ISSN: 0975-8232

IJPSR (2010), Vol. 1, Issue 5 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received 13 February, 2010; received in revised form 20 April, 2010; accepted 25 April, 2010

HERBAL REMEDIES FOR TREATMENT OF HYPERTENSION

Manish Agrawal [*1], D. Nandini[2], Vikas Sharma [1] and N. S. Chauhan

Department of Pharmaceutical Sciences, Dr. H. S. Gour University[1], Sagar (MP), India

Sagar Institute of Pharmaceutical Sciences [2], Sagar (MP), India

Keywords:

Antihypertensive activity, herbal remedies, Phytochemical

Correspondence to author:

Nagendra Singh Chauhan

Department of Pharmaceutical Sciences,

Dr. H. S. Gour University, Sagar (MP) India

Email: chauhan.nagendra@gmail.com

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