-synthetic nutraceuticals. Plant-derived products constitute one of the largest categories because of their abundance of polyphenols, flavonoids, alkaloids, terpenoids, vitamins, minerals, and other bioactive substances. Animal and marine sources provide omega-3 fatty acids, peptides, and other cardiovascular-related compounds, while microbial sources mainly include probiotics and fermentation-derived bioactive substances (Nasri et al., 2014).

3.5 Classification According to Their Potential Cardiovascular Action

For hypertension-focused research, nutraceuticals can also be grouped according to their principal biological actions, including vasodilatory agents, ACE-inhibitory compounds, antioxidant agents, anti-inflammatory compounds, lipid-modulating agents, nitric-oxide-enhancing agents, and gut-microbiota-modulating agents. This classification is particularly useful for understanding how different nutraceuticals may influence the multifactorial pathophysiology of hypertension (Borghi and Cicero, 2017).

Overall, nutraceuticals represent a heterogeneous group of bioactive substances with diverse mechanisms and varying levels of clinical evidence. Their classification according to source and biological activity provides a useful framework for evaluating their potential role in hypertension. However, clinical application requires standardized preparations, defined doses, adequate bioavailability, reliable quality control, and evidence from appropriately designed human studies.

4. Pathophysiology of Hypertension

Hypertension is a multifactorial disorder resulting from persistent alterations in the mechanisms that regulate arterial blood pressure. Blood pressure is primarily determined by cardiac output and systemic vascular resistance, which are influenced by renal sodium handling, sympathetic nervous system activity, the renin-angiotensin-aldosterone system (RAAS), vascular endothelial function, and hormonal regulation (Unger et al., 2020). Dysregulation of these mechanisms can increase vascular resistance and blood volume, leading to sustained elevation of blood pressure.

4.1 Regulation of Blood Pressure

Normal blood pressure is maintained through coordinated interactions between the heart, blood vessels, kidneys, nervous system, and endocrine pathways. The kidneys regulate extracellular fluid volume and sodium balance, while the autonomic nervous system controls

heart rate and vascular tone. The baroreceptor system provides rapid regulation, whereas renal and hormonal mechanisms contribute to long-term blood-pressure control (Hall, 2016).

In hypertension, these regulatory mechanisms may become persistently altered, resulting in increased vascular resistance or inappropriate retention of sodium and water. Genetic susceptibility, excessive dietary sodium, obesity, physical inactivity, and metabolic abnormalities can further disturb normal blood-pressure regulation (Oparil et al., 2018).

4.2 Role of the Renin-Angiotensin-Aldosterone System

The RAAS plays a central role in the regulation of blood pressure and fluid homeostasis. Renin released from the kidneys initiates the conversion of angiotensinogen to angiotensin I, which is subsequently converted to angiotensin II by angiotensin-converting enzyme. Angiotensin II promotes vasoconstriction and stimulates aldosterone secretion, resulting in increased sodium and water retention (Unger et al., 2020).

Persistent activation of the RAAS contributes to hypertension through increased vascular resistance, fluid retention, oxidative stress, inflammation, and vascular remodeling. Consequently, inhibition of this pathway forms an important therapeutic strategy in hypertension and represents a potential target for several bioactive nutraceutical compounds (Oparil et al., 2018).

4.3 Sympathetic Nervous System Activation

The sympathetic nervous system contributes to blood-pressure regulation by controlling cardiac activity and peripheral vascular resistance. Increased sympathetic activity can elevate heart rate, myocardial contractility, and vasoconstriction, thereby increasing arterial pressure. Chronic sympathetic activation may also promote renin release and contribute to structural vascular changes (Oparil et al., 2018).

Enhanced sympathetic activity is particularly relevant in individuals with obesity, metabolic abnormalities, and stress-related cardiovascular risk. Nutritional interventions capable of improving metabolic health and reducing oxidative and inflammatory stress may therefore have complementary effects on pathways associated with sympathetic overactivity.

4.4 Endothelial Dysfunction

The vascular endothelium plays an essential role in regulating vascular tone through the production of vasodilatory and vasoconstrictory mediators. Nitric oxide is a major endogenous vasodilator that promotes smooth-muscle relaxation and maintains vascular

homeostasis. Reduced nitric oxide bioavailability and impaired endothelial signaling contribute to increased vascular resistance and hypertension (Rajendran et al., 2013).

Oxidative stress can further reduce nitric oxide availability by promoting its interaction with reactive oxygen species. Consequently, nutraceuticals possessing antioxidant or nitric-oxide-enhancing properties, including certain polyphenols, flavonoids, and dietary nitrates, have been investigated for their potential to improve endothelial function and blood-pressure regulation (Cicero et al., 2015).

4.5 Oxidative Stress and Inflammation

Oxidative stress occurs when the production of reactive oxygen species exceeds the capacity of endogenous antioxidant systems. Excess reactive oxygen species can impair endothelial function, reduce nitric oxide bioavailability, promote vascular smooth-muscle proliferation, and stimulate inflammatory pathways (Montezano et al., 2014).

Chronic low-grade inflammation is also involved in the development and progression of hypertension. Inflammatory mediators can promote endothelial dysfunction, vascular remodeling, and renal abnormalities, creating a cycle that sustains elevated blood pressure. These mechanisms provide a biological rationale for investigating antioxidant and anti-inflammatory nutraceuticals in hypertension (Montezano et al., 2014).

4.6 Renal Dysfunction and Sodium Retention

The kidneys are critical for long-term blood-pressure regulation through control of sodium and water excretion. Impaired renal sodium handling can increase extracellular fluid volume and cardiac output, contributing to persistent hypertension (Hall et al., 2012).

Excessive dietary sodium intake can further promote fluid retention and increase blood pressure in salt-sensitive individuals. Conversely, adequate dietary potassium may enhance renal sodium excretion and contribute to blood-pressure reduction, supporting the potential importance of dietary mineral balance in hypertension management (Aburto et al., 2013).

4.7 Vascular Remodeling and Arterial Stiffness

Persistent hypertension induces structural changes in the arterial wall, including smooth-muscle hypertrophy, increased collagen deposition, and reduced arterial elasticity. These changes increase vascular resistance and arterial stiffness, further aggravating blood pressure and creating a self-perpetuating cycle of vascular injury (Laurent and Boutouyrie, 2007).

Arterial stiffness is particularly important in ageing and cardiometabolic disorders and is associated with increased cardiovascular risk. Nutraceuticals that improve endothelial

function, reduce oxidative stress, or modulate inflammation may potentially influence some of these vascular abnormalities, although clinical evidence remains variable.

4.8 Gut Microbiota and Hypertension

Emerging evidence indicates that alterations in the gut microbiota may contribute to hypertension through interactions involving microbial metabolites, intestinal permeability, immune regulation, inflammation, and vascular function. Short-chain fatty acids and other microbial metabolites may influence blood pressure through effects on the immune, renal, and cardiovascular systems (Yang et al., 2015).

This emerging **gut-vascular axis** has increased interest in probiotics, prebiotics, dietary fiber, and fermented foods as potential nutraceutical approaches. However, further human clinical studies are needed to establish whether targeted microbiota modulation produces clinically meaningful and sustained reductions in blood pressure.

4.9 Interrelationship of Pathophysiological Mechanisms

The mechanisms involved in hypertension do not operate independently. RAAS activation, sympathetic overactivity, oxidative stress, inflammation, endothelial dysfunction, renal sodium retention, and vascular remodeling interact to maintain elevated blood pressure. This complex pathophysiology provides a rationale for investigating nutraceuticals with multitarget effects, rather than focusing on a single biological pathway.

Nutraceuticals containing polyphenols, flavonoids, omega-3 fatty acids, dietary nitrates, potassium, magnesium, probiotics, and other bioactive compounds may potentially influence several of these pathways simultaneously. Nevertheless, mechanistic plausibility should be distinguished from demonstrated clinical efficacy, and well-designed randomized controlled trials remain essential for establishing their therapeutic value.

5. Role of Nutrition in Hypertension Management

Nutrition plays a fundamental role in the prevention and management of hypertension because dietary factors can directly influence blood pressure, vascular function, sodium-water balance, body weight, and cardiometabolic health. Dietary modification is therefore considered an essential component of non-pharmacological hypertension management (Unger et al., 2020). Diets rich in fruits, vegetables, whole grains, legumes, nuts, and other plant-based foods provide potassium, magnesium, dietary fiber, and bioactive phytochemicals that may contribute to improved cardiovascular health.

5.1 Dietary Patterns and Blood Pressure

Dietary patterns rather than individual nutrients are increasingly recognized as important determinants of blood-pressure control. The Dietary Approaches to Stop Hypertension (DASH) diet, characterized by high consumption of fruits, vegetables, whole grains, legumes, nuts, and low-fat dairy products with reduced saturated fat and sodium, has demonstrated significant blood-pressure-lowering effects (Appel et al., 1997).

Similarly, Mediterranean-style dietary patterns emphasizing vegetables, fruits, whole grains, legumes, nuts, fish, and unsaturated fats have been associated with favorable cardiovascular outcomes. Such dietary approaches may reduce oxidative stress, improve endothelial function, and support healthy body weight (Estruch et al., 2018).

5.2 Role of Sodium Restriction

Excessive sodium intake is an important dietary risk factor for elevated blood pressure, particularly among salt-sensitive individuals. High sodium consumption promotes water retention, increases extracellular fluid volume, and may adversely affect vascular function and arterial stiffness (He et al., 2019).

Reduction of dietary sodium is therefore an important component of hypertension management. Evidence suggests that reducing sodium intake can produce meaningful reductions in blood pressure, with greater effects generally observed among individuals with hypertension (Filippini et al., 2021).

5.3 Importance of Dietary Potassium

Potassium plays an important role in maintaining electrolyte balance and vascular function. Increased potassium intake can promote renal sodium excretion, reduce vascular resistance, and potentially attenuate the pressor effects of excessive sodium consumption (Aburto et al., 2013).

Fruits and vegetables such as bananas, oranges, tomatoes, leafy vegetables, pulses, and potatoes are important dietary sources of potassium. However, potassium supplementation or substantial dietary increases should be considered cautiously in individuals with impaired renal function or those receiving medicines that increase serum potassium.

5.4 Role of Magnesium and Calcium

Magnesium contributes to vascular smooth-muscle relaxation, endothelial function, and regulation of cellular calcium transport. Adequate magnesium intake has therefore been associated with favorable effects on blood-pressure regulation, although the magnitude of benefit varies among studies (Zhang et al., 2016).

Calcium also participates in vascular contraction and intracellular signaling. Adequate dietary calcium intake may contribute to normal blood-pressure regulation, particularly in individuals with insufficient dietary intake. Food-based sources are generally preferred over unnecessary supplementation (Cicero et al., 2015).

5.5 Dietary Fiber and Whole Grains

Dietary fiber is an important component of a cardioprotective diet and is abundant in whole grains, legumes, fruits, vegetables, and seeds. Soluble and fermentable fibers may influence blood pressure through improvements in body weight, lipid metabolism, insulin sensitivity, and gut microbial activity (Anderson et al., 2009).

Whole-grain consumption has also been associated with improved cardiovascular health. Increased dietary fiber intake may provide additional benefits when incorporated into an overall dietary pattern emphasizing minimally processed plant foods.

5.6 Fruits, Vegetables and Bioactive Phytochemicals

Fruits and vegetables provide potassium, magnesium, fiber, vitamins, minerals, and numerous phytochemicals, including flavonoids, carotenoids, and other polyphenols. These compounds may exert antioxidant, anti-inflammatory, and endothelial-protective effects that are relevant to hypertension (Cicero et al., 2015).

Regular consumption of plant-based foods may therefore provide benefits beyond their individual nutrient content. Foods such as berries, citrus fruits, grapes, tomatoes, leafy vegetables, beetroot, and Indian fruits such as amla (Phyllanthus emblica) represent potential sources of cardiovascular bioactive compounds.

5.7 Role of Dietary Nitrates

Dietary nitrates, particularly those obtained from green leafy vegetables and beetroot, can contribute to nitric oxide production through the nitrate-nitrite-nitric oxide pathway. Increased nitric oxide availability promotes vascular relaxation and may reduce peripheral vascular resistance (Lundberg et al., 2008).

Clinical investigations of beetroot juice and nitrate-rich foods have reported reductions in blood pressure in some populations, although the magnitude and duration of the response vary. Dietary nitrates therefore represent an important link between conventional nutrition and nutraceutical approaches to hypertension.

5.8 Omega-3 Fatty Acids and Cardiovascular Health

Omega-3 polyunsaturated fatty acids, particularly **EPA and DHA**, are obtained from fatty fish and selected dietary supplements. They may influence vascular tone, inflammation, lipid metabolism, and other cardiovascular pathways. Meta-analytical evidence suggests that omega-3 fatty acids may produce modest reductions in blood pressure, particularly at higher intakes (Miller et al., 2014).

Incorporating appropriate dietary sources of omega-3 fatty acids may therefore complement other dietary strategies for cardiovascular-risk reduction. However, supplementation should be individualized according to overall cardiovascular status and dietary intake.

5.9 Dietary Approaches Relevant to Indian Populations

Dietary management of hypertension in India should consider regional food habits, cultural preferences, affordability, and the increasing consumption of processed foods. Traditional Indian diets can provide beneficial sources of legumes, whole grains, vegetables, fruits, nuts, seeds, spices, and fermented foods when appropriately prepared.

Greater emphasis on millets, pulses, vegetables, fruits, unsalted nuts, seeds, and minimally processed foods, together with reduced consumption of high-sodium packaged foods, pickles, papads, processed snacks, and excessive refined carbohydrates, may support healthier dietary patterns. Such culturally appropriate approaches may improve the feasibility and long-term adherence of nutritional interventions in Indian populations.

5.10 Nutrition and Nutraceutical Integration

Nutrition provides the foundation for hypertension prevention, while nutraceuticals may offer concentrated sources of selected bioactive compounds. A distinction should therefore be maintained between obtaining nutrients through a balanced diet and using concentrated nutraceutical supplements. Nutraceuticals should preferably be considered as adjuncts to dietary and pharmacological management, rather than substitutes for prescribed antihypertensive treatment (Borghi and Cicero, 2017).

Overall, dietary modification can influence several mechanisms involved in hypertension, including sodium balance, endothelial function, oxidative stress, inflammation, vascular tone, and metabolic health. Integrating evidence-based nutrition with appropriately evaluated nutraceutical interventions may therefore provide a comprehensive approach to hypertension management.

Table 1. Indian Medicinal Plants and Nutraceuticals Investigated for Hypertension

S.	Plant/Nutraceutical	Major	Potential	Key Reference

No.		**Bioactive Constituents**	**Antihypertensive Mechanisms**	
1	**Garlic (*Allium sativum*)**	Allicin, S-allyl cysteine, sulfur compounds	NO/H_2S enhancement, ACE inhibition, antioxidant activity, vasodilation	Borghi & Cicero (2017); Stabler et al. (2022)
2	**Amla (*Phyllanthus emblica*)**	Polyphenols, tannins, vitamin C, emblicanin	Antioxidant, anti-inflammatory, endothelial protection	Upadhyay et al. (2019)
3	**Moringa (*Moringa oleifera*)**	Flavonoids, phenolics, carotenoids	Antioxidant, anti-inflammatory, possible vascular effects	Gopalakrishnan et al. (2023)
4	**Fenugreek (*Trigonella foenum-graecum*)**	Fiber, saponins, flavonoids	Metabolic improvement, antioxidant and vascular effects	Asbaghi et al. (2023)
5	**Turmeric (*Curcuma longa*)**	Curcumin, curcuminoids	Antioxidant, anti-inflammatory, vascular and RAAS modulation	Kandhare et al. (2013)
6	**Green tea (*Camellia sinensis*)**	Catechins, EGCG	↑ NO, antioxidant activity, endothelial protection	Borghi & Cicero (2017)
7	**Sesame (*Sesamum indicum*)**	Sesamin, sesamolin, unsaturated fatty acids	Antioxidant, vascular and lipid-modulating effects	Borghi & Cicero (2017)
8	**Beetroot (*Beta vulgaris*)**	Dietary nitrates	Nitrate-nitrite-NO pathway, vasodilation	Borghi & Cicero (2017)
9	**Millets**	Dietary fiber, polyphenols, minerals	Improved dietary quality, metabolic and vascular effects	Nutritional evidence
10	**Pulses/legumes**	Fiber, potassium, magnesium, polyphenols	Improved sodium balance, metabolic health and vascular function	Dietary-pattern evidence

Abbreviations: ACE, angiotensin-converting enzyme; BP, blood pressure; EGCG, epigallocatechin gallate; H_2S, hydrogen sulfide; NO, nitric oxide; RAAS, renin-angiotensin-aldosterone system.

8. Mechanisms of Antihypertensive Action of Nutraceuticals

Nutraceuticals may influence blood pressure through several interconnected mechanisms involving vascular, renal, neurohormonal, metabolic, and inflammatory pathways. Unlike many conventional antihypertensive drugs that primarily act on specific molecular targets, nutraceuticals may exert multitarget effects, including enhancement of nitric oxide (NO) availability, modulation of the renin-angiotensin-aldosterone system (RAAS), reduction of oxidative stress, and improvement of endothelial function (Cicero and Colletti, 2015; Borghi and Cicero, 2017).

The potential antihypertensive activity of nutraceuticals is particularly relevant because hypertension is a multifactorial disorder involving several pathological processes simultaneously. Clinical evidence indicates that selected nutraceuticals, including potassium, magnesium, L-arginine, cocoa flavonoids, beetroot juice, CoQ10, and aged garlic extract, may produce measurable reductions in blood pressure, although the magnitude of benefit differs between interventions (Borghi and Cicero, 2017).

8.1 Enhancement of Nitric Oxide Bioavailability

Nitric oxide is an important endogenous vasodilator synthesized primarily by endothelial nitric oxide synthase (eNOS). It promotes relaxation of vascular smooth muscle and helps maintain normal vascular resistance. In hypertension, oxidative stress and endothelial dysfunction reduce NO bioavailability, contributing to impaired vasodilation and increased peripheral vascular resistance (Förstermann and Münzel, 2006).

Several nutraceuticals may improve NO signaling through different pathways. Dietary nitrates from beetroot and green leafy vegetables are converted to nitrite and subsequently NO, whereas L-arginine provides the substrate for endogenous NO synthesis. Flavonoids may additionally improve eNOS activity and protect NO from oxidative degradation (Lundberg et al., 2008; Ravan et al., 2020).

8.2 Modulation of the Renin-Angiotensin-Aldosterone System

The RAAS is a major regulator of blood pressure and fluid homeostasis. Excessive angiotensin II activity promotes vasoconstriction, aldosterone secretion, sodium retention, oxidative stress, inflammation, and vascular remodeling, thereby contributing to sustained hypertension.

Several food-derived compounds and plant phytochemicals have demonstrated potential ACE-inhibitory activity. Garlic compounds, polyphenols, flavonoids, and bioactive peptides may interfere with components of the RAAS, although the clinical magnitude of these effects is generally less established than that of conventional ACE inhibitors and ARBs (Borghi and Cicero, 2017).

8.3 Antioxidant Activity

Oxidative stress is an important contributor to hypertension because excessive reactive oxygen species (ROS) can reduce NO availability, impair endothelial function, and promote vascular smooth-muscle proliferation and inflammation. Increased ROS generation has been associated with activation of the RAAS, sympathetic pathways, and vascular inflammatory processes (Montezano and Touyz, 2014).

Nutraceuticals containing polyphenols, flavonoids, carotenoids, vitamin C, vitamin E, and sulfur-containing compounds may help counteract oxidative stress. Garlic, amla, turmeric, green tea, cocoa, and grape-derived products have therefore been investigated for vascular antioxidant effects; however, antioxidant activity demonstrated experimentally should not automatically be interpreted as clinical antihypertensive efficacy (Ravan et al., 2020).

8.4 Anti-inflammatory Effects

Chronic low-grade inflammation contributes to endothelial dysfunction, vascular remodeling, and progression of hypertension. Inflammatory mediators can stimulate oxidative stress, impair endothelial signaling, and promote structural changes in blood vessels, thereby maintaining elevated vascular resistance.

Several nutraceuticals possess anti-inflammatory properties that may complement their direct vascular actions. Curcumin, omega-3 fatty acids, flavonoids, and other polyphenols have been investigated for their ability to modulate inflammatory signaling pathways and cytokine production, providing a potential mechanism for their cardiovascular effects (Ravan et al., 2020).

8.5 Improvement of Endothelial Function

The vascular endothelium regulates vascular tone through the release of NO, prostacyclin, endothelin, and other vasoactive mediators. Endothelial dysfunction results in reduced vasodilatory capacity and increased vascular resistance and is considered an important feature of hypertension.

Nutraceuticals such as cocoa flavonoids, dietary nitrates, garlic-derived compounds, omega-3 fatty acids, and other polyphenols may improve endothelial function by increasing NO bioavailability and reducing oxidative and inflammatory damage. Flavonoids have been particularly studied for their ability to enhance NO signaling and modulate vascular ion channels (Ravan et al., 2020).

8.6 Modulation of Vascular Smooth-Muscle Tone

Vascular smooth-muscle contraction is a major determinant of systemic vascular resistance. Calcium-dependent signaling, potassium channels, NO-cGMP pathways, and other intracellular mechanisms regulate vascular tone, and abnormalities in these pathways can contribute to increased peripheral resistance. Magnesium may influence calcium transport and promote vascular smooth-muscle relaxation, while NO-producing nutraceuticals stimulate the soluble guanylate cyclase-cGMP pathway. A meta-analysis of randomized controlled trials involving magnesium supplementation demonstrated a modest but significant reduction in blood pressure, supporting its potential role as an adjunctive nutritional intervention (Zhang et al., 2016).

8.7 Regulation of Renal Sodium and Water Balance

The kidneys play a central role in long-term blood-pressure regulation by controlling sodium and water excretion. Excessive sodium retention increases extracellular fluid volume and cardiac output, thereby contributing to elevated blood pressure. Potassium is particularly important because increased potassium intake promotes renal sodium excretion and can reduce the pressor effects of excessive sodium intake. A systematic review of randomized trials found that increased potassium intake was associated with reductions in blood pressure, particularly in individuals with elevated sodium consumption (Aburto et al., 2013).

8.8 Modulation of Sympathetic Nervous System Activity

Increased sympathetic nervous system activity can elevate heart rate, cardiac output, vascular resistance, and renin secretion. Persistent sympathetic activation is therefore an important contributor to the development and maintenance of hypertension.

Some nutraceuticals may influence neurovascular regulation indirectly through antioxidant, metabolic, or circadian mechanisms. Melatonin has received particular attention because of its potential effects on sympathetic activity and nocturnal blood-pressure regulation, although evidence remains insufficient for routine clinical use as an antihypertensive nutraceutical (Borghi and Cicero, 2017).

8.9 Improvement of Arterial Stiffness

Chronic hypertension promotes structural changes in arterial walls, including increased collagen deposition, vascular smooth-muscle hypertrophy, and loss of arterial elasticity. Increased arterial stiffness can further elevate systolic blood pressure and contributes independently to cardiovascular risk.

Nutraceuticals with antioxidant, anti-inflammatory, and endothelial-protective properties may potentially improve arterial compliance. Omega-3 fatty acids, cocoa flavonoids, and selected polyphenols have therefore been investigated for vascular effects, although evidence regarding sustained improvement in arterial stiffness remains heterogeneous.

8.10 Modulation of Lipid and Glucose Metabolism

Hypertension commonly occurs together with obesity, insulin resistance, dyslipidemia, and metabolic syndrome. These conditions can promote oxidative stress, inflammation, endothelial dysfunction, and vascular injury, thereby increasing overall cardiovascular risk.

Nutraceuticals such as omega-3 fatty acids, dietary fiber, polyphenols, and selected plant-derived compounds may improve lipid and glucose metabolism in addition to their vascular effects. Their potential clinical importance may therefore extend beyond direct blood-pressure reduction to broader cardiovascular-risk modification (Ravan et al., 2020).

8.11 Gut Microbiota Modulation

The gut microbiota has emerged as an important regulator of cardiovascular and metabolic health. Alterations in microbial composition and microbial metabolites may influence blood pressure through immune signaling, intestinal permeability, renal mechanisms, and vascular function.

Probiotics, prebiotics, and dietary fibers may modify gut microbial composition and increase production of short-chain fatty acids such as acetate, propionate, and butyrate. Although these mechanisms are biologically plausible, the clinical antihypertensive effects of microbiota-targeted nutraceuticals remain relatively modest and strain-specific, requiring further controlled studies.

8.12 Reduction of Vascular Inflammation and Remodeling

Persistent hypertension causes vascular injury and promotes smooth-muscle hypertrophy, extracellular-matrix deposition, fibrosis, and arterial stiffening. Angiotensin II, oxidative stress, inflammatory mediators, and altered endothelial signaling contribute to this progressive vascular remodeling.

Plant-derived polyphenols, curcuminoids, omega-3 fatty acids, and other anti-inflammatory nutraceuticals may attenuate some of these processes through antioxidant and signaling effects. However, evidence demonstrating reversal of established vascular remodeling in humans remains limited, and further long-term clinical studies are required.

8.13 Modulation of Calcium Channels and Ion Transport

Calcium influx into vascular smooth-muscle cells is essential for contraction and regulation of vascular resistance. Nutraceuticals containing magnesium and certain plant-derived bioactive compounds may influence calcium-dependent signaling and ion-channel activity, potentially reducing vascular smooth-muscle contraction.

Flavonoids have also been reported to interact with vascular ion channels and endothelial signaling pathways, providing an additional mechanism for their antihypertensive effects (Ravan et al., 2020). However, the extent to which these molecular effects translate into clinically significant BP reductions varies substantially between compounds.

8.14 Integrated Multitarget Mechanism

The antihypertensive effects of nutraceuticals should be viewed as the result of interactions among several biological pathways rather than a single mechanism. For example, a polyphenol-rich nutraceutical may simultaneously reduce oxidative stress, improve NO availability, suppress inflammation, and enhance endothelial function.

This multitarget activity provides a biological rationale for using nutraceuticals as adjunctive interventions in hypertension. Nevertheless, mechanistic plausibility does not establish clinical efficacy, and current evidence supports their complementary rather than replacement role alongside appropriate antihypertensive therapy (Borghi and Cicero, 2017; Borghi et al., 2020).

12. Overall Mechanistic Perspective

Collectively, nutraceuticals may influence blood pressure through NO enhancement, RAAS modulation, antioxidant activity, anti-inflammatory effects, endothelial protection, vascular relaxation, renal sodium regulation, metabolic improvement, and gut microbiota modulation. Recent reviews continue to identify omega-3 fatty acids, garlic, magnesium, CoQ10, and other nutraceuticals as promising complementary interventions, although the reported BP reductions are generally modest and depend on dose, formulation, baseline BP, and patient characteristics (Liu et al., 2025).

Therefore, future research should focus on standardized preparations, dose optimization, bioavailability, long-term safety, and well-designed randomized controlled trials. Particular

attention should also be given to Indian medicinal plants and food-derived nutraceuticals, where extensive traditional use exists but clinical evidence is still comparatively limited.

13. Future Perspectives and Emerging Trends

The future of nutraceutical-based hypertension management is moving toward personalized, standardized, and evidence-based interventions that complement conventional pharmacotherapy. Advances in nutrigenomics and nutrigenetics may help identify individuals who respond differently to specific nutrients according to their genetic, metabolic, and dietary characteristics, supporting personalized nutrition strategies (Ordovas et al., 2018). At the same time, increasing evidence linking gut microbiota with blood-pressure regulation has stimulated interest in probiotics, prebiotics, synbiotics, and dietary fibers as potential therapeutic approaches (Yang et al., 2015). Development of standardized nutraceutical preparations with defined concentrations of active constituents is essential because variations in plant source, extraction method, formulation, and dose currently limit reproducibility between studies (Borghi et al., 2020). Advanced delivery systems such as nanoformulations, phytosomes, liposomes, and self-emulsifying systems may further improve the bioavailability of poorly absorbed phytochemicals such as curcumin, resveratrol, and CoQ10. Artificial intelligence, digital health technologies, wearable devices, and home blood-pressure monitoring may also facilitate individualized assessment of dietary interventions and long-term treatment responses. In India, considerable opportunities exist for investigating indigenous resources such as garlic, amla, moringa, turmeric, fenugreek, millets, and other traditional foods as sources of standardized cardiovascular nutraceuticals. Future research should prioritize large multicentric randomized controlled trials, standardized doses, long-term cardiovascular outcomes, pharmacokinetic evaluation, safety assessment, herb-drug interaction studies, and cost-effectiveness analysis (Cicero et al., 2015; Borghi and Cicero, 2017). Greater collaboration among clinicians, nutritionists, pharmacologists, pharmaceutical scientists, food technologists, and traditional medicine researchers could facilitate the translation of promising Indian nutraceuticals into clinically validated interventions. Ultimately, nutraceuticals are likely to have their greatest value as part of an integrated strategy involving healthy dietary patterns, physical activity, weight management, conventional antihypertensive therapy, and individualized cardiovascular-risk reduction rather than as replacements for established treatment (Borghi et al., 2020).

14. Conclusion

Nutraceuticals represent a promising complementary approach to hypertension management because of their ability to influence multiple mechanisms involved in blood-pressure regulation, including endothelial dysfunction, oxidative stress, inflammation, nitric oxide availability, vascular tone, and renal sodium balance. Several nutraceuticals, including garlic, potassium, magnesium, omega-3 fatty acids, beetroot-derived nitrates, cocoa flavonoids, and selected plant-based bioactive compounds, have demonstrated potential blood-pressure-lowering effects. India offers considerable opportunities in this field because of its rich diversity of medicinal plants, traditional foods, spices, and indigenous dietary resources such as garlic, amla, moringa, turmeric, fenugreek, and millets. However, the clinical evidence for many Indian nutraceuticals remains limited, particularly because of variations in dosage, formulation, bioavailability, standardization, study duration, and population characteristics. Therefore, nutraceuticals should currently be considered adjuncts to established antihypertensive therapy rather than replacements for conventional treatment. Future research should focus on standardized formulations, large multicentric clinical trials, long-term safety, herb-drug interactions, cardiovascular outcomes, improved bioavailability, and personalized nutritional approaches. Strengthening evidence for indigenous Indian nutraceuticals may ultimately support the development of affordable, culturally acceptable, safe, and scientifically validated strategies for comprehensive hypertension prevention and man.

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16 Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this review.

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