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HERBAL REMEDIES FOR TREATMENT OF HYPERTENSION

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ABSTRACT

Hypertension is a common problem facing many peoples today. Although billions of dollars are spent annually for the treatment and detection of cardiovascular disease, current conventional treatments have done little to reduce the number of patients with hypertension. Alternative medicine offers an effective way to decrease the rising number of people with high blood pressure. Research has found a variety of alternative therapies to be successful in reducing high blood pressure including diet, exercise, stress, management, supplements and herbs. Every year, more and more studies are being performed on herbal remedies for high blood pressure. There are many herbal drugs like Punarnava, Barberry, Rouwolfia, Garlic, Ginger, Ginseng and Arjuna which can safely use for the treatment of hypertension. This review highlight the herbs proved scientifically for the treatment of hypertension.

INTRODUCTION: Natural products from plants, animals and minerals have been the basis of the treatment of human disease. Today estimate that about 80 % of people in developing countries still relays on traditional medicine based largely on species of plants and animals for their primary health care. Herbal medicines are currently in demand and their popularity is increasing day by day. About 500 plants with medicinal use are mentioned in ancient literature and around 800 plants have been used in indigenous systems of medicine. India is a vast repository of medicinal plants that are used in traditional medical treatments [1]. There has been an increase in demand for the Phytopharmaceutical products of Ayurveda in Western countries, because of the fact that the allopathic drugs have more side effects. Many pharmaceutical companies are now concentrating on manufacturing of herbal and Phytopharmaceutical products [2]. In India, around 20,000 medicinal plants have been recorded. Chemical principles from natural sources have become much simpler and have contributed significantly to the development of new drugs from medicinal plants **[3-4].** There are many herbal drugs which are used for the treatment of hypertension some of them are listed in the following table 1:

Chemical Classification of Antihypertensive Herbs:

- Alkaloids- Rauwolfia, Papaver, Avis tolochladebis, Loptis, jayonica, Withenia, Golden seal, Bhringaraj
- Terpenoids- Jatamansi, Inula helenicum. Arnica montana, Coleus, Jalbrahmi, Black cohosh forskohlii, Sania syriaca
- Steroid- Veratrum, Holarrhena pubescens, satavari, bhringraj ,Clerodendroon trichotomum
- Flavanoids -Devis scandens, Mitragyna ciliate, Yaroow, Olive leaf, Hawthorn, Arjuna, Ginkgo, Vitis vinifera, Alpinia
- Volatile Oil - Black cumin seed, Ginger
- Sterols - Cat's claw
- Tannin- African mistletoe, Arjuna

Pharmacological Classification of Antihypertensive Herbs:

- Centrally Acting- Withania (CNS acting); Rauwolfia (catcholamine depeleters); Hypericum (dopamine and norepinephrine reuptake inhibitors); Black cumin seed (CNS acting and antioxidant)
- Vasodialators- Garlic (via hyperpolarisation through H_2S); Ginseng (direct smooth muscle relaxant); Hawthorn, Vitis, Yarrow, Olive leaf (endothelium dependent vasodilation); Forskolin (Adenyl cyclase pathway), Lotus
- Diuretic –Punarnava
- Ace Inhibitors- Garlic (by allicin)
- Cholesterol Synthesis Inhibitors- Cat's claw, African mistletoe

TABLE 1: LIST OF PLANT USED AS ANTIHYPERTENSIVE AGENTS

COMMON NAME	BOTANICAL NAME	FAMILY	PART USED	CHEMICAL CONSTITUENT	OTHER USES
Snakeroot	*Rouvolfia serpentina*	Apocynaceae	root	ajmaline, rescinnamine, serpentinine, sarpagine, deserpidine, and chandrine	Also has been used for anxiety and psychosis , Cushing's Disease,dyskinesia
Garlic	*Alium sativum*	Liliacae	Bulbils	sulfur containing compounds alliin, ajoene, diallylsulfide, dithiin, S-allylcysteine,	Antibacterial,insecticidal,used in digestive disorder,causes lowering of cholesterol level
Ginseng	*Panex ginseng*	Araliaceae	root	ginsenoside	Adeptogen, pherodisiac,stimulant
St. John's wort	*Hypericum perforatum*	Hyperi -caceae.	aerial parts	hypericin and hyperforin	Antidepressant, sedative, relaxing nervine, anti-inflammatory. Used in anxiety, stress, depression, menopausal nervousness, menstrual cramps, neuralgia and rheumatism
African mistletoe	*Lorentus ben-wensis*	Lorentheacae	leaves	Tender shoots—contain 10% tannins	Bark—astringent and narcotic.
Scotch broom	*Cystisus scoparius*	Papilionaceae	Seeds	quinolizidine alkaloids; main alkaloids are (−)-sparteine, lupanine, ammodendrine and various derivatives; biogenic amines, including tryramine, epinine, dopamine; isoflavone glycosides including genistein, scoparin; flavonoids; essential oil; caffeic acid and p-coumaric acids; tannins. Seeds contain lectins	Diuretic and cathartic. Emetic in large doses The herb is used chiefly in the form of sulphate in tachycardia and functional palpitation
Black cohosh	*Cimicifuga racemosa*	Renanculaceae	Root	triterpene glycosides- cycloartanes	Osteoporosis, gynacological disorders,kidney problems and in premenstrual tension.
Cat's claw	*Uncaria tomantosa*	Rubeacae	Leaves	Rhynchophylline, hirsutine, and mitraphylline. Rhynchophylline . Three sterols — beta sitosterol (80%), stigmasterol, and campesterol—	Analgesic,Antibacterial,Anticancerous,Anticoagulant,Antidepressant, Antidysenteric,,anti-inflammatory,antileukemic,antimutagenic
Lotus	*Nelumbo nucifera*	Nelumbo-naceae	Arial parts	alkaloids including liensinine, isoliensinine, referine, lotusine, methylcorypalline, and demethylcoclaurine. Among them, referine has been shown to have a vasodilating effect and liensinine has antihypertensive and antiarrhymic abilities.	Tranquilizer, cardiotonic and in kidney and skin diseases.
Ginger	*Gingiber officinalis*	Zingiberaceae	rhizomes	Volatile oil ; 3sesquiterpines:- bisaboline, zingiberene and zingiberol	Flavour, as a condiment, aromatic, carminative
Ginkgo	*Ginkgo biloba*	Ginkgoaceae	Seed, leaf.	Phenolic acids; ginkgolic acid, hydroginkgolic acid, ginkgolides Flavonoids. Biflavonoids; sciadopitysin, ginkgetin, bilobetin .	Asthma, sputum and cough, leucorrhoea.
Golden seal	*Hydrastis canadensis*	Ranuculaceae	Rhizomes and roots	3 alkaloid hydrastine, berberine,canadine	As an astringent in inflammation of mucous membranes
Hawthorn	*Crataegus laevigata/ Crataegus oxycantha*	Rosaceae	Dried flowers,frFruits, leaves	flavonoids, catechins, triterpene saponins, amines, and oligomeric proanthocyanidins (OPCs)	In angina pectoris , hypertension

COMMON NAME	BOTANICAL NAME	FAMILY	PART USED	CHEMICAL CONSTITUENT	OTHER USES
	and monogyna)		and twigs		
Mistletoe	*Viscum album*	Loranthaceae	leaves	Toxic protines,designated phoratoxin,viscotoxin	cardiotonic, vasodilatory, antispasmodic, tumor-inhibiting, and thymus stimulating
Stinging nettie	*Urtica dioica*	*Urticaceae.*	leaves, rootlets, rhizomes and cortex	acetylcholine, histamine and 5-hydroxytryptamine (5-HT). Acetylcholine is present in the leaves, rootlets, rhizomes and cortex in the ascending order of concentration.	Diuretic, astringent, antihaemorrhagic; eliminates uric acid from the body, detoxifies the blood. Externally, astringent and haemostatic. Used internally for the treatment of nephritis, haemoptysis and other haemorrhages.
Jalbrahmi	*Centella ascitica*	Apiaceae	Whole plant	pentacyclic triterpenes derivatives-madecassosides and asiaticosides.	Used in insomnia,anxity,scleroderma and vericosa vein disease
Black Cumin Seeds	*Nigella sativa*	Ranunculaceae	seed	thymoquinone, dithymoquinone, thymohydroquinone, thymol, carvacrol, tanethole and 4-terpineol.	Hypotensive action - due to its volatile oils Diuretic agent
Arjuna	*Termenalia arjuna*	Combretaceae.	bark	tannins, triterpenoid saponins, flavonoids, gallic acid, ellagic acid, OPCs, phytosterols, calcium, magnesium, zinc, and copper.	Bark—used as a cardioprotective and cardiotonic in angina and poor coronary circulation; as a diuretic in cirrhosis of liver and externally in skin diseases, herpes and leukoderma.
Ashwagandha	*Withania somnifera*	Solanaceae.	Whole plant	Alkaloids including withanine, withananine, withananinine, pseudo-withanine, somnine, somniferine, somniferinine. The leaves of Indian chemotype contain withanolides, including withaferin A.	Root—used as an anti-inflammatory drug for swellings, tumours, scrofula and rheumatism; and as a sedative and hypnotic in anxiety neurosis. Leaf— anti-inflammatory, hepatoprotective, Antibacterial. Fruits and seeds—diuretic
Bhingaraj	*Eclipta prostrata /Eclipta alba*	Asteraceae	leaves	wedelolactone and dimethyl wedelolactone, ascorbic acid. Alkaloid, ecliptine. thiophene derivatives mono-, di- and trithiophene acetylenes together with a-terthenyl in ß-sitosterol. The roots are very rich in thiophene acetylenes. active constituent, culumbin, exhibited remarkable antihypertensive activity	Rheumatism,hair fall, fever, hepatitis, edema possessing potent antihepatotoxic properties
Punarnava (Hogweed)	*Boerhavia diffusa,*	Nyctaginaceae	Whole plant	Punarnava contains b-Sitosterol, a-2-sitosterol, palmitic acid, ester of b-sitosterol, tetracosanoic, hexacosonoic, stearic, arachidic acid, urosilic acid, Hentriacontane, b-Ecdysone, triacontanol. Punarnavoside (antifibrinolytic glycoside, 0.03-0.05%); oeravinones, Lignans (liridodendrin, boeravine & hypoxanthine deriv .) ; Flavones, Sterols; Root contains Alanine, Arachidic acid, Aspartic acid, Behenic acid, Boerhavic acid, Boerhavone, Pot.nitrate (6.5 %), Oxalic acid, Punarnavine 1 and 2 etc.	Diuretic, bitter, cooling, astringent to bowels, useful in leucorrhoea, inflammations, asthma etc.

COMMON NAME	BOTANICAL NAME	FAMILY	PART USED	CHEMICAL CONSTITUENT	OTHER USES
Satawari	*Asperagus recemosus*	Asparagaceae.	tuberous dried root	saponins—shatavarins I–IV. Shatavarin IV is a glycoside of sarsasapogenin. dried root yields sitosterol; (dihydroxy-O hydroxyisobutyl) benzaldehyde and undecanyl cetanoate, and contains a large amount of saccharine matter, mucilage and minerals	Used as a galactagogue and for disorders of female genitourinary tract; as a styptic and ulcer-healing agent; as an intestinal disinfectant and astringent in diarrhoea; as a nervine tonic, and in sexual debility for permatogenesis.
Alpinia	*Alpinia zerumbet*	Zingibaraeceae	Whole plant	flavonoids [(+)-catechin; (-)-epicatechin; rutin; quercetin; kaempferol 3-O-rutinosideo; kaempferol 3-O-glucoronide; kaempferol] and kava pyrones (dihydro-5,6-dehydrokawain and 5,6-dehydrokawain)	diuretic and antiulcerogenic
Ma Huang (Herba Ephedra)	*Ephedra sinica, Ephedra intermedia or Ephedra equisetina.*	Ephedraceae	Stem	Contain the phenylproamine alkaloids, l-ephedrine, d-pseudoephdrine. E. sinica contains 55-78% ephedrine and 12-23% pseudoephedrine.	In bronchospasm, asthma, and bronchitis and in allergic Rhinitis.
Chinese Angelica	*Angelicae Gigantis*	Apiaceae	Dried root	Root contains about 0.2-0.4% of essential oil , ferulic acid, ligusticide, angelicide, brefeldin A, butylphthalide, nicotinic acid, succinic acid and several coumarin constituents.	Gynaecological disorders and infertility.In rheumatism, ulcers, anemia, and constipation; and in the prevention and treatment of allergic attacks.
Forskolin	*Coleus forskohlii*	Lamiaceae.	Root	ditermene coleonol,	Antispasmodic
Hibiscus	*Hibiscus sabdariffa*	Malvaceae	calyxes	Oxalic,malic,citric,tarteric andhibiscic acid	Aromatic and mild laxative action
Raisins	*Vitis vinifera*	vitaceae	Seed extract	Grape skin produces endothelium dependent aorta relaxation possibly by its flovonoids (quercetin)	Antioxidant,hypolipidemic,uterine relaxent
Olive leaf	*Olea africana and Olea europea*	Oleacae	Leaf	Oleuropein, a complex structure of flavonoids, esters, and multiple iridoid glycosides,	Sore throat, kidney problems and backache. Leaf infusions are lotion to treat eye infections or a gargle to relieve sore throat, internally as a remedy for colic or urinary tract infections; powdered leaf is used as styptic.
Yarrow	*Achillea wilhelmsii*	Asteraceae	Dried arial parts with flower.	flavonoids and sesquiterpene lactone	Antihyperlipidemic diaphoretic and antipyretic, intestinal colic , diuretic and urinary antiseptic for urinary retention or cystitis, vulnerary and topical anti-inflammatory

Specific Botanicals for treatment of Hypertension:

Arjuna bark (*Terminalia arjuna*): *Terminalia arjuna* is a deciduous tree found throughout India. Its bark has been used in Ayurvedic medicine for over three centuries. Terminalia's active constituents include tannins, triterpenoid saponins, flavonoids, gallic acid, ellagic acid, OPCs, phytosterols, calcium, magnesium, zinc, and copper [5]. Several studies have elucidated Terminalia's effects on various

cardiac disorders including congestive heart failure, coronary artery disease, and hypertension. A study on its effects on stable and unstable angina patients found it effective for those with stable angina, with a 50-percent reduction in angina episodes and significant decrease in systolic blood pressure [6].

In a double-blind crossover study, 12 subjects with refractory chronic congestive heart failure (idiopathic dilated cardiomyopathy (n=10); previous myocardial infarction (n=1), or peripartum cardiomyopathy (n=1)), received *Terminalia arjuna*, at a dose of 500 mg every eight hours, or placebo for two weeks, each treatment protocol separated by a two-week washout period, as an adjuvant to conventional therapy. Clinical, laboratory, and echocardiographic evaluations were carried out at baseline and at the end of therapy. *Terminalia*, compared to placebo, was associated with improvement in symptoms and signs of heart failure, decrease in echo-left ventricular end diastolic and end systolic volume indices, increase in left ventricular stroke volume index, and increase in left ventricular ejection fractions [7]. A study with similar dosing on primarily post-myocardial infarction angina patients found improvements in cardiac function. Prolonged use resulted in no adverse side effects or signs of renal, hepatic, or hematological abnormalities [8].

It has been widely used in Ayurvedic system of medicine for cardiac disorders since ancient times [9, 10]. Extensive reviews on various aspects of *T. arjuna* have been published [11, 12]. Both experimental and clinical studies showed the beneficial effects of the bark in congestive heart failure and in ischemic heart disease and other cardiovascular complications [13]. The aqueous extract of *T. arjuna* showed contraction followed by relaxation on isolated rat thoracic aorta [14]. Results from our laboratory demonstrated that 70% alcoholic extract of *T. arjuna* reduced the platelet count on chronic treatment to dogs. Singh et al. reported that aqueous solution of 70% alcoholic bark extract of *T. arjuna* produced dose-dependent decrease in heart rate and blood pressure in dogs, though the mechanism was not determined [15]. In the present investigation, a systematic study was performed to find the probable mechanism of hypotension produced by 70% alcoholic extract of *T. arjuna* in thiopental anaesthetized dogs.

The hypotension produced by 6 mg/kg body weight dose of the extract was not blocked by atropine which could block the response of selected dose of acetylcholine indicating that the muscarinic mechanism was not involved. Studies with mepyramine maleate indicate that histaminergic mechanism was also not involved in the hypotension produced by the extract. Studies with propranolol which blocked the hypotensive response of the extract indicated that it may contain compounds having adrenergic ß-receptor agonist action. Even though propranolol is a non-specific ß-blocker, it is clear that the compounds present in the extract might be adrenergic $ß_2$-agonists, since adrenergic $ß_2$-receptor stimulation produces hypotension. Moreover, with

the limitations of our study, one cannot completely ruled out the possibility that the observed hypotensive responsive could also be due to the effect of *T. arjuna* directly on the heart there by reducing the cardiac load. Earlier, it was reported that aqueous soluble fraction of 70% alcoholic extract (dried) of *T. arjuna* produced dose-dependent hypotension and decrease in heart rate [16] and were attributed to principles of the extract acting centrally. Our studies with 70% alcoholic extract dissolved in propylene glycol indicate the likely presence of compounds acting peripherally through adrenergic $ß_2$-receptor mechanism and/or by direct action on the cardiac muscle. Mallikarjuna and co-workers studied the influence of aqueous extract of *T. arjuna* on isolated rat thoracic aorta and found contraction followed by relaxant effect. It was felt that the vasorelaxant effect of *T. arjuna* extract could contribute to the reported decrease in blood pressure in anaesthetized dogs as observed [17]. The same experiment on isolated vascular smooth muscle lends support for our observation that the hypotension could be of peripheral origin.

However, Mallikarjuna and co-workers indicated that the vasorelaxant effect of the extract was not blocked by propranolol. The possible reason for this variable effect could be due to the difference in the active principles present in different types of extracts used. This indicates that the 70% alcoholic extract might contain compounds to a higher degree whose activity was blocked by propranolol while the activity produced by the constituents of aqueous extract were not blocked by propranolol[18]. Further investigations are needed on the isolates of *Terminalia arjuna* to study their cardiovascular effects in order to explain more in detail of the observed results [19].

Hawthorne (*Crataegus oxycantha and Crataegus monogyna*): Hawthorne has been used traditionally for cardiovascular disorders in many cultures. It contains a number of active constituents including flavonoids, catechins, triterpene saponins, amines, and oligomeric proanthocyanidins (OPCs). Hawthorne has been shown to exert a mild blood pressure lowering effect that can take up to four weeks for maximal results [20]. It is believed that the herb dilates coronary blood vessels [21] .One *in vitro* study on rat aorta found proanthocyanidins extracted from hawthorn relaxed vascular tone via endothelium-dependent nitric oxide-mediated relaxation [22].

Olive Leaf (*Olea africana and Olea europea*): Olive leaf extract is derived from the leaves of the olive tree. The entire leaf extract contains several phytochemicals, including 20-percent oleuropein, a complex structure of flavonoids, esters, and multiple iridoid glycosides, which acts as a vasodilator, lowering blood pressure and preventing angina attacks. Oleuropein is also being recognized as a potent antioxidant [23, 24]. The hypotensive action of olive leaf has been studied for two decades. A clinical study of *Olea europaea* aqueous extract was conducted on two groups of hypertensive patients, 12 patients consulting for the first time, and 18 patients on conventional antihypertensive

treatment. An aqueous extract was given for three months, after 15 days of placebo supplementation. Researchers noted a statistically significant decrease of blood pressure ($p<0.001$) for all patients, without side effects [25].

One of olive leaf's mechanisms of action is vasodilation. In an *in vitro* study a decoction of olive leaf caused relaxation of isolated rat aorta endothelium. The relaxant activity was independent of the integrity of the vascular endothelium. Oleuropeoside was found to be a component responsible for vasodilator activity; however, the researchers felt at least one other principle was either a vasodilator itself or potentiated the relaxant effect of oleuropeoside [26].

European Mistletoe (*Viscum album*): The use of mistletoe in medicine has become popular, not only because of its hypotensive activity, but also because of its anti-cancer properties. Mistletoe is known to possess hypotensive, cardiotonic, vasodilatory, antispasmodic, tumor-inhibiting, and thymus stimulating activity [27]. Its pharmacological effects, including diuretic and hypotensive activity, were studied using an alcohol extract of Japanese and European mistletoe. Both extracts showed blood pressure lowering effects when administered intravenously and orally to cats [28]. Other researchers have reported similar hypotensive effects of mistletoe in experimental animal studies [29].

Yarrow (*Achillea wilhelmsii*): *Achillea wilhelmsii* (Asteraceae) has flavonoids and sesquiterpene lactone constituents, which have been found effective in lowering blood pressure and lipids. A double-blind, placebo-controlled trial examined the antihyperlipidemic and antihypertensive effects of *Achillea*. The researchers randomly selected 120 men and women, aged 40-60 years, and divided them into two groups: (1) moderate hyperlipidemic and (2) hypertensive subjects. Each study group was treated either with an alcohol extract of *Achillea* or placebo at a dose of 15-20 drops twice daily for six months [30]. Blood pressure and serum lipids (total cholesterol, triglycerides, LDL- cholesterol and HDL- cholesterol) were measured at the end of two, four, and six months. A significant decrease was noted in triglycerides after two months, and significant decreases in triglycerides and total- and LDL- cholesterol after four months. Levels of HDL-cholesterol were significantly increased after six months' treatment. A significant decrease was observed in diastolic and systolic blood pressure after two and six months, respectively ($p<0.05$).

Black Cumin Seeds (*Nigella sativa*): *Nigella sativa* (Ranunculaceae) has a long history of use in folk medicine as a diuretic and hypotensive agent. In an animal study, an oral dose of either *Nigella sativa* extract (0.6 mL/kg/day) or furosemide (5 mg/kg/day) significantly increased diuresis by 16 and 30 percent, respectively, after 15 days of treatment. In the same rat study, a comparison between *Nigella sativa* and nifedipine found mean arterial pressure decreased by 22 and 18 percent in the *Nigella sativa* and nifedipine treated rats, respectively [31].

The essential oil of *Nigella sativa* seed has an antioxidant property that

makes it useful in treating cardiovascular disorders. Active constituents of *Nigella sativa* are thymoquinone, dithymoquinone, thymohydroquinone, thymol [32], carvacrol, t- anethole and 4-terpineol. Hypotensive action of Nigella is mainly due to its volatile oils. An animal study found the volatile oil has the potential of being a potent, centrally acting antihypertensive agent. Thin-layer chromatography (TLC) has confirmed Nigella's antioxidant properties [33].

Forskolin (*Coleus forskohlii*): *Coleus forskohlii* has been used in Ayurvedic medicine for many years. In 1974 the Indian Central Drug Research Institute discovered that forskolin, a component of this plant, has hypotensive and antispasmodic action. Forskolin's blood pressure lowering effects appear to be due to relaxation of arterial vascular smooth muscle. In a study with isolated heart tissue, forskolin activated membrane-bound adenylatecyclase and cytoplasmic cAMP-dependent protein kinase. The researchers postulated the positive inotropic effect was via an enhanced calcium uptake by the heart muscle cell. Another constituent from Coleus, ditermene coleonol, has been found to lower blood pressure in both rat and cat models [34].

Indian Snakeroot (*Rauwolfia serpentina*): Rauwolfia is cultivated for the medicinal use of its 30 alkaloids (particularly reserpine found in the root), many used in treating hypertension [35] .Besides reserpine, other alkaloids used in hypertension and other cardiac disorders are ajmaline, rescinnamine, serpentinine, sarpagine, deserpidine, and chandrine. Rauwolfia alkaloids work by controlling nerve impulses along certain pathways that affect heart and blood vessels, lowering blood pressure. Rauwolfia depletes catecholamines and serotonin from nerves in the central nervous system. In a controlled intervention trial, 389 subjects, ages 21-55 years, with diastolic blood pressures 90-115 mm Hg were examined for 7-10 years. Subjects were randomly assigned to either a combination of a diuretic and *Rauwolfia serpentina*, or an identical placebo. Diastolic blood pressure was reduced an average of 10 mm Hg and systolic by 16 mm Hg in the active treatment group, with no change in the placebo group [36].

The Rauwolfia constituent ajmaline not only lowers blood pressure, but also has a potent antiarrhythmic effect. Studies have shown that ajmaline specifically depresses intraventricular conduction, suggesting this would be particularly effective in the treatment of re-entrant ventricular arrhythmias [37].

In one study of 100 patients with essential hypertension, it was determined that serum cadmium levels were 43-percent higher and serum zinc levels 28-percent lower in hypertensives when compared with normotensive controls. When the patients were put on ajmaloon, a preparation from *Rauwolfia serpentina*, blood pressure was lowered significantly. It also appeared to decrease the elevated serum cadmium levels in these individuals [38].

Rauwolfia has been used for anxiety and psychosis because at higher doses it tends to calm a person and slow them down. Several studies have shown

reserpine to be effective in helping people with Cushing's disease. (Cushing's disease is a disorder in which the adrenal gland makes too much cortisone). Tardive dyskinesia, a side of certain antipsychotic drugs, has been treated with reserpine.

Ginseng (*Panax Ginseng*): A very popular plant root grown originally in China and today also in Japan, Korea and North America. Ginseng is commonly used as an adaptogenic agent for fatigue, insomnia, anxiety, depression and immune enhancement. It is also used for increasing resistance to environmental stress and as a general enhancer of well-being [39]. This herb is also used for improving physical and athletic performance, improving cognitive function, concentration and memory. Ginseng has a variety of active ingredients, consisting mainly of ginsenoid saponins.

Ginseng is marketed either as a single herb compound or in combination with other herbs. The single herb compound is available in tablet as well as in alcoholic extracts (known as tinctures) [40].Experiments in dogs showed that intravenous administration of ginseng extract caused an immediate drop in blood pressure. The effect was long lasting suggesting that it might be facilitated by a Calcium channel blocking like effect [41] and interference with calcium mobilization into vascular smooth muscle cells [42]. Rg1, one of the active ingredients in Ginseng can stimulate the production and release of nitric oxide (NO) from endothelial cells. Another ingredient, Ginsenoside Rb1 lowers blood pressure and acts as a CNS depressant. It also interferes with platelet aggregation and coagulation. Interestingly, Ginseng extracts exhibit a peripheral vasoconstricting effect in low doses and peripheral vasodilatation in high doses. However, in cerebral and coronary vessels it exhibits only a vasodilating effect resulting in improvement in cerebral and coronary blood flow [43]. These varying effects can probably be attributed to the many different saponins that present as the active ingredients in this herb. The potential of Ginseng to increase BP should be emphasized as this herb is not suitable for patients with hypertension and may interfere with blood pressure lowering medications. There is some evidence that *Panax ginseng* can inhibit the cytochrome P450 2D6 (CYP2D6) enzyme by approximately 6% [44]. However, contradictory research suggests that *Panax ginseng* might not inhibit CYP2D6 (21). Until more is known, *Panax ginseng* should be used cautiously in patients taking drugs metabolized by these enzymes [45]. Some of these drugs include amitriptyline (Elavil), clozapine (Clozaril), codeine, desipramine (Norpramin), donepezil (Aricept), fentanyl (Duragesic), flecainide(Tambocor), fluoxetine (Prozac), meperidine (Demerol), methadone (Dolophine), metoprolol (Lopressor, Toprol XL).

Ginkgo (*Ginkgo Biloba*): The fruit and leaves of the Ginkgo tree are commonly used orally for dementia, including Alzheimer's, vascular, and mixed dementia. Ginkgo leaf is also used for conditions associated with cerebral vascular insufficiency, especially in the elderly, including memory loss, headache, tinnitus, vertigo, dizziness, concentrating

difficulty [46], mood disturbances and hearing disorders. It is also used orally for ischemic stroke. Ginkgo is also used for cognitive disorders secondary to depression and to improve cognitive behavior and sleep patterns in patients with depression and chronic fatigue syndrome (CFS); eye problems, including mascular degeneration and glaucoma; attention deficit-hyperactivity disorder (ADHD); [47]thrombosis; heart disease; arteriosclerosis and angina pectoris. The major active ingredients in the herb are flavonoids and glycosides. Ginkgo is marketed either as a single herb compound or in combination with other herbs [48].

The single herb compound is available in tablets. The vascular effect of Ginkgo extract is very well established. Considerable clinical as well as experimental evidence suggest that extracts from Ginkgo leaves induce vasodilation and improve vascular blood flow, particularly in the regions of the deep seated medium and small arteries [49]. Overall, ginkgo leaf acts to increase cerebral and peripheral blood flow microcirculation, and reduce vascular permeability [50, 51]. Ginkgo also has a moderate blood pressure lowering effect. Evidence suggests that ginkgo leaf extract seems to increase pancreatic beta-cell function in response to glucose loading and modestly reduce blood pressure [52]. There is conflicting evidence about whether ginkgo induces or inhibits CYP3A4 [53] .Ginkgo does not appear to affect hepatic CYP3A4 [54]. However, it is not known if ginkgo affects intestinal CYP3A4. Preliminary clinical research suggests that taking ginkgo does not significantly affect levels of donepezil, a CYP3A4 substrate. Although the evidence regarding the effect of Ginkgo on cytochrome P450 is not conclusive, it is best that this herb be used cautiously in patients taking drugs metabolized by CYP3A4.

Garlic (*Allium Sativum*): The bulb of garlic is commonly used for a variety of ailments. Garlic is used for hypertension, hyperlipidemia, coronary heart disease, age-related vascular changes and atherosclerosis, earaches, chronic fatigue syndrome (CFS), and menstrual disorders. Garlic is regarded as a potent platelet aggregation inhibitor. Many of the pharmacological effects of garlic are attributed to the allicin, ajoene, and other organosulfur constituents such as S- allyl-L-cysteine. Fresh garlic contains approximately 1% alliin [55].One milligram of alliin is converted to 0.458 mg allicin which is regarded as the major active compound in garlic. Further conversion yields ajoene. The amount of allicin in garlic preparations is dependent upon the method of preparation. Taking low doses of garlic powder orally, 300 mg per day seems to slow the age-related aortic elasticity decrease. Higher doses of 900 mg per day seem to slow development of atherosclerosis in both aortic and femoral arteries when used over a four-year period [56]. Evidence suggests that taking garlic orally can modestly reduce blood pressure by 2% to 7% after 4 weeks of treatment [57].Garlic is thought to reduce blood pressure by causing smooth muscle relaxation and vasodilation by activating production of endothelium-derived relaxation factor [EDRF, nitric oxide. Clinical research suggests garlic oil can

inhibit the activity of CYP2E1 by 39% [58] .Garlic oil should be used cautiously in patients taking drugs metabolized by these enzymes. There is inconsistent information about the effects of garlic on cytochrome P450 3A4 (CYP3A4) isoenzymes [59].Garlic is eaten in Asia, the Middle East, and in many other cultures on a daily basis. It is an ancient home remedy that has been used for many different purposes, including hypertension, and reduces a number of risk factors associated with cardiovascular disease including [60]: (1) reducing total and LDL-cholesterol, (2) increasing HDL-cholesterol, (3) lowering triglycerides and fibrinogen, (4) lowering blood pressure, (5) improved circulation, (6) enhancing fibrinolysis, (7) inhibition of platelet aggregation, and (8) reducing plasma viscosity. The blood pressure effect is thought to be due to an opening of (Ca) ion channels in the membrane of vascular smooth muscle, affecting hyperpolarization, resulting in vasodilation [61].

A garlic preparation containing 1.3-percent allicin at a large dose (2400 mg) was evaluated in an open-label study in nine severely hypertensive patients (diastolic blood pressure 115 mm Hg or greater). Approximately five hours after taking the garlic, the systolic blood pressure fell an average of 7 mm Hg while diastolic BP dropped an average of 16 mm Hg. A significant decrease in diastolic blood pressure lasted from 5-14 hours after the dose and no significant side effects were reported [62].

Ma Huang (*Ephedra sinica/Ephedra intermedia*): The dried herbaceous stem of *Ephedra sinica, Ephedra intermedia* or *Ephedra equisetina* [63] . Small doses of this herb are commonly used In Traditional Chinese medicine for the treatment of asthma. All three Ephedra herbs contain the phenylproamine alkaloids [64] l-ephedrine, d-pseudoephdrine. *E. sinica* contains 55-78% ephedrine and 12-23% pseudoephedrine.However, this herb is available for purchase in a variety of exercise performance enhancing formulas as well as weight loss formulas imported for private non commercial use [65, 66].Ephedrine, having a similar structure to epinephrine, is a well known sympathomimetic agent, acting on both α and β -adrenergic receptors. By its β-adrenergic action, it relaxes bronchial muscles and produces the antiasthmatic action. It produces myocardial stimulation by its α- 1agonist effect [67].Ephedrine also constricts blood vessels by its α-agonistic effect, causing an increase in blood pressure and heart rate and increasing myocardial contractility and cardiac output [68].Use of this herb has been associated with severe adverse reactions such as myocardial infarcts and cerebral accidents. The ability of Ma Hunag to increase BP should be emphasized as this herb may possibly interfere with blood pressure lowering medications [69].

Dang Gui / Dong Quai/ Chinese Angelica (*Angelica sinesis)*: Dang Gui is the dried root of *Angelica sinesis*. [70].Dang Gui is also used to manage hypertension, rheumatism, ulcers, anemia, and constipation; and in the prevention and treatment of allergic attacks. The root of Dang Gui contains about 0.2- 0.4% of essential oil. The major active ingredients include ferulic acid, ligusticide, angelicide,

brefeldin A, butylphthalide, nicotinic acid, and succinic acid. The herb also contains several coumarin constituents [71].Dang Gui is usually marketed as a single herb compound administered as powder extract in capsules. This herb is used extensively by the general population due to its potent effects on gynecological related disorders [72].Dang Gui has a number of known cardiovascular and hematological effects: the essential oil caused an increase in coronary blood flow and decreased myocardial oxygen consumption; it also has mild antiarrhythmic effect [73].

Some of the coumarin constituents of this herb can act as vasodilators and antispasmodics. Osthol appears to inhibit platelet aggregation and smooth muscle contraction and cause hypotension. An Intravenous administration of 1-4 gr/kg of the aqueous extract of the root significantly decreased arterial pressure and reduced the resistance of coronary, cerebral and femoral arteries in dogs thus significantly increasing blood flow [74] .Preliminary research suggests Dang Gui might protect against ischemia-reperfusion injury . Dang Gui has been reported to inhibit platelet aggregation and its concomitant use with coumadin increases the drug's anticoagulant effects, increases INR and may increase the risk of bleeding.

Grapes (*Vitis vinifera)*: Reports have shown the antioxidant, hypotensive, hypolipidemic and vasodilatory effects of grape (*Vitis vinifera*) seed extract. We have recently shown the relaxatory effect of grape leaf extract on rat uterus and reduction of frog heart rate and contractility. [75] .The aim of the present study was to investigate the relaxant effect of *Vitis vinifera* leaf hydroalcoholic extract (VLHE) on rat thoracic aorta contractions induced by phenylephrine and KCl and the role of aorta endothelium on this action. Rat aorta was removed and placed in an organ bath containing Krebs-Henseleit solution and aorta contractions were recorded isometrically.

The results demonstrate that VLHE (0.125-2 mg/ml) reduces the endothelial intact aorta reconstructed by phenylephrine (1 µM) dose-dependently ($P<0.0001$). Extract induced the same response in endothelial denuded aorta, but in a much lesser extent. The IC50 for both groups were 0.45±0.08 and 1.73±0.23 mg/ml, respectively. However, the contractile responses of these groups were similar. VLHE (0.125-2 mg/ml) reduced the contractions induced by KCl (80 mM) dose-dependently ($P<0.0001$). The relaxatory effect of VHLE on KCl–induced contractions was less than those evoked by Phenylephrine. Vasorelaxatory effect of VHLE on intact aorta was attenuated by nitric oxide synthase inhibitor (L-NAME, 100 µM) and gaunyl cyclase inhibitor (methylene blue, 10 µM) significantly, but was unaffected by atropine (1 µM). The results suggest that the greatest vasorelaxant effect of VHLE on rat aorta is endothelium dependent [76].

Punarnava (*Boerhavia diffusa)*: *Boerhavia diffusa*, commonly called hog weed, is known as 'erimmirii' (which literally means water-food). Punarnava is found throughout India and Brazil. It is a very important plant for urinary system. Throughout the tropics, it is used as a

natural remedy for Guinea worms.The roots and leaves are considered to have an expectorant action, to be emetic and diuretic in large doses and are used in the treatment of asthma [77]. The thick roots, softened by boiling are applied as a poultice to draw abscesses and to encourage the extraction of guinea worm.

Punarnava contains b-Sitosterol, a-2-sitosterol, palmitic acid, ester of b-sitosterol, tetracosanoic, hexacosonoic, stearic, arachidic acid, urosilic acid, Hentriacontane, b- Ecdysone, triacontanol [78]. Punarnavoside (antifibrinolytic glycoside, 0.03-0.05%); Boeravinones, Lignans (liridodendrin, boeravine & hypoxanthine deriv .); Flavones, Sterols; Root contains Alanine, Arachidic acid, Aspartic acid, Behenic acid, Boerhavic acid, Boerhavone, Pot. nitrate (6.5%), Oxalic acid, Punarnavine 1 and 2 etc.

Anti-hypertensive Liridodendrin & Hypoxanthine are active antihypertensive agents and the former is Ca channel antagonist. This plant is a powerful Rasayana dravya (longevity enhancer. Punarnava enhances the quality of bodily tissues, including nutrient plasma (Rasa Dhatu), blood (Rakta Dhatu), muscle (Mamsa Dhatu), fat (Meda Dhatu), bone marrow and nerves (Majja Dhatu), and reproductive fluids (Shukra Dhatu). According to Ayurveda, Punarnava is diuretic by increasing renal blood flow [79]. It is bitter, cooling, astringent to bowels, useful in leucorrhoea, inflammations, asthma etc. Each part has a different therapeutic value and must be prepared in its own way for maximum benefits.

Cat´s Claw (*Uncaria tomentosa*): *Uncaria tomentosa* proliferates spontaneously all over the Amazon rainforest, especially in the upper Amazon region of Peru and neighboring countries, and other tropical areas of South and Central America, including Peru, Colombia, Ecuador, Guyana, Trinidad, Venezuela, Suriname, Costa Rica, Guatemala, and Panama. It has also been reported as far North as Belize, and South into Paraguay. There are as many as 60 species related to this plant [80]. Several different phytochemicals found in the water extract of Uncaria tomentosa have demonstrated different actions in the blood and heart.Some alkaloids contained in the extract have demonstrated hypotensive and vasodilating properties. These alkaloids are rhynchophylline, hirsutine, and mitraphylline [81].

Rhynchophylline also has shown to inhibit platelet aggregation and thrombosis. The analyses conducted there show that rhynchophylline has the ability to inhibit the accumulation of platelets and may also prevent and reduce blood clots in blood vessels and relax the blood vessels of endothelial cells, dilate peripheral blood vessels, lower the heart rate, and lower blood cholesterol. Three sterols —beta sitosterol (80%), stigmasterol, and campesterol—have been identified and proven to be mild inhibitors of cholesterol synthesis *in vitro*[80] This also means that could help to prevent atherosclerosis, inhibiting the formation of the atherosclerotic plaque that occurs during the progression of atherosclerosis. Various chemicals in it are known to promote the loss of water from the body,

relax smooth muscles, and widen small blood vessels in the hands and feet. All these effects may help to lower blood pressure. It has also been proposed that the water extract of *Uncaria tomentosa* could help prevent strokes, diseases of the circulatory system, and heart attacks (due to its lowering C-reactive protein level activity).

Bhringraj (*Eclipta Alba/Eclipta prostrate*): The herb contains wedelolactone and dimethyl wedelolactone possessing potent antihepatotoxic properties .The herb is a rich source of ascorbic acid. It also contains an alkaloid, ecliptine. The occurrence of mono-, di- and trithiophene acetylenes together with a-terthenyl in this species is noteworthy. The petroleum ether extract of aerial parts contains a trithienyl aldehyde, ecliptal, besides stigmasterol and ß- sitosterol. The roots are very rich in thiophene acetylenes [82] . *Eclipta* is an effective anti-inflammatory agent. It inhibited the higher levels of histamine due to chronic inflammation upto 58.67 percent. The ethanolic extract of the dried whole plant *E.prostrata* and its active constituent, culumbin, exhibited remarkable antihypertensive activity on anesthetized rats. No significant side effects or toxicities have been found either on histopathology of liver, kidney, spleen, heart or on biochemical parameters like SGOT, SGPT, BUN, etc. Moreover, no appreciable changes have been found in body weight and in specific organ weight during the course of investigation on Long Evans rats [83].

Alpinia (*Alpinia zerumbet*): *Alpinia zerumbet* is a medicinal plant originated from West Asia, is used in the northeast and southeast of Brazil as infusions or decoctions as a diuretic, antihypertensive, and antiulcerogenic. Experiments were undertaken to determine whether a hydroalcoholic extract obtained from leaves of *Alpinia zerumbet* (AZE) induces vasodilation in the mesenteric vascular bed (MVB), and an antihypertensive effect was also assessed in rats with DOCA-salt hypertension. In MVB precontracted with norepinephrine, AZE induces a long-lasting endothelium-dependent vasodilation that is not reduced by indomethacin. [84, 85] Inhibition of NO synthase by N-nitro-L-arginine methyl ester (L-NAME) and guanylyl cyclase by 1H- [1, 2, 3] oxadiazolo [4, 4- a] quinoxalin-1-one (ODQ) reduces the vasodilator effect of AZE.

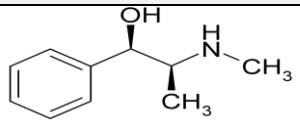
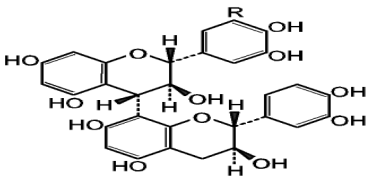
In vessels precontracted with norepinephrine, the vasodilator effect of AZE was not changed by 4-aminopyridine, glibenclamide or by charybdotoxin plus apamin. Concentrations of atropine, pyrilamine, and yohimbine that significantly reduced the vasodilator effect of acetylcholine, histamine, and clonidine, respectively, did not change the vasodilator effect of AZE. HOE 140, which significantly reduced the vasodilator effect of bradykinin, induced a slight but significant reduction on the vasodilator effect of AZE [86.] Chronic oral administration of AZE induced a significant reduction in systolic, mean, and diastolic arterial pressure in rats with DOCA-salt hypertension. Probably the vasodilator effect of AZE is dependent on the activation of the NO- cGMP pathway and independent of activation of ATP-dependent, voltage-dependent, and calcium-dependent K^+ channel.

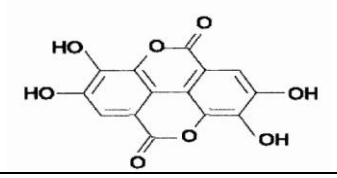
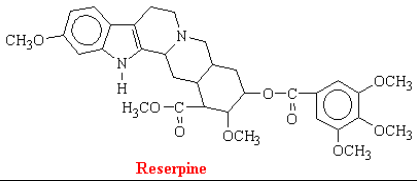
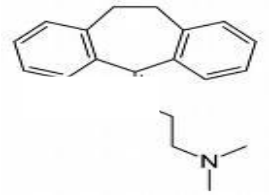
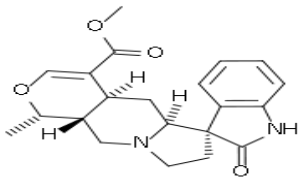
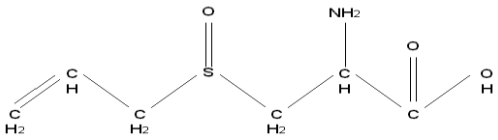
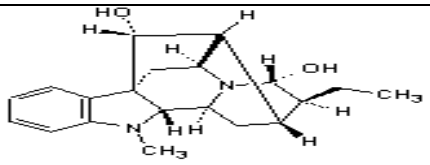
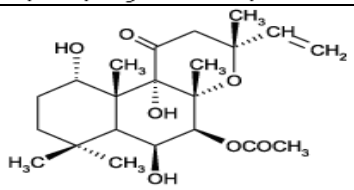
Bradykinin receptors may also participate in the vasodilator effect of AZE. Finally, the vasodilator and antihypertensive effects of AZE demonstrated in the present study provide experimental support for the indication of *Alpinia zerumbet* as an antihypertensive medicinal plant.Biochemical analysis performed has shown that leaves of *Alpinia zerumbet* are rich in flavonoids [(+) - catechin; (-) - epicatechin; rutin; quercetin; kaempferol 3- O- rutinosideo; kaempferol 3-O-glucoronide; kaempferol] and kava pyrones (dihydro-5, 6-dehydrokawain and 5, 6-dehydrokawain). Recently, many experimental data have suggested that polyphenols that occur in many vegetables may participate in the mechanism of beneficial effect of some medicinal plants. It is also demonstrated that in alcohol-free red wine and products obtained from the skin of vinifera grapes, both rich in polyphenols, have vasodilator and antihypertensive effects in experimental animals [87] .

CONCLUSION: Lifestyle changes, including diet, exercise, and stress management, may contribute significantly to lowering of blood pressure. Supplements such as potassium, magnesium, CoQ10, omega-3 fatty acids, amino acids Aarginine and taurine, and vitamins C and E have been effectively used in the treatment of cardiovascular disease, including hypertension. They have proven effective in lowering blood pressure and improving heart functions. Among the most researched and frequently utilized for hypertension are Hawthorne, *Arjuna*, Olive leaf, European mistletoe, Yarrow, Black cumin seeds, Forskolin, Indian snakeroot, and Garlic.

More research is indicated to determine the full potential that alternative medicine has to offer in the management of hypertension. With the increasing numbers of patients suffering from hypertension and conventional medicine failing to effectively control the problem, alternative therapies offer hope.

CHEMICAL CONSTITUENTS AND THEIR STRUCTURE:

Plant	Chemical constituents	structure
Ephedra sinica/Ephedra intermedia	Ephedrine	
Hawthorn	ProcynadinB-3 R=H prodelfinidinB-3 R=OH	 Procyanidin B-3 (R = H) Prodelphinidin B-3 (R = OH)

Terminalia arjuna	Ellagic acid	
Rouwolfia serpentine	Reserpine	 Reserpine
Panax Ginseng	Amitryptylin	
Uncaria tomentosa bark	Mitraphylline	
Alium sativum	Alliin	
Rouwolfia serpentine	Ajmaline	 (17*R*,21*R*)-Ajmalan-17,21-diol
Coleus forskohlii	Forskolin	

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