Int. J. Sci. R. Tech., 2026 3(5)
A Multidisciplinary peer-reviewed Journal
www.ijsrtjournal.com [ISSN: 2394-7063]

Original Article

A Review On The Role Of Herbal Medicine In Modulating Hypertension-Related Complications: Mechanistic Insights

Bhoomika Swarnkar, Abhishek Nand, Lokprabha Hirwani, Harkesh Dadsena, Pushpendra Kumar, Chhavi Rahangdale, Yashika Israni, Helina Tandon, Umakant Sahu, Vishal Jain*, Narendra Kumar

University Institute Of Pharmacy, Pt. Ravishankar Shukla University, Raipur, Chhattisgarh- 492010

ABSTRACT

One of the most common chronic conditions in the world, hypertension significantly increases the risk of kidney, cardiovascular, and neurological problems. Despite the wide availability of synthetic antihypertensive medications, adverse effects, high prices, and poor adherence-particularly in areas with limited resources—often restrict long-term control. Due to these restrictions, there is now more interest in herbal remedies, many of which have long been essential components of traditional Chinese medicine, Ayurveda, and Unani. Vascular reconstruction, dysfunction of endothelial cells, oxidative stress, and abnormalities in signalling molecules like nitric oxide & hydrogen sulphide are some of the underlying causes of hypertension that are examined in this review. It also emphasizes how particular medicinal plants alter these pathways. Herbs with a variety of mechanisms of action, such as calcium channel inhibition, renin-angiotensin-aldosterone system regulation, nitric oxide enhancement, and antioxidant effects, such as Terminalia arjuna, Crataegus monogyna, Ginkgo biloba, Withania somnifera, Boerhaavia diffusa, Tribulus terrestris, Allium sativum, and Camellia sinensis, have antihypertensive activity. Their phytoconstituents, including withanolides, ginsenosides, allicin, and punarnavine, have demonstrated promise in reducing the risk of problems such as erectile dysfunction, nephropathy, atherosclerosis, stroke, and left ventricular hypertrophy. By combining pharmacological facts and molecular insights, this review emphasizes the importance of herbal drugs as long-term and effective adjuncts or alternatives for managing hypertension and its associated difficulties.

Keywords: Renin-angiotensin-aldosterone system (RAAS), Phytoconstituents, Hypertension (HTN), Endothelial dysfunction, Vascular smooth muscle cell (VSMC).

INTRODUCTION

Hypertension, often known as high blood pressure, is a major public health issue around the world. By 2025, it is expected that more than 1.5 billion persons worldwide—or almost one in every three people aged 30 to 79—will have hypertension6. Despite advances in diagnosis and care, less than 20% of these people successfully control their blood pressure7. The issue is particularly grave in India, where around 24% of adult men and 21% of adults are affected[1]. Urban populations have prevalence rates that range from 25% to 30%, while rural areas have a bit lower estimate between 10% and 14%[2]. Even more concerning is that only about 37% of persons with hypertension obtain a diagnosis, 30% receive treatment, and less than 15% maintain ongoing blood pressure management[3].

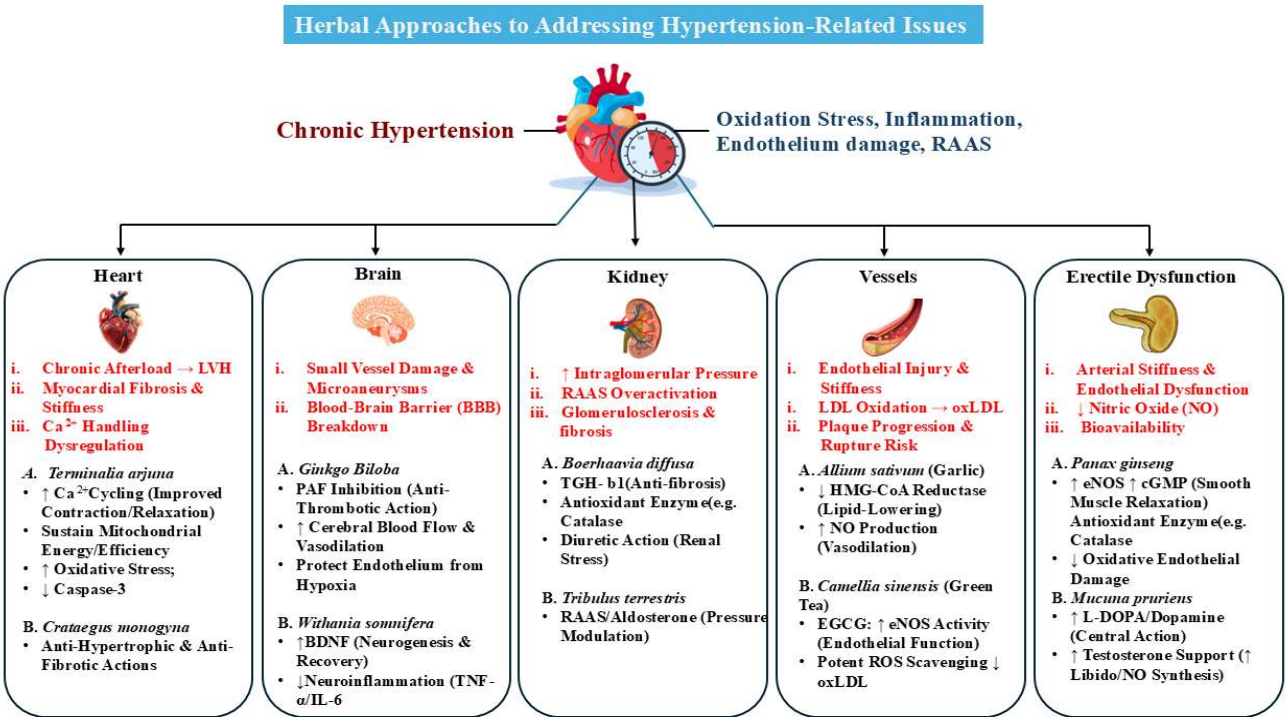
This growing burden, along with limited treatment accessibility and low long-term adherence, has rekindled interest in both traditional and alternative therapies, particularly those involving medicinal plants. Herbal therapies have been used for millennia in traditional practices such as Ayurveda, Traditional Chinese Medicine (TCM), and Unani, where botanicals are used to lower blood pressure, relieve stress, and improve [6]vascular health. Recent pharmacological investigations have verified the blood pressure-lowering properties of several plants, include Rauwolfia serpentina, Allium sativum (garlic), and Hibiscus sabdariffa. These kinds of plants are high in bioactive substances-such as

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

alkaloids, flavonoids, polyphenols, and saponins, which give antihypertensive benefits via mechanisms such ACE inhibition, vasodilation, antioxidant effects, and increased urine output[4].

Given the prevalence of hypertension worldwide and the disadvantages of synthetic medications—such as side effects, increased costs, and the possibility of polypharmacy—herbal treatments for hypertension are gaining recognized as viable and sustainable supplementary solutions[5,6,7]. This review evaluates the existing evidence on herbal antihypertensive therapies, stressing their pharmacological effects, clinical effectiveness, safety profiles, and potential role in the holistic management of hypertension[8].

Even though there are different therapeutic options to manage hypertension and cholesterol using regular drugs, blood pressure control remains unsatisfactory, particularly in low and middle-income countries[9]. This may be due to delays in intensifying treatment regimens like lifestyle changes and traditional medications, as well as a lack of awareness regarding the significance of adhering to prescribed treatments[10,11]. Worldwide, it has been discovered that 80% of individuals are open to the idea of using herbs for treating health issues, while the exclusive use of traditional herbal medicine among those with hypertension stood at 38.6%, with 47.5% using it in conjunction with antihypertensive medications[12,13].



GRAPHICAL ABSTRACT

2. METHODS

2.1 Search Strategy and Method for Identification of Studies

A literature search of published papers, periodicals, magazines, monographs, dissertations, and theses was part of this project. This time range was extended in certain cases because of incomplete information using the search terms "hypertensive," "hypotensive," "anti-hypertensive," and "blood pressure," along with their corresponding translations, the researchers identified medicinal plants that can alter blood pressure for this study through literature and other resources found in the Professor Eurico Back Library at UNESC. Research was also conducted using Medline, PubMed, Science Direct, academic Google, and Scientific Electronic Library Online to survey plant/drug interactions. The terms "antihypertensive drugs" (antihypertensives), "high blood pressure" (hypertension), and "drug interactions" were linked to the scientific names of plants that were found to alter blood pressure.The Gray search was conducted using Google Scholar as an extra platform, and substantial reference mining was done from the chosen papers.

This was done to make sure that this systematic review did not omit any pertinent publications.

2.2 Pathophysiology of hypertension

The pathophysiological processes linked to the development of hypertension include increased vascular resistance, which is primarily identified by reduced vascular diameter due to increased arterial remodelling and vascular contraction[14].Various elements play a role in the pathophysiology of hypertension (HTN), such as heightened activity of the renin-angiotensin-aldosterone system (RAAS), increased sympathetic nervous system stimulation, vasopressin effects, disruption of G protein-coupled receptor signalling, inflammatory responses, various functions of T-cells, and the range of vasoactive peptides released by other endothelial and smooth muscle cells[15].

Hypertension is defined by abnormalities in the arteries throughout the vascular system, impacting major arteries like the aorta, smaller resistance vessels (150–400µm), and the microcirculation, which includes arterioles and capillaries. Heightened arterial reactivity (responsiveness and strength) results from a lack of proper regulation in the presence of endothelial nitric oxide synthase (e-NOS) and pro-oxidant enzymes, along with heightened basal and stimulated calcium levels resulting from excessive transmembrane calcium permeability via calcium channels, and/or the simultaneous occurrence of vascular smooth muscle cell (VSMC) hyperplasia and hypertrophy (vascular remodelling), can result in increased vasoconstriction. These pathological processes contribute to a greater ratio of the thickness of the vessel wall compared to the size of the arterial lumen[16]. The heightened ratio significantly contributes to the onset of hypertension.

Molecular Pathogenesis of Hypertension

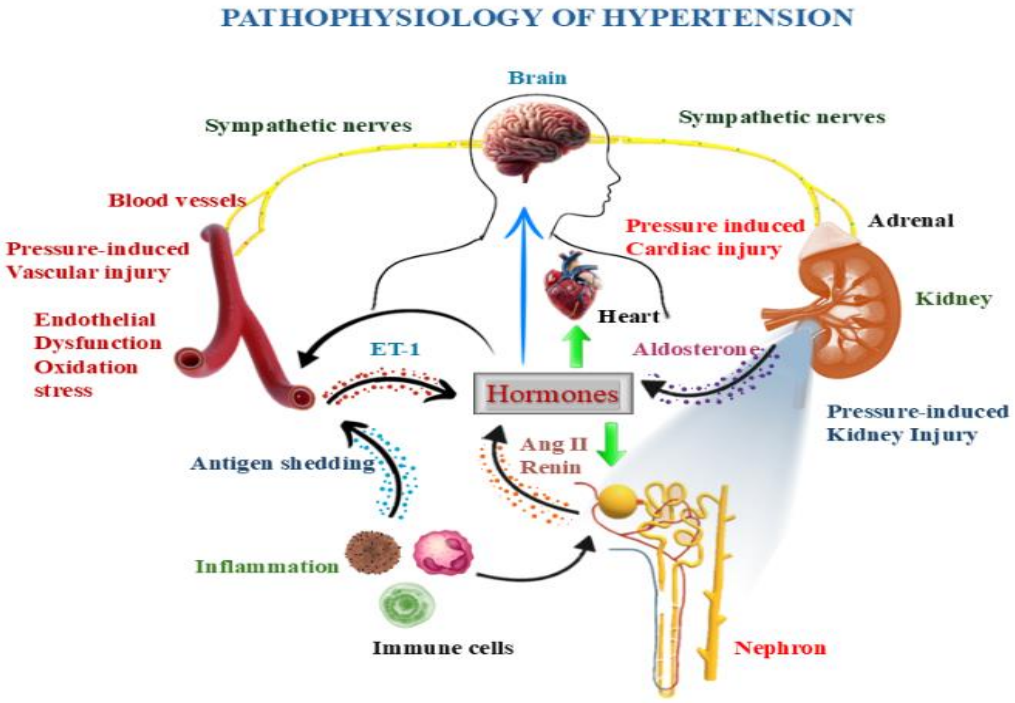


Figure. 1 Pathophysiology of Hypertension

2.2.1. Vascular Smooth Muscle Cell (VSMC) Proliferation

Vascular smooth muscle cells (VSMCs) play a role in the development of hypertension, and their growth leads to heightened peripheral resistance by reducing the diameter of arteries[17]. To gain an understanding of these complex changes, it is necessary to investigate the modifying variables that encourage or inhibit VSMC formation in the therapy of hypertension. Growth factors stimulate the cell to enter the cell cycle until the G1 phase, the first checkpoint. VSMC changes are a primary contributor to the development

of hypertension. Normally, these cells are contractile and relaxed, which helps to regulate blood flow and vascular tone. However, in hypertension conditions, VSMCs become more active and lose their contractile properties. This shift, known as phenotypic flipping, allows them to proliferate, migrate, and produce more structural proteins, resulting in larger and more rigid blood vessels[19].

Another signal, platelet-derived growth factor (PDGF), functions similarly by activating pathways that lead to enhanced VSMC proliferation and remodeling[19]. High blood pressure exerts mechanical pressures on VSMCs as well. Mechanosensitive molecules detect these stresses and activate pathways such as YAP/TAZ and RhoA/ROCK, promoting cell growth and shape alterations[20]. These modifications help to restrict and harden the arteries. Inflammation and oxidative stress exacerbate the situation. Increased amounts of reactive oxygen species (ROS) can activate pathways such as EGFR/AKT/ERK, resulting in additional cell growth. In addition, inflammatory molecules like as TLR4 and NF-KB are activated, promoting inflammation and driving VSMCs into an active, synthetic state[21].

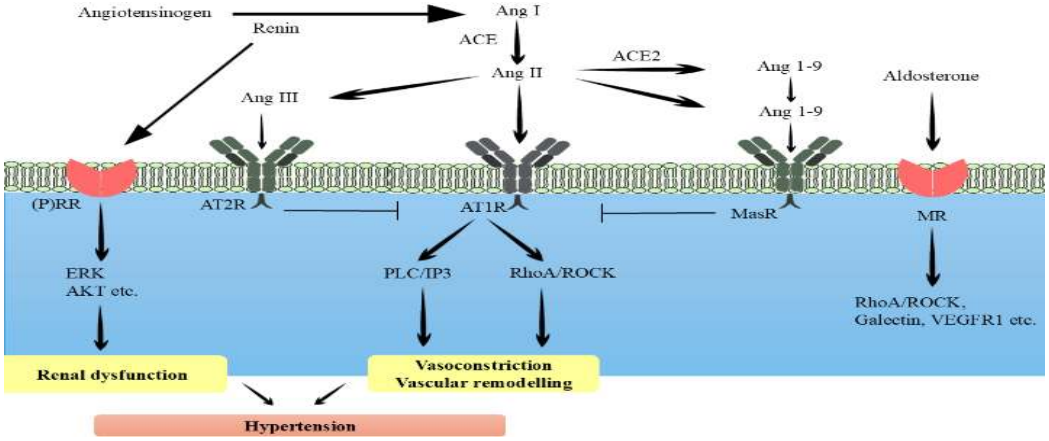


Figure. 2 Receptor-Mediated RAAS Pathways Contributing to Hypertension

A new study published in 2025 revealed the role of a protein known as ZFP36. This protein reduces the quantity of RGS2, which normally inhibits cell proliferation. When RGS2 is reduced, signals that induce contraction and cell growth become more powerful, exacerbating hypertension. In animal models, inhibiting ZFP36 in VSMCs helped lower blood pressure and enhance vascular shape[22]. Various signals cause this behaviour. One of the most significant is angiotensin II (Ang II), a chemical that causes high blood pressure. It activates the AT1R receptor on VSMCs, which stimulates intracellular pathways such as ERK and elevates calcium levels in the cells, boosting their development and migration[23].

Several potential therapeutics are being investigated to prevent or treat VSMC overgrowth. One of these is Resolving D1, a molecule that reduces inflammation and inhibits damaging signalling pathways. Research indicates that it can inhibit Ang II-induced vascular remodelling and lower blood pressure in animals[23].

2.2.2. Endothelial Cells

Endothelial cells form a single layer that lines the interior surface of blood arteries and are critical for vascular function. These cells control processes like blood flow, vascular tone, inflammation, blood coagulation, and barrier permeability. In healthy settings, endothelial cells release chemicals like nitric oxide (NO), which helps relax blood arteries and prevent clot formation or severe inflammation[24].

Endothelial cells frequently fail in the presence of hypertension and cardiovascular disease. This dysfunction can be caused by high levels of angiotensin II (Ang II), oxidative stress, and disrupted blood flow. Ang II not only increases blood pressure but also disturbs the protective role of endothelial cells by increasing the formation of reactive oxygen species (ROS), lowering nitric oxide bioavailability, and harming the inner lining of blood vessels[25].

According to recent research, Ang II can cause endothelial cells to die through a process known as ferroptosis. This process is initiated by lipid

peroxidation and involves receptors such as CD36, which absorb oxidized lipids and decrease the protective barrier created by these cells. As a result, the vascular wall is more susceptible to inflammation and injury[26].

Oxidative stress is a primary cause of endothelial damage. When ROS levels rise due to mitochondrial malfunction or NADPH oxidase activation, they activate inflammatory pathways such as NF-KB, JAK/STAT, and MAPK. These signalling pathways promote the production of adhesion molecules like ICAM-1 and VCAM-1, which attract immune cells to the vascular wall and increase inflammation and remodeling[27].

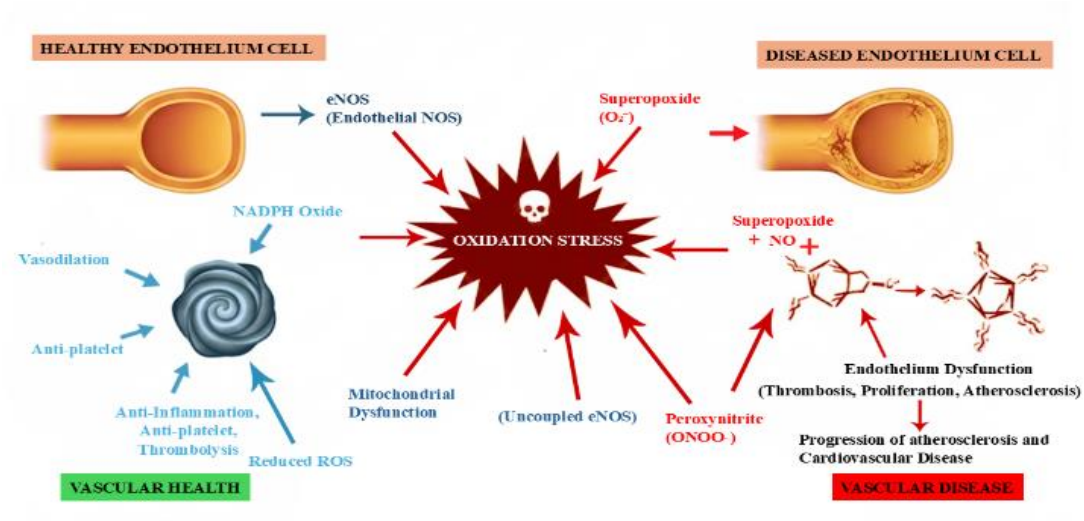


Figure. 3 Oxidative stress and role of NOS on blood vascular system

2.2.3. Repertoire of Signalling Molecules

The following signalling molecules become essential to the pathophysiology of hypertension assuming a homeostatic imbalance[28]. Fortunately, various plant and herbal extracts, along with their individual metabolites, can influence signalling cascades related to the physiology of the cardiovascular system (refer to Section Herbs and Spices Most Commonly Used for Treatment of Hypertension, below). These herbs not only protect blood vessels but could also potentially reverse the changes associated with hypertension. This is especially true if changes in hypertensive patients are dealt with before they reach a decompensated state.

A. Reactive Oxygen Species

In a healthy state, pro-oxidant activity is counterbalanced by antioxidative agents. Nevertheless, when this balance is disrupted, the disorganized environment gives rise to pathological conditions like hypertension, atherosclerosis, and various other vascular complications[29]. ROS, such as superoxide anions (O•− 2) and hydroxyl ions (OH−), play a critical role in hypertension pathophysiology by causing oxidative stress[30]. Reactive oxygen species (ROS) are produced by nicotinamide-adenine dinucleotide phosphate (NADPH) oxidase and other enzymatic activities, particularly those associated with the electron transport chain in mitochondria[31]. ROS are also liable for the oxidation of low- density lipoprotein (LDL), which causes inflammation and increases VSMC proliferation. Inflammation and increased proliferation both play important roles in causing plaque formation, which may contribute to high blood pressure. Interestingly, in animals, blood pressure drops when ROS generation is reduced with antioxidant treatment[32].

B. Nitric Oxide

Nitric oxide (NO), a key chemical produced by endothelial cells, has a direct effect on vascular smooth muscle cells (VSMCs) and is required for the control of vascular tone, blood pressure, and pathologic remodelling. Under normal settings, No is mainly generated by endothelial nitric oxide synthesis (e-NOS) and spreads into vascular smooth muscle cells (VSMCs), which activates soluble guanylate cyclase (sGC). This activation increases the quantity of cyclic guanosine monophosphate (cGMP), which

stimulates protein kinase G (PKG). PKG reduces cellular calcium levels, smooth muscle elasticity, and decreases VSMC proliferation and migration[33].

Beyond the typical cGMP-dependent mechanisms, NO has cGMP-independent actions. One important method is S-nitrosation, in which NO covalently changes proteins such as RhoA and Raf-1, inhibiting their signaling capabilities. These proteins are implicated in the ERK/MAPK pathway, which typically promotes VSMC development and migration. Inhibiting this mechanism causes cell cycle arrest and decreased proliferation[34].

Recent research has demonstrated that NO can control VSMC growth by modulating ubiquitin-proteasome pathways. Specifically, NO promotes the degradation of UbcH10, an E2 enzyme required for cell cycle progression. Downregulating UbcH10 causes arrest during the G1/S phase transition and lessens neointimal thickening after vascular damage[35]. Stimulating NADPH oxidase produces superoxide anion (O•− 2), which combines with NO to form peroxynitrite, a potent oxidant. This peroxynitrite then induces oxidative breakdown of the e-NOS cofactor tetrahydrobiopterin (BH4), yielding the inactive dihydrobiopterin (BH2). This produces more superoxide anion, which eventually lowers BH4 levels. As a result, a shift in balance from NO to superoxide production occurs, which is known as the uncoupling of NOS[36].

C. Hydrogen Sulphide

In VSMCs and perhaps endothelial cells, cystathionine γ-lyase (CSE) converts L-cysteine to produce hydrogen sulphide (H2S)[37]. H2S has a vasorelaxant impact on VSMCs via increasing intracellular cGMP levels and activating ATP-dependent potassium channels[37,38].

Hydrogen sulphide (H_2S) is recognized as an important gas transmitter for maintaining vascular health. In VSMCs, H_2S regulates physiological activities such relaxation, proliferation, migration, and oxidative stress resistance. The circulatory system manufactures it naturally through the enzyme cystathionine γ-lyase (CSE).H_2S relaxes vascular smooth muscle by activating ATP-sensitive potassium (K_ATP) channels, resulting in membrane hyperpolarization and decreased calcium influx. This reduces intracellular Ca^{2+} and promotes vasodilation[39]. H_2S prevents vascular calcification by activating the KEAP1-NRF2-NQO1 pathway, a key antioxidant mechanism. This reduces oxidative damage and inhibits signals that promote calcification in VSMCs[40], H_2S's actions make it an attractive target for therapies to prevent vascular disorders such as hypertension, atherosclerosis, and restenosis.

3. Herbal Approaches to Addressing Hypertension-Related Issues: An In-Depth Physiological Analysis

1. Left Ventricular Hypertrophy (LVH) and Heart Failure: -

Pathophysiology of Disease - Chronic high blood pressure increases afterload, which is the pressure the left ventricle must overcome to pump blood. As a result, myocardial cells expand, causing left ventricular hypertrophy (LVH) to maintain cardiac output. Nonetheless, this favorable hypertrophy can turn maladaptive over time, resulting in increased stiffness of the myocardium, fibrosis, poor relaxation (diastolic dysfunction), and eventually heart failure, whether with preserved or reduced ejection fraction[41].

At the cellular level, elevated blood pressure activates hypertrophic signalling pathways such MAPKs and alters calcium control, resulting in contractile dysfunction and poor energy efficiency[42].

Herbal Solutions and Mechanisms: -

A. ***Terminalia arjuna*** - The deciduous tree *Terminalia arjuna,* also referred to as Arjuna, is indigenous to the Indian subcontinent and has long been used as a cardiac tonic in Ayurvedic medicine. Its effectiveness in treating cardiovascular disorders, especially left ventricular hypertrophy (LVH) and heart failure (HF), which are frequently brought on by chronic hypertension, is supported by recent pharmacological and clinical research.

Pathophysiology of *Terminalia arjuna* - The cardiotonic properties of *Terminalia arjuna* are well established. According to clinical research, taking 400 mg of Oxyjun® (standardized Arjuna extract) daily enhanced cardiac output by 6.3%, decreased tiredness by 22.5%, and improved left ventricular ejection

fraction[43]. Mechanistically, its triterpenoids and flavonoids modulate intracellular calcium cycling, enhance myocardial contractility, and reduce oxidative stress-induced apoptosis in cardiac cells[42].

The heart uses left ventricular hypertrophy to make up for elevated systemic vascular resistance in persistent hypertension. After maintaining cardiac output for a while, this adaptive mechanism turns maladaptive because of fibrosis, higher myocardial oxygen demand, and poorer diastolic relaxation. Eventually, these alterations lead to cardiac failure with a preserved or decreased ejection fraction[43].

Key Pathways Involved include –

- Activation of MAPK and NF-KB, which results in the production of inflammatory and fibrotic genes.
- Oxidative stress and malfunctioning mitochondria.
- Diastolic filling and contractility are hampered by improper calcium management[43].

Phytoconstituents like Triterpenoids (arjunic acid, arjunolic acid), Flavonoids (arjunone, arjunolone), Glycosides, tannins, and minerals (especially CoQ10-like activity) constituents contribute to Arjuna's antioxidant, anti-inflammatory, and cardiotonic properties. Terminalia arjuna modulates calcium ion channels and sarcoplasmic reticulum function, improving myocyte relaxation and contraction cycles, thus supporting both systolic and diastolic function. By downregulating caspase-3 and maintaining mitochondrial membrane potential, it prevents myocardial cell death. This is important for sustaining cardiac energy metabolism, particularly during ischemia stress[44].

B. ***Crataegus monogyna*** - Native to Europe and Asia, hawthorn (*Crataegus monogyna*) is a medicinal shrub that has long been used in both traditional and contemporary herbal therapy to treat circulatory disorders[45]. It is highly relevant for the treatment of heart failure (HF) and left ventricular hypertrophy (LVH), two common complications of long-term hypertension, because its berries, leaves, and flowers contain a wide variety of bioactive compounds that have cardiotonic, anti-hypertrophic, and vasodilatory effects[46,47].

Pathophysiology of *Crataegus monogyna* - To maintain cardiac output, chronic hypertension raises afterload over time, which induces adaptive myocardial hypertrophy. This process eventually turns pathological because of:

- Fibrosis of the heart.
- Stiffness of the left ventricle increased.
- Calcium signalling impairment.
- Modified expression of some genes in cardiomyocytes[48].

These changes disrupt diastolic function, promote electrical remodelling, and increase the risk of systolic heart failure.

2. Stroke (Ischemic and Haemorrhagic): -

Pathophysiology of Disease - Chronic hypertension harms small blood vessels in the brain, leading to arteriosclerosis, lipohyalinosis, and the development of microaneurysms. This vascular condition increases the risk of haemorrhagic stroke because of blood vessel due to vessel blockage. Furthermore, hypertension weakens cerebral autoregulation, affects the integrity of the blood–brain barrier (BBB), elevates levels of inflammatory cytokines, and triggers neuronal apoptosis[49,50].

Herbal Solutions and Mechanisms: -

A. ***Ginkgo biloba*** - In the search for complementary or alternative therapies, Ginkgo biloba, a traditional medicinal plant native to China, has received interest for its neuroprotective properties. The standardized extract, notably EGb 761, contains flavonoids (such as quercetin and kaempferol) and terpenoids (such as ginkgolides and bilobalide) with antioxidant, anti-inflammatory, antiplatelet, and vasodilatory properties that are useful in stroke therapy. Extracts, notably ginkgo diterpene lactone meglumine (GDLM), have been shown to help with stroke rehabilitation. In a randomized research involving 3,448 individuals with ischemic stroke, there was a 6.8% increase in the rate of positive recovery (as defined by the modified Rankin Scale

scores of 0-1) compared to those receiving a placebo[49].

Pathophysiology of *Ginkgo biloba* - GDLM enhances cerebral blood flow, inhibits platelet activating factor reducing thrombosis, protects endothelial cells, and promotes neuronal resistance to hypoxia through antioxidant mechanisms[50]. Ischemic stroke is caused by arterial obstruction, which leads to diminished cerebral blood flow, ATP depletion, glutamate-induced excitotoxicity, oxidative stress, and neuronal death. Hemorrhagic stroke occurs when blood vessels break, resulting in hematoma formation, oxidative damage, and inflammation. Ischemic stroke is caused by arterial obstruction, which leads to diminished cerebral blood flow, ATP depletion, glutamate-induced excitotoxicity, oxidative stress, and neuronal death. Hemorrhagic stroke occurs when blood vessels break, resulting in hematoma formation, oxidative damage, and inflammation.[51] Ginkgo biloba, particularly its extract EGb 761, provides neuroprotection via antioxidant, anti-inflammatory, and vasodilating properties. Its flavonoids and terpenoids absorb free radicals, enhance mitochondrial activity, and increase nitric oxide-mediated vasodilation[52]. In hemorrhagic stroke, Ginkgo decreases edema and maintains the blood-brain barrier, limiting neuronal damage[53].

B. Withania somnifera - *Withania somnifera* (Ashwagandha), an important plant in Ayurvedic medicine, is recognized for its adaptogenic, anti-inflammatory, neuroprotective, and antioxidant effects. The root extract contains bioactive substances such as withanolides, sitoindosides, and alkaloids, which enhance its medicinal potential. Recent experimental and clinical research have highlighted its neurorestorative efficacy in central nervous system illnesses, including stroke[54].

Pathophysiology of *Withania somnifera* - In ischemic stroke, the cessation of cerebral blood flow causes oxidative stress, excitotoxicity, and activation of the inflammatory cascade. Ashwagandha mitigates these effects by reducing lipid peroxidation**,** inhibiting pro-inflammatory cytokines (e.g., TNF-α, IL-6), and enhancing endogenous antioxidant defences (e.g., superoxide dismutase, catalase)[55].

In haemorrhagic stroke, where bleeding into brain tissue causes edema and neuronal injury, Ashwagandha reduces neuroinflammation and supports the integrity of the blood-brain barrier. Its ability to upregulate brain-derived neurotrophic factor (BDNF) promotes neurogenesis and neuronal recovery post-stroke[56].

3. Chronic Kidney Disease (Hypertensive Nephropathy) –

Pathophysiology of Disease - Renal arteriole constriction and thickening brought on by hypertension results in ischemia and damage to the glomeruli and tubules. Proteinuria, a decline in glomerular filtration rate (GFR), and a gradual loss of nephrons lead to chronic kidney disease (CKD)[57].

Herbal Solutions and Mechanisms: -

A. *Boerhaavia diffusa* - Punarnava, also known as Boerhaavia diffusa, is a traditional Ayurvedic herb that is widely used for its nephroprotective, diuretic, anti-inflammatory, and antioxidant qualities. Important bioactive substances found in the plant, including flavonoids, lignans, boeravinones, and punarnavine, have been shown to have protective effects on renal tissues[58]. Long-term uncontrolled hypertension causes glomerular sclerosis and tubulointerstitial fibrosis, which in turn causes hypertensive nephropathy, a progressive form of chronic kidney disease (CKD). Punarnava has shown promise in decreasing these side effects while maintaining renal function.

Pathophysiology of *Boerhaavia diffusa* - Glomerular ischemia, arteriolar constriction, glomerulosclerosis, and progressive nephron loss because of persistently elevated intraglomerular pressure are the hallmarks of hypertensive nephropathy. The processes behind these changes include oxidative stress, fibrosis, inflammation, and activation of the renin-angiotensin-aldosterone system (RAAS)[59].

Boerhaavia diffusa has nephroprotective properties by:

- Reducing oxidative damage by increasing the levels of endogenous antioxidant enzymes, such as superoxide dismutase and catalase.

- Inhibiting pro-inflammatory cytokines including TNF-α and IL-6 to modify inflammatory pathways.
- Displaying diuretic properties that alleviate renal stress and reduce systemic blood pressure.
- Reducing fibrotic signaling (such as TGF-β1), which prevents the formation of extracellular matrix in renal tissues.

B. ***Tribulus terrestris*** **-** lowers intraglomerular pressure and promotes natriuresis[60] by inhibiting RAAS and lowering aldosterone levels. In Ayurvedic and traditional medical systems, Tribulus terrestris, also referred to as Gokshura, is a well-known medicinal plant that has nephroprotective, antihypertensive, diuretic, and anti-inflammatory qualities. Glycosides[61], alkaloids, flavonoids, and saponins—particularly protodioscin—are the main bioactive components. Tribulus terrestris has been investigated for its potential to treat renal problems, notably those brought on by chronic hypertension, and has long been used as a renal tonic.

Pathophysiology of *Tribulus terrestris* - Consequently, the strain on the renal vasculature is reduced. By increasing the quantities of endogenous enzymes such as glutathione peroxidase and superoxide dismutase, it also strengthens antioxidant defences and combats oxidative damage. Additionally, it helps prevent immune-related tissue damage through its anti-inflammatory properties, which are mediated by the reduction of cytokines including TNF-α and IL-6. Crucially, new research indicates that T. terrestris may block pathways linked to fibrosis, including the TGF-β1/Smad axis, which is essential for the development of chronic renal scarring.[62,63].

4. Atherosclerosis and Vascular Dysfunction: -

Pathophysiology of Disease - The endothelium deteriorates more quickly due to high blood pressure, which causes LDL to oxidize and plaque to form. Because of the increased arterial stiffness and clot formation, this increases the risk of peripheral artery disease and heart attacks. High blood pressure-induced endothelial damage leads to LDL oxidation and the formation of atherosclerotic plaques, increasing the risk of cardiovascular events[42]. Chronic arterial disease known as atherosclerosis is brought on by endothelial dysfunction, which is frequently brought on by smoking, diabetes, hypertension, or hyperlipidaemia[64]. Endothelial damage promotes the migration of low-density lipoprotein (LDL) into the intima, where it is oxidatively modified to become oxidized LDL (oxLDL), which sets off an inflammatory cascade[65]. When monocytes enter the artery wall, mature into macrophages, and generate foam cells, early fatty streaks are created. Fibrous plaque development is facilitated by the proliferation of smooth muscle cells and the deposition of extracellular matrix. TNF-α and IL-1β are examples of inflammatory mediators that increase matrix metalloproteinase activity, weakening plaques and raising the chance of rupture[66]. Reduced nitric oxide (NO) bioavailability, oxidative stress, and decreased vasodilation all contribute to vascular dysfunction, which in turn encourages thrombosis and vascular stiffness. Acute ischemia episodes and thrombus development are brought on by plaque rupture, which reveals thrombogenic material[65].

Herbal Solutions and Mechanisms: -

A. ***Allium sativum*** **(garlic): -** Garlic, or Allium sativum, is a popular medical herb known for its heart-healthy properties. Garlic is rich in bioactive sulfur-containing compounds that have anti-inflammatory, anti-thrombotic, antioxidant, and lipid-lowering properties, including allicin, ajoene, and S-allyl cysteine[67]. Its medical benefits are particularly notable in cardiovascular disease, where it helps to lower risk factors such as hyperlipidemia, hypertension, and oxidative stress. It has traditionally been utilized in both a culinary and therapeutic environment[68].

Pathophysiology of *Allium sativum* **-** Plaques in atherosclerosis form because of endothelial dysfunction and lipid accumulation. Oxidized low-density lipoprotein (oxLDL) causes an inflammatory response that draws monocytes, which then change into foam cells, resulting in the creation of fatty streaks and the progression of plaques[69]. Garlic counteracts this process by blocking HMG-CoA reductase, lowering LDL cholesterol production, and

decreasing LDL oxidation via antioxidant activity[70]. It increases nitric oxide (NO) generation, improves endothelial function and vasodilation, and lowers oxidative stress. Reducing cytokines like IL-6 and TNF-α can reduce plaque destabilization and vascular damage[71,72]. Allium sativum regulates lipid metabolism, oxidative stress, and vascular inflammation via various pathways, thereby addressing the fundamental pathophysiological causes of atherosclerosis and vascular dysfunction.

B. ***Camellia sinensis*** **(Green Tea)** - Green tea, referred to as Camellia sinensis, is a rich source of polyphenolic compounds, especially catechins like epigallocatechin-3-gallate (EGCG), which have powerful antioxidant, anti-inflammatory, and lipid-modifying actions[73]. Green tea is linked to lower cardiovascular morbidity and mortality, according to epidemiological studies, because it improves lipid profiles, endothelial function, and reduces oxidative stress. Catechins, particularly EGCG, improve arterial flexibility and prevent plaque formation by decreasing LDL oxidation and increasing endothelial NO synthase (eNOS) activity42[74]. Green tea's cardiovascular advantages originate from its capacity to decrease LDL oxidation, increase vascular responsiveness, and regulate important signalling pathways involved in vascular health.

Pathophysiology of *Camellia sinensis* - Endothelial damage triggers atherosclerosis, which is then followed by the entry of LDL cholesterol into the intima, oxidative modification, and the recruitment of monocytes, which develop into foam cells and aid in the creation of plaque[75]. Vascular dysfunction is sustained by oxidative stress and inflammation, which lowers the bioavailability of nitric oxide. By scavenging reactive oxygen species, preventing LDL oxidation, and increasing endothelial nitric oxide synthase (eNOS) activity, green tea catechins—EGCG in particular—oppose these processes and improve vasodilation[76]. Additionally, catechins reduce vascular inflammation and stabilize plaques by downregulating inflammatory mediators such NF-κB, TNF-α, and interleukins[77].

5. Erectile Dysfunction (ED) –

Pathophysiology of Disease - Hypertension-induced arterial stiffness and endothelial dysfunction impair blood flow to the penile tissue. Nitric oxide (NO) deficiency inhibits the smooth muscle relaxation necessary for erection. Reduced nitric oxide availability and increased vascular stiffness, which hinder blood flow to the erectile tissue, are the causes of erectile dysfunction[42,78]. Furthermore, cGMP is broken down more quickly by elevated phosphodiesterase type 5 (PDE5) activity, which restricts smooth muscle relaxation. Hormonal abnormalities like low testosterone can lower libido and erectile function, while chronic inflammation and vascular stiffness further impair penile hemodynamics[79,80].

Herbal Solutions and Mechanisms: -

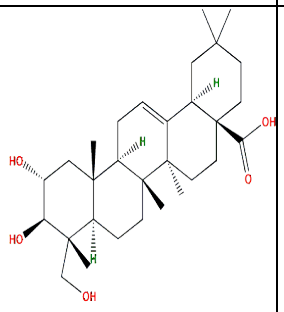
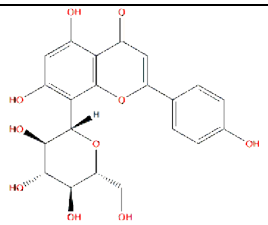
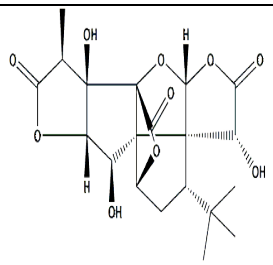
A. ***Panax ginseng*** - Panax ginseng, sometimes referred to as Korean or Asian ginseng, is a herb used extensively in East Asian traditional medicine to improve sexual health, energy, and general physiological robustness. Ginsenosides, its active components, have neuroendocrine-modulating, vasodilatory, and antioxidant properties, making it a promising treatment for erectile dysfunction (ED)[81]. According to preclinical and clinical research, P. ginseng promotes nitric oxide (NO) generation, enhances endothelial function, and increases libido, all of which lead to better erectile performance[82].

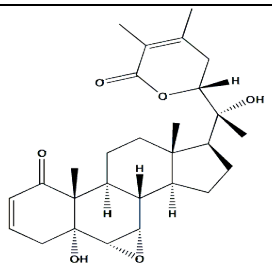
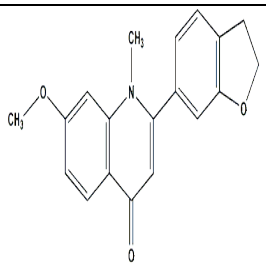
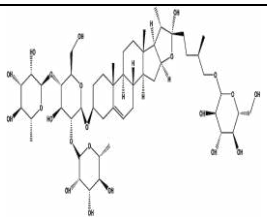
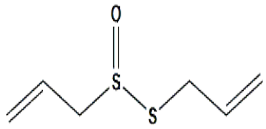
Pathophysiology of *Panax ginseng* - Endothelial dysfunction, reduced NO bioavailability, oxidative damage, hormonal dysregulation, and neurovascular impairment all contribute to poor penile hemodynamics[83]. Ginsenosides have been shown in animal studies to improve erectile function by influencing central dopaminergic pathways and increasing erectile responses. Ginsenosides also increase the activity of endothelial nitric oxide synthase (eNOS) and cyclic guanosine monophosphate (cGMP), which relaxes smooth muscles in the corpus cavernosum and improves penile blood flow. Additionally, ginsenosides prevent oxidative damage to the vascular endothelium, which preserves erectile capacity[84].

B. ***Mucuna pruriens*** **-** *Mucuna pruriens*, often known as velvet bean, is a traditional Ayurvedic herb used to improve male sexual performance. Its seeds are rich in L-DOPA, the natural precursor to dopamine, and contain antioxidant

constituents such as flavonoids and alkaloids. Emerging research suggests these components contribute to improved erectile function by acting on central and peripheral neuroendocrine pathways[85].

Pathophysiology of *Mucuna pruriens* - Erectile function depends critically on nitric oxide (NO)-mediated vasodilation in penile tissue. *M. pruriens* enhances dopamine levels in the brain, activating the hypothalamic–pituitary–gonadal axis, leading to increased gonadotropins and testosterone release, which in turn supports NO synthesis and endothelial function. It also mitigates oxidative stress in the corpus cavernosum via antioxidant actions, protecting NO availability and penile tissue structure[85,86].

S. N.	Botanical Name (Common Name)	Mechanism(s) of Action (Target receptor)	Part Used	Antihypertensive Phytoconstituents (Major Active)	Chemical Structure	References
1.	*Terminalia arjuna* (Arjuna)	PPARα receptor activation Ca^{2+}-handling proteins Endothelial nitric oxide (NO)	Stem bark	**Arjunolic acid**, arjunic acid, arjunosides (glycosides), tannins, ellagic acid, gallic acid, flavonoids and oligomeric proanthocyanidins		**87, 88, 89**
2.	*Crataegus monogyna* (Hawthorn)	Na^+/K^+-ATPase inhibition Endothelial NO synthase (eNOS) activation TGF-β1/Smad signaling inhibition	Leaves/flowers, and berries	**Vitexin**, Hyperoside, rutin, quercetin, procyanidins.		**90, 91, 92, 93, 94**
3.	*Ginkgo biloba* (Ginkgo)	Endothelial NO synthase (eNOS) activation Platelet-activating factor (PAF) receptor antagonism NF-κB pathway inhibition	Leaves	**Ginkgolide B** Flavonoids (quercetin, kaempferol), ginkgolides, bilobalide		**95, 96, 97, 98**

4.	*Withania somnifera* (Ashwagandha)	NMDA receptor modulation Nrf2/ARE pathway activation NF-κB pathway inhibition	Roots, leaves	**Withanolides** Withaferin A, withanolide A sitoindosides		**99, 100, 101**
5.	*Boerhavia diffusa* (Punarnava)	TGF-β1/Smad signaling inhibition Renin–Angiotensin–Aldosterone System (RAAS) modulation	Roots, leaves	**Punarnavine**, boeravinones Flavonoids alkaloids		**102, 103, 104, 105**
6.	*Tribulus terrestris* (Puncture Vine)	TGF-β1/Smad signaling inhibition Renin–Angiotensin–Aldosterone System (RAAS) modulation Nrf2/ARE pathway activation	Fruits, roots	**Protodioscin** Saponins (dioscin), flavonoids Diosgenin, Polyphenols, alkaloids		**106, 107, 108, 109**
7.	*Allium sativum* (garlic)	HMG-CoA reductase inhibition NF-κB inhibition eNOS activation → ↑ NO	Bulb	**Allicin**, S-allyl cysteine, ajoene, diallyl disulfide, flavonoids, diallyl trisulfide, Organosulfur compounds		**110, 111, 112, 113**

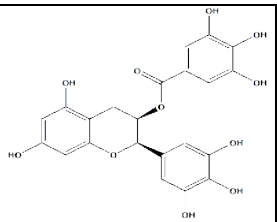
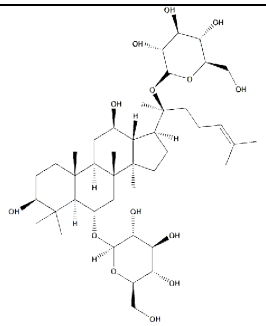
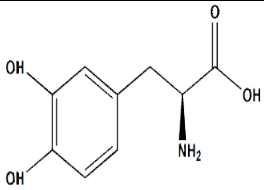
8.	*Camellia sinensis* (Green Tea)	HMG-CoA reductase inhibition NF-κB pathway inhibition eNOS activation → ↑ NO	Leaves	**Epigallocatechin gallate (EGCG)**, catechins, theaflavins, flavonoids		**114, 115, 116, 117**
9.	*Panax ginseng* (Ginseng)	eNOS activation → ↑ NO release Nitrergic nerve signaling modulation Nrf2/ARE pathway activation, ↓ ROS	Root	**Ginsenosides Rg1** (Rb1, Rg3, Re, Rd), polysaccharides, flavonoids, Total ginsenosides		**118, 119, 120,**
10.	*Mucuna pruriens* (Velvet Bean)	Dopamine D2 receptor activation Hypothalamic–pituitary–gonadal (HPG) axis activation Nrf2/ARE pathway activation	Seeds	**L-DOPA (Levodopa)**, alkaloids, flavonoids, saponins, phenolic compounds, antioxidants (quercetin, catechins)		**121, 122, 123**

Table No. 1 Herbal Approaches for Managing Hypertension with Their Mechanisms of Action.

4. Herbal medicines used for the treatment of hypertension

Side effects are common with several antihypertensive medications used to treat hypertension. To treat it, scientific research suggests a variety of lifestyle changes as well as the application of appropriate medicinal plants.[41] Certain herbs and spices contain secondary metabolites that have antihypertensive effects. Many herbal remedies help manage and lower hypertension by providing antioxidant, anti-inflammatory, and anti-apoptotic benefits, activating the e-NOS-NO signalling pathway, reducing endothelial permeability, and promoting angiogenesis.[42]

The list of medicinal plants that have been found to be useful in managing and treating hypertension is provided in Table 1.

S.N.	Botanical Name	Common Name	Mechanism(s) of Action	Part Used	Antihypertensive Phytoconstituents (Major Active)	Reference
1.	***Allium sativum***	Garlic	Vasodilation, ACE inhibition, antioxidant	Bulb	Allicin, S-allyl cysteine, diallyl disulfide	**124**
2.	***Hibiscus sabdariffa***	Rosella	Vasodilation via Anthocyanins, ACE inhibition, diuretic	Calyx	Anthocyanins (delphinidin-3-sambubioside), protocatechuic acid	**125**
3.	***Crataegus oxyacanthine***	Hawthorn	Ca^{2+} Channel blockage, Antioxidant, Vasodilation	Berry	Flavonoids (vitexin, rutin), oligomeric procyanidins	**126**
4.	***Nigella sativa***	Black Cumin	↓SNS stimulation, antioxidants, Ca^{2+} blockage	Seed	Thymoquinone, α-hederin, nigellidine	**127**
5.	***Rauwolfia serpentina***	Sarpa Gandha	Sympatholytic via reserpine, catecholamine depletion	Root	Reserpine, ajmaline, serpentine (indole alkaloids)	**128**
6.	***Boerhavia diffusa***	Punarnava	Diuretic, Ca^{2+} channel blockade, antioxidant	Root	Punarnavine, boeravinones (rotenoids)	**129**
7.	***Moringa oleifera***	Drumstick	Vasodilation, ACE inhibition, antioxidant	Leaf	Quercetin, chlorogenic acid, isothiocyanates	**130**
8.	***Coptis chinensis***	Goldthread	ACE inhibition, ↓Ang II, ↑e-NOS	Rhizome	Berberine, palmatine, coptisine	**131**
9.	***Panax ginseng***	Ginseng	↑NO production, vasorelaxation, anti-inflammatory	Root	Ginsenosides (Rb1, Rg1, Re)	**132**

10.	***Apium graveolens***	Celery	Ca^{2+} channel inhibition, diuretic	Seed	3-n-butylphthalide, apigenin, luteolin	**133**
11.	***Salvia Miltiorrhiza***	Red sage	K^+ channel activation, ACE inhibition, antioxidant	Root	Tanshinones, salvianolic acid B, rosmarinic acid	**134**
12.	***Peganum harmala***	Esfand	NO modulation, vasodilation, monoamine oxidase inhibition	Seed	Harmine, harmaline (β-carboline alkaloids)	**135**
13.	***Peperomia pellucida***	Shiny Bush	ACE inhibition, antioxidant, diuretic	Whole Plant	Pellucidin A, quercetin, tannins	**136**
14.	***Syzygium polyanthum***	Indonesian Bay-leaf	Vasorelaxation via phenolics, NO-dependent pathways	Leaf	Phenolic acids, flavonoids (quercetin, rutin)	**137**
15.	***Bidens Pilosa***	Blackjack	Diuretic, NO pathway enhancement, Ca^{2+} channel inhibition	Leaf	Polyacetylenes, rutin, caffeic acid	**138**
16.	***Andrographis paniculata***	Kalmegh	ACE inhibition, Ca^{2+} & β-blockade, ↑NO	Leaf/Aerial Parts	Andrographolide, neoandrographolide	**139**
17.	***Terminalia arjuna***	Arjuna	Vasorelaxation, antioxidant, cardiotonic	Bark	Arjunolic acid, arjunosides, tannins	**140**
18.	***Camellia sinensis***	Green Tea	Antioxidant, vasorelaxant(polyphenols), ACE inhibition	Leaf	EGCG (epigallocatechin gallate), catechins, theaflavins	**141**

19.	***Ocimum sanctum***	Holy basil	Diuretic, antioxidant, vasodilatory flavonoids	Leaf	Eugenol, rosmarinic acid, ursolic acid	**142**
20.	***Glycyrrhiza glabra***	Licorice	Mineralocorticoid effect, though use limited due to ↑BP risk	Root	Glycyrrhizin, liquiritigenin *(note: ↑BP risk)*	**143**
21.	***Cinnamomum zeylanicum***	Cinnamon	Insulin sensitization, vasodilation, antioxidant	Bark	Cinnamaldehyde, procyanidins	**144**
22.	***Withania Somnifera***	Ashwagandha	↓Cortisol, antioxidant, ↑NO	Root	Withanolides, sitoindosides	**145**
23.	***Valeriana officinalis***	Valerian	CNS depressant, ↓SNS, sedative	Root	Valerenic acid, flavonoids	**146**
24.	***Crocus sativus***	Saffron	Ca^{2+} channel blocker, antioxidant	Stigma	Crocin, safranal, crocetin	**147**
25.	***Phyllanthus amarus***	Bhumi amla	Antioxidant, ACE inhibition	Whole Plant	Phyllanthin, hypophyllanthin, ellagic acid	**148**
26.	***Justicia gendarussa***	Willow-leaved justicia	Vasodilation, Ca^{2+} blockade	Leaf	Gendarusin A, flavonoids	**149**
27.	***Tribulus terrestris***	Gokshura	Diuretic, vasorelaxant saponins	Fruit	Protodioscin, saponins	**150**
28.	***Eclipta alba***	Bhringraj	Vasodilator, NO activation	Whole plant	Wedelolactone, ecliptine	**151**

29.	***Vitex negundo***	Nirgundi	Vasodilator, anti-inflammatory	Leaf	Flavonoids (luteolin, casticin), iridoids	**152**
30.	***Barleria prionitis***	Vajradanti	Diuretic, vasorelaxant	Leaf	Barlerin, iridoid glycosides	**153**
31.	***Azadirachta indica***	Neem	ACE inhibition, antioxidant, vasodilation	Leaf	Nimbin, nimbolide, quercetin	**154**
32.	***Piper betle***	Betel leaf	Vasorelaxation, calcium antagonism	Leaf	Hydroxychavicol, eugenol	**155**
33.	***Leea indica***	Bandicoot berry	Ca^{2+} channel blocker, anti-inflammatory	Leaf	Flavonoids, phenolic acids	**156**
34.	***Centella asiatica***	Gotu Kola	NO-mediated vasodilation, diuretic	Laef	Asiaticoside, madecassoside	**157**
35.	***Sida cordifolia***	Bala	Adrenergic modulation, mild hypotensive	Leaf	Ephedrine, vasicinol (low doses hypotensive)	**158**
36.	***Aegle marmelos***	Bael	Antioxidant, vasodilation via polyphenols	Leaf	Marmelosin, aegeline, flavonoids	**159**
37.	***Cissampelos pareira***	velvetleaf	ACE inhibition, diuretic, antioxidant	Root	Cissampeline, hayatin (alkaloids)	**160**
38.	***Solanum nigrum***	Black nightshade	Diuretic, β-blocking potential	Leaf	Solamargine, solanine, flavonoids	**161**

39.	***Cassia occidentalis***	Coffee senna	Ca^{2+} channel blockade, diuretic	Leaf	Emodin, chrysophanol, anthraquinones	**162**
40.	***Mentha piperita***	Pepper mint	Vasodilation, NO modulation	Leaf	Menthol, rosmarinic acid	**163**
41.	***Tamarindus indica***	Tamarind	ACE inhibition, diuretic, antioxidant	Fruit pulp	Procyanidins, tartaric acid, catechins	**164**
42.	***Rosmarinus officinalis***	Rosemary	Vasodilation, ACE inhibition, Ca^{2+} blockade	Leaf	Rosmarinic acid, carnosic acid, ursolic acid	**165**
43.	***Mangifera indica***	Mango	Polyphenol-mediated vasodilation	Leaf/fruit	Mangiferin, gallic acid, quercetin	**166**
44.	***Curcuma longa***	Turmeric	Antioxidant, NO modulation, anti-inflammatory	Rhizome	Curcumin, demethoxycurcumin	**167**
45.	***Avena sativa***	Oats	Diuretic, endothelial function improvement	Grain	Avenanthramides, β-glucan	**168**
46	***Olea europaea***	Olive leaf	ACE inhibition, vasodilation, antioxidant	Leaf	Oleuropein, hydroxytyrosol, verbascoside	**169**
47	***Orthosiphon stamineus (syn. O. aristatus)***	Java tea	Diuretic, RAAS modulation, antioxidant	Aerial	Rosmarinic acid, sinensetin, eupatorin	**170**
48	***Apocynum venetum***	Luobuma	β-blocker–like, Ca^{2+} antagonism,	Leaf	Flavonoids (hyperoside), quercetin glycosides	**170**

			anxiolytic (↓SNS)			
49	***Eucommia ulmoides***	Du-zhong	ACE inhibition, NO↑, vasodilation	Bark/Leaf	Geniposidic acid, pinoresinol diglucoside	**171**
50	***Zingiber officinale***	Ginger	Ca^{2+} channel blockade, ACE↓, vasodilation	Rhizome	6-Gingerol, shogaols	**170**
51	***Allium cepa***	Onion	ACE↓, vasodilation, antioxidant	Bulb	Quercetin, sulfur compounds	**170**
52	***Elettaria cardamomum***	Green Cardamom	Diuretic, vasodilation, antioxidant	Seed	1,8-Cineole, terpinyl acetate, flavonoids	**172, 173**
53	***Beta vulgaris***	Beetroot	Dietary nitrate → NO↑ vasodilation	Root/juice	Nitrate, betalains	**174, 175**
54	***Vitis vinifera (seed)***	Grape seed	Endothelial function, ACE↓, antioxidant	Seed Extract	Procyanidins (OPCs), catechins	**176, 177**
55	***Linum usitatissimum***	Flaxseed	NO↑, anti-inflammatory, RAAS modulation	Seed	α-Linolenic acid, lignans (SDG)	**178, 179**
56	***Theobroma cacao***	Cocoa	NO↑ (endothelial), ACE↓	Bean	Flavanols (epicatechin, catechin)	**180, 181**
57	***Punica granatum***	Pomegranate	ACE↓, antioxidant, endothelial protection	Juice/Peel	Punicalagins, ellagic acid	**182, 183**

58	***Vaccinium myrtillus / spp.***	Bilberry /Blueberry	NO↑, antioxidant	Berry	Anthocyanins (delphinidin/cyanidin glycosides)	**170**
59	***Glycine max***	Soybean	Endothelial/estrogenic, RAAS modulation	Seed	Isoflavones (genistein, daidzein)	**170**
60	***Sesamum indicum***	Sesame	Antioxidant, NO/endothelial effects	Seed/Oil	Sesamin, sesamolin, lignans	**170**
61	***Coriandrum sativum***	Coriander	Ca^{2+} blockade, diuretic	Seed/leaf	Linalool, flavonoids	**170**
62	***Cuminum cyminum***	Cumin	Vasodilation, antioxidant	Seed	Cuminaldehyde, terpenes	**170**
63	***Trigonella foenum-graecum***	Fenugreek	Insulin sensitization, diuretic, NO↑	Seed	Saponins (diosgenin), 4-hydroxyisoleucine	**170**
64	***Passiflora incarnata***	Passionflower	Anxiolytic (↓SNS), vasodilation	Aerial Parts	Flavonoids (vitexin), harmala alkaloids (trace)	**170**
65	***Achillea millefolium***	Yarrow	Vasodilation, diuretic	Aerial Parts	Flavonoids, azulenes	**170**
66	***Tilia cordata/platyphyllos***	Linden	Vasodilation, mild diuretic, anxiolytic	Flower/bract	Flavonoids (tiliroside), volatile oils	**170**
67	***Leonurus cardiaca***	Motherwort	Negative chronotropy, vasodilation	Aerial parts	Leonurine, stachydrine	**170**
68	***Urtica dioica***	Stinging nettle	Diuretic, RAAS modulation	Leaf/root	Flavonoids, lignans, sterols	**170**
69	***Cynara scolymus***	Artichoke leaf	Endothelial protection, diuretic	Leaf	Cynarin, chlorogenic acid	**170**

70	***Petroselinum crispum***	Parsley	Diuretic, vasodilation	Leaf/seed	Apiol, myristicin, flavonoids	**170**
71	***Berberis vulgaris***	Barberry	ACE↓, vasodilation	Root/Bark	Berberine, berbamine	**170**
72	***Berberis aristata***	Tree Turmeric	ACE↓, vasodilation	Root/Bark	Berberine, palmatine	**170**
73	***Salvia officinalis***	Sage	ACE↓, antioxidant	Leaf	Rosmarinic acid, carnosol	**170**
74	***Melissa officinalis***	Lemon Balm	Anxiolytic, vasodilation	Leaf	Rosmarinic acid, flavonoids	**170**
75	***Morus alba***	White Mulberry	ACE↓, vasodilation	Leaf	DNJ, quercetin, chlorogenic acid	**170**
76	***Nelumbo nucifera***	Lotus leaf	Diuretic, lipids↓, vasodilation	Leaf/embryo	Nuciferine, flavonoids	**170**
77	***Stephania tetrandra***	Fangji	Ca^{2+} channel blockade	Root	Tetrandrine, fangchinoline	**170**
78	***Panax notoginseng***	Notoginseng	Endothelial NO↑, anti-inflammatory	Root	Notoginsenosides R1, Rg1, Rb1	**184**
79	***Vernonia amygdalina***	Bitter Leaf	Vasodilation, antioxidant	leaf	Vernodalin, flavonoids	**170**
80	***Uncaria tomentosa***	Cat's claw (Peru)	Vasodilation, anti-inflammatory	Bark	Oxindole alkaloids	**170**
81	***Hibiscus rosa-sinensis***	Chinese hibiscus	Vasodilation, diuretic	Flower/leaf	Anthocyanins, flavonoids	**170**

82	***Houttuynia cordata***	Fish Mint	Diuretic, endothelial effects	Aerial parts	Houttuynoside, quercitrin	**170**
83	***Bacopa monnieri***	Brahmi	Anxiolytic (↓SNS), NO↑	Aerial parts	Bacosides	**170**
84	***Tinospora cordifolia***	Guduchi	Endothelial/anti-inflammatory	Stem	Tinosporaside, berberine-like alkaloids	**170**
85	***Persea americana***	Avocado	Vasodilation, antioxidant	Leaf/seed	Flavonoids, phenolics	**170**
86	***Satureja khuzestanica/hortensis***	Savory	ACE↓, antioxidant	Aerial parts	Carvacrol, thymol, rosmarinic acid	**170**
87	***Carica papaya***	Papaya	Ca^{2+} blockade (preclinical), antioxidant	Leaf/Seed	Benzyl isothiocyanate, flavonoids	**170**
88	***Eleutherococcus senticosus*** **(syn.** ***Acanthopanax senticosus*****)**	Siberian ginseng	Endothelial/NO modulation, adaptogenic (↓SNS)	Root	Eleutherosides	**170**
89	***Nardostachys jatamansi***	Spikenard	Sedative (↓SNS), vasodilation	Rhizome	Jatamansone (valeranone)	**170**
90	***Cydonia oblonga***	Quince	Vasodilation, antioxidant	Leaf/ 95fruit	Quercetin, chlorogenic acid	**170**
91	***Angelica sinensis***	Dong-quai	Vasodilation, anti-platelet	Root	Ferulic acid, ligustilide	**184**
92	***Plantago major/asiatica***	Plantain	Diuretic, anti-inflammatory	Leaf/ Seed	Aucubin, acteoside	**170**

93	***Alisma orientale***	Ze-xie	Diuretic, RAAS modulation	Rhizome	Alisol A/B (triterpenes)	**184**
94	***Aspalathus linearis***	Rooibos	ACE↓, antioxidant	Leaf	Aspalathin, nothofagin	**170**
95	***Scutellaria baicalensis***	Chinese skullcap	ACE↓, vasodilation	Root	Baicalin, baicalein	**184**
96	***Portulaca oleracea***	Purslane	NO↑, K^+ channel activation, diuretic	Aerial parts	Omega-3s, flavonoids	**170**
97	***Ammi visnaga***	Khella	Ca^{2+} channel blockade, vasodilation	Fruit	Khellin, visnagin	**170**
98	***Gynostemma pentaphyllum***	Jiaogulan	AMPK/NO/endothelial effects	Leaf	Gypenosides (saponins)	**185**
99	***Nigella arvensis***	Wild black cumin	Antioxidant, vasodilation, Ca^{2+} channel modulation	Seed	Thymoquinone derivatives, alkaloids	**186**
100	***Erythrina variegata***	Indian coral tree	Ca^{2+} channel blockade, CNS depressant (↓SNS activity)	Baak/ Leaf	Isoflavonoids (erycristagallin), alkaloids	**187**

Table No. 2 Other Effective medicinal plants on Hypertension:

Abbreviations:

ACE – Angiotensin-Converting Enzyme

Ang II – Angiotensin II

AT1R – Angiotensin II Type 1 Receptor

BBB – Blood–Brain Barrier

CKD – Chronic Kidney Disease

CNS – Central Nervous System

CoQ10 – Coenzyme Q10

CSE – Cystathionine γ-Lyase

ED – Erectile Dysfunction

EGCG – Epigallocatechin-3-Gallate

GDLM – Ginkgo Diterpene Lactone Meglumine

GFR – Glomerular Filtration Rate

HPG Axis – Hypothalamic–Pituitary–Gonadal Axis

H_2S – Hydrogen Sulphide

IL – Interleukin

LDL – Low-Density Lipoprotein

LVH – Left Ventricular Hypertrophy

MAPK – Mitogen-Activated Protein Kinase

NO – Nitric Oxide

NOS – Nitric Oxide Synthase

PAF – Platelet-Activating Factor

PDE5 – Phosphodiesterase Type 5

PDGF – Platelet-Derived Growth Factor

PKG – Protein Kinase G

RAAS – Renin–Angiotensin–Aldosterone System

ROS – Reactive Oxygen Species

SNS – Sympathetic Nervous System

TGF-β1 – Transforming Growth Factor Beta 1

TNF-α – Tumour Necrosis Factor Alpha

VSMC – Vascular Smooth Muscle Cell

CONCLUSION

One of the most difficult worldwide health problems is still hypertension, which has a major role in neurological, renal, and cardiovascular problems. While traditional antihypertensive medications continue to be the mainstay of treatment, their drawbacks in terms of adverse effects, cost, and patient compliance underscore the need for safer and more long-lasting substitutes. The renin-angiotensin-aldosterone system modulation, calcium channel blockade, nitric oxide enhancement, and antioxidant defence are some of the mechanisms by which herbal medicines, enhanced with a variety of phytoconstituents like flavonoids, alkaloids, saponins, and polyphenols, offer promising antihypertensive effects.

Terminalia arjuna, Crataegus monogyna, Ginkgo biloba, Withania somnifera, Allium sativum, and Camellia sinensis are important medicinal plants that show promise in managing hypertension and reducing its secondary complications, like cardiac hypertrophy, renal impairment, cerebrovascular injury, vascular dysfunction, and erectile disorders.

To fully realize the benefits of these herbal compounds, future research should focus on thorough clinical validation, standardized formulations, and long-term safety monitoring. By acting through a variety of pathways, their diverse phytoconstituents provide a comprehensive therapeutic strategy. By combining these ancient therapies with modern biomedical research, they can be used as supportive or complementary interventions.

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HOW TO CITE: Bhoomika Swarnkar, Abhishek Nand, Lokprabha Hirwani, Harkesh Dadsena, Pushpendra Kumar, Chhavi Rahangdale, Yashika Israni, Helina Tandon, Umakant Sahu, Vishal Jain*, Narendra Kumar, A Review On The Role Of Herbal Medicine In Modulating Hypertension-Related Complications: Mechanistic Insights, Int. J. Sci. R. Tech., 2026, 3 (6), 457-490. https://doi.org/10.5281/zenodo.20567000