

Treatment of Hypertension by Using Herbal Drugs

Yogesh Madhukar Patil

Department of Pharmacy,
Shastry Institute of pharmacy, Erandol, Jalgaon

Abstract- Today, a lot of people struggle with hypertension. Despite billions of dollars spent annually on cardiovascular disease treatment and detection, conventional treatments have not reduced the number of hypertensive patients. The rising number of people with high blood pressure can be effectively reduced with alternative medicine. Diet, exercise, stress management, herbs, supplements, and other alternative therapies have all been shown to reduce high blood pressure successfully in research. Herbal treatments for high blood pressure are the subject of increasing numbers of research studies each year. Punarnava, Barberry, Rauwolfia, Garlic, Ginger, Ginseng, and Arjuna are just a few of the herbal medicines that can be safely used to treat hypertension. The herbs that have been scientifically proven to treat high blood pressure are highlighted in this review. The medical term for high blood pressure is hypertension (HTN). In addition to raising the risk of heart disease and stroke, it makes the heart work too hard and contributes to atherosclerosis, or artery hardening. Other conditions like congestive heart failure, kidney disease, and blindness can result from HTN. There are typically a lot of side effects associated with conventional antihypertensives. Due to their better compatibility with the human body and fewer side effects, herbal medicines are utilized for primary health care by approximately 75 to 80 percent of the world's population, primarily in developing nations. Local plants with hypotensive and antihypertensive therapeutic potential have been the subject of extensive research over the past three decades. Some of these medicinal plants' hypotensive and antihypertensive effects have been confirmed, while others have been disproved. However, more scientific research is required to verify the effectiveness and elucidate the safety profile of such herbal remedies for their antihypertensive potential, and ayurvedic knowledge must be combined with modern medicine.

Keywords- Antihypertensive activity, herbal remedies, Phytochemical, medicinal plants

INTRODUCTION:

The treatment of human disease has been based on natural products made from plants, animals, and minerals. It is estimated that approximately 80% of people in developing countries still rely on traditional medicine for their primary health care, which is largely based on species of plants and animals. Natural medications are right now popular and their notoriety is expanding step by step. In ancient literature, approximately 500 medicinal plants are mentioned, and approximately 800 plants have been utilized in indigenous medical practices. The vast repository of medicinal plants that are utilized in traditional medical procedures can be found in India []. Due to the increased risk of adverse effects associated with allopathic medications, Western nations have seen an increase in demand for Ayurvedic phytopharmaceutical products. The production of herbal and phytopharmaceutical products is currently the primary focus of numerous pharmaceutical companies[]. Around 20,000 medicinal plants have been identified in India. Chemical principles derived from natural sources are now much simpler and have significantly aided in the creation of new drugs derived from medicinal plants. []. There are numerous herbal medicines that are used to treat hypertension.

● 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 , Clerodendron trichotomum
- ✓ Flavanoids -Devis scandens, Mitragyna ciliate, Yarow, 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 H₂S); Ginseng (direct smooth muscle relaxant); Hawthorn, Vitis, Yarrow, Olive leaf (endothelium dependent vasodilation); Forskolol (Adenyl cyclase pathway), Lotus
- ✓ Diuretic -Punarnava
- ✓ Ace Inhibitors- Garlic (by allicin)
- ✓ Cholesterol Synthesis Inhibitors- Cat's claw, African mistletoe

Table 1: Conventional medicines used in the treatment of hypertension**Diuretics:**

Loop diuretics: Bumetanide, Ethacrynic acid, Furosemide, Torsemide
 Thiazide diuretics: Epitezide, Hydrochlorothiazide, Chlorothiazide, Bendroflumethiazide
 Thiazide-like diuretics: Indapamide, Chlorthalidone, Metolazone
 Potassium-sparing diuretics: Amiloride, Triamterene, Spironolactone

Adrenergic receptor antagonists:

Beta blockers: Atenolol, Metoprolol, Nadolol, Oxprenolol, Pindolol, Propranolol, Timolo
 Alpha blockers: Doxazosin, Phentolamine, Indoramin, Phenoxybenzamine, Prazosin, Terazosin, Tolazoline
 Mixed Alpha + Beta blockers: Bucindolol, Carvedilol, Labetalol

Adrenergic receptor agonists:

Alpha-2 agonists: Clonidine, Methyldopa, Guanfacine

Calcium channel blockers:

Dihydropyridines: Amlodipine, Felodipine, Isradipine, Lercanidipine, Nicardipine, Nifedipine, Nimodipine, Nitrendipine
 Non-dihydropyridines: Diltiazem, Verapamil

ACE inhibitors: Captopril, Enalapril, Fosinopril, Lisinopril, Perindopril, Quinapril, Ramipril, Trandolapril, Benazepril.

Angiotensin II receptor antagonists: Valsartan, Candesartan, Eprosartan, Irbesartan, Losartan, Olmesartan, Telmisartan.

Aldosterone antagonists: Eplerenone, Spironolactone.

Vasodilators: Sodium nitroprusside, Hydralazine.

Centrally acting adrenergic drugs: Clonidine, Guanabenz, Methyldopa, Moxonidine.

Table no.1

Naturally occurring medicinal plants, herbs having hypotensive/antihypertensive potential:-✓ *Agathosma betulina*

(Family: Rutaceae; Common name: Buchu). It is a South African medicinal plant and has been used by the indigenous people of the area for centuries to treat wider ailments. It is an effective diuretic and anti-inflammatory agent. Early Dutch settlers used buchu to make a brandy tincture, which is still used today to treat many disorders [25]

✓ *Allium sativum*

(Family: Alliaceae or Liliaceae; Common name: Garlic). Garlic has long been used for a variety of cardiovascular conditions, especially hyperlipidemia. It has also been reported to have hypotensive action. It is thought to increase nitric oxide production, resulting in smooth muscle relaxation and vasodilatation. One of the primary active compounds that gives garlic its characteristic odor and many of its healing benefits is called allicin. Meta-analysis of randomly chosen literary data has demonstrated that garlic is related to decrease of BP in patients with increased systolic pressure, but not in patients without increased systolic pressure.[] Garlic preparations have been found to be superior to placebo in reducing BP in individuals with HTN.[] The antioxidative and antihypertensive effect of garlic has been observed in 20 patients with HTN compared to 20 patients with normal pressure, who have been receiving garlic pearls preparation for a period of two months. The results have revealed decreased BP, significant reduction of 8-hydroxy-2-deoxyguanosin, level of nitric oxide, and lipid peroxidation, and an increased level of antioxidative vitamins (C and E). This study points to the beneficial cardioprotective action of garlic in essential HTN .

✓ *Annona muricata*

(Family: Annonaceae; Common name: Prickly Custard apple). *A. muricata* is a member of the family of custard apple trees called Annonaceae and a species of the genus *Annona*, known mostly for its edible fruits *Annona*. The tree grows natively in the Caribbean and Central America. The leaf extract of the plant has been reported to lower an elevated BP by decreasing the peripheral vascular resistance.[]

✓ *Apium graveolens*

(Family: Apiaceae; Common name: Celery). According to Chinese theory, Celery is effective for HTN because it acts upon the liver; one type of HTN is associated with liver. In Mainland China, celery was useful in reducing HTN in 14 of 16 patients. The juice was mixed with equal amount of honey and about 8 ounces were taken orally three times each day for up to one week.[] It has also been reported to reduce systolic and diastolic BP. The difference of BP in human beings before and after treatment has been found to be significant t (P<0.05), indicating that seeds of *A. graveolens* can be used as a safe and effective treatment of high BP.[] Fresh celery juice can be mixed with vinegar to relieve dizziness and headache and shoulder pain associated with HTN. It is also administered in HTN associated with pregnancy and climacteric.[]

✓ *Aristolochia manshuriensis*

(Family: Aristolochiaceae; Common name: Guan Mu Tong). This Chinese plant is being used as a diuretic and antiphlogistic for the treatment of edema and rheumatic pain. The extract of this plant has been reported to contain aristolochic acid, aristolosite, magnoflorine, oleanolic acid, hederagenin, and tannins. Magnoflorine has been found to possess hypotensive properties.[]

✓ *Artocarpus altilis*

(Family: Moraceae; Common name: Breadfruit). The plant is native to the Malay Peninsula and western Pacific islands. A study has shown that the leaf extract of the plant decreased the tension of phenylephrine-stimulated isolated guinea pig aorta rings by 15 to 35% []

✓ Blond psyllium

(Family: Plantaginaceae; Common name: Indian plantago). Preliminary clinical research shows that taking a B. psyllium (Plantago species) supplement 15 g daily can modestly lower BP; systolic by about 8 mmHg and diastolic by 2 mmHg. []

✓ Camellia sinensis

(Family: Theaceae; Common name: Tea). There are many potential health benefits from drinking tea. There is lots of interest among researchers on the effect of tea on cardiovascular disease. Research on tea and HTN is contradictory. Research on black tea (fermented tea) (Camellia sinensis) shows no effect on BP in people with HTN. Population research links consumption of green tea (unfermented) (Camellia sinensis) and oolong tea (partially fermented) (Camellia sinensis) with a decreased risk of developing HTN.[]

✓ Capparis cartilaginea

(Family: Capparaceae; Common name: Lasaf). It is a prostrate or scrambling shrub found in rocky ground, sometimes hanging from cliffs. It has been reported that crude extract of C. cartilaginea produces a dose-dependent decrease in BP and slight bradycardia in anesthetized rats . []

✓ Carum copticum

(Family: Umbelliferae; Common name: Ajwain). The crude extract of C. copticum (1-30 mg/kg) produces a fall in BP and heart rate (HR) of anesthetized normotensive (NMT) rats. Hypotension produced is very brief and returns to normal within a minute. At the low dose (up to 1 mg/kg), the crude extract produces negligible change in the HR. However, bradycardia has been reported at the higher doses (10-30 mg/kg) . []

✓ Cassia absus

(Family: Caesalpiniaceae; Common name: Chaksu). This plant is found in the tropical region and is found everywhere in India. It has been reported that an intravenous administration of a crude extract of C. absus produces a dose-related (1-30 mg/ kg) decrease in BP, accompanied with a decrease in HR at the higher doses (10 and 30 mg/kg). Repeated injections of the same dose of the crude extract have been seen to produce tachyphylaxis. A sustained fall in BP of anesthetized animals and weak antiacetylcholine effect has been reported . []

✓ Zingiber officinale

Family: Zingiberaceae; Common name: Ginger). Ginger root is commonly used in Asian cooking. It acts to improve blood circulation and relaxes muscles surrounding blood vessels. The crude extract of ginger (Zo.Cr) induced a dose-dependent (0.3-3 mg/kg) fall in the arterial BP of anesthetized rats. In guinea pig paired atria, Zo.Cr exhibited a cardiodepressant activity on the rate and force of spontaneous contractions. In rabbit thoracic aorta preparation, Zo.Cr relaxed the phenyl ephrine-induced vascular contraction at a dose ten times higher than that required against K⁺ (80 mM)-induced contraction. Ca²⁺ channel-blocking activity was confirmed when Zo.Cr shifted the Ca²⁺ dose-response curves to the right, like the effect of verapamil. These data indicate that the BP-lowering effect of ginger is mediated through blockade of voltage-dependent calcium channels. []

Chronic administration of Pet ether extract (PE) (50 mg/kg/day; po), toluene fraction (10 mg/kg/day; po) of ginger rhizome, and Korean ginseng extract (KGE) (30 mg/ kg/day; po) significantly reduced the BP in deoxycorticosterone acetate salt-induced hypertensive rats, whereas PE (50 mg/ kg/day; po) and KGE (30 mg/kg/day; po) reduced the BP in fructose-induced hypertensive rats. The mechanism of action may partly involve the serotonergic antagonistic property.[] Human trials for hypotensive effect of ginger have been few and generally used a low dose with inconclusive results.[] The renewed interest in the search for new drugs from natural sources, especially from plant sources, has gained global attention during the last two decades. The tropical rain forests have become an important point of this activity, primarily due to the rich biodiversity they harbor, which promises a high diversity of chemicals with the potential novel structures. However, of this rich biodiversity, only a small portion has been studied for its medicinal potential. Thus, natural plants and herbs can be our source of drugs, with fewer side effects and better bioavailability for treatment of HTN in future.

✓ Pueraria lobata

(Family: Fabaceae; Common name: Kudzu). The dry root of this plant is officially listed and used in China as a muscle relaxant, antipyretic, and for the treatment of dysentery and HTN.[] The total isoflavones, from the ethanol extract of roots, have shown hypotensive effect on anesthetized dogs and unanesthetized hypertensive dogs.[] The isoflavone-puerarin, when administered intravenously at a dose range of 100 to 200 mg, in clinical trials to patients suffering from HTN or angina pectoris, showed a decrease in blood catecholamine levels, BP, and HR[]

✓ Punica granatum

(Family: Lythraceae; Common name: Pomegranate). Pomegranate juice is becoming a more popular fruit drink. Research shows that pomegranate reduces the activity of angiotensin converting enzymes (ACE) by about 36%. Clinical research reveals contradictory results. One study shows modest reduction in systolic BP after drinking 50 ml/day of pomegranate juice for a year. Another study shows no benefit after drinking 240 ml/day of the juice for 3 months.[]

✓ Raphanus sativus

(Family: Cruciferae; Common name: Radish): The plant has been found to have antihypertensive activity. Isolated tissue preparations were suspended in tissue baths containing Krebs solution, while acute toxicity study was performed in mice for 24 hours. The extract caused a dose-dependent (0.1-3 mg/ kg) fall in BP and HR of rats that was mediated through an atropine-sensitive pathway. In isolated guinea-pig atria, it showed dose-dependent (0.03-3.0 mg/ml) inhibition of force and rate of contractions.

In the atropine-treated tissues, the inhibitory effect was abolished and a cardiac stimulant effect was unmasked, which was resistant to adrenergic and serotonergic receptor blockade. In the endothelium-intact rat aorta, it inhibited phenylephrine induced contractions, which was blocked by atropine. The extract was safe in mice up to the dose of 10 g/kg. The study showed that the

cardiovascular inhibitory effects of the plant are mediated through activation of muscarinic receptors, thus possibly justifying its use in HTN. []

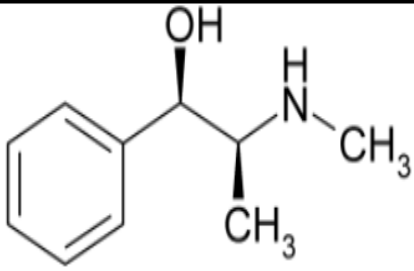
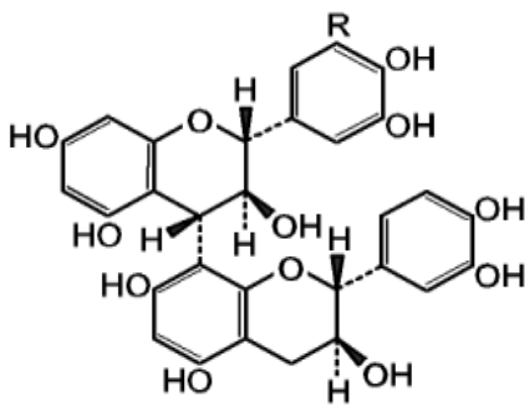
✓ *Lycopersicon esculentum*

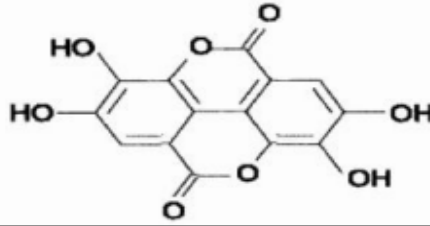
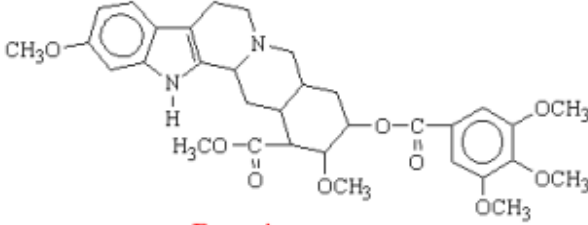
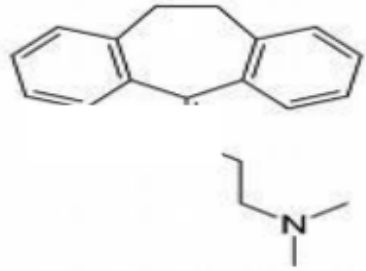
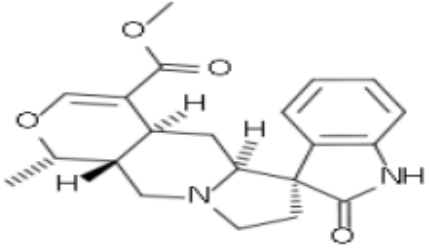
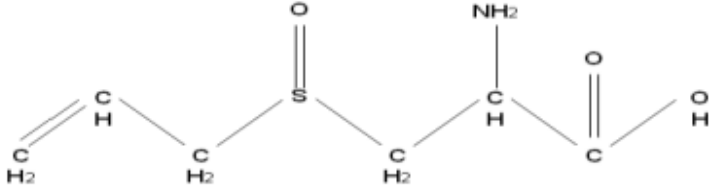
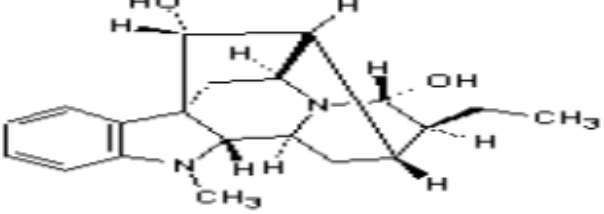
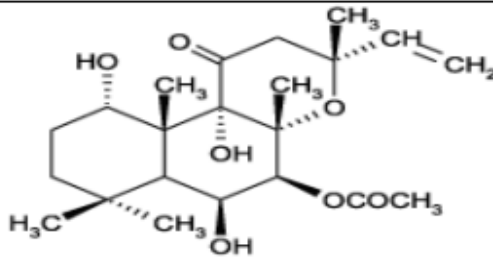
(Family: Solanaceae; Common name: Tomato). Tomato extract contains carotenoids, such as lycopene, beta carotene, and vitamin E, which are known as effective antioxidants, to inactivate free radicals and to slow the progress of atherosclerosis. A study showed that extract of tomato (Lyc-O-Mato) modestly reduces BP in patients with mild, untreated HTN. [] A significant correlation has been observed between systolic BP and lycopene levels. Tomato extract when added to patients treated with low doses of ACE inhibition, calcium channel blockers, or their combination with low-dose diuretics had a clinically significant effect-reduction of BP by more than 10 mmHg systolic and more than 5 mmHg diastolic pressure. No side effects to treatment were recorded and the compliance with treatment was high. []

✓ *Lumnitzera racemosa*

Family: Combretaceae; Common name: Black Mangrove). It is a handsome shrub or a small tree found on the coast of India and on the Andaman and Nicobar Island. According to folk medicine, the fruits of this plant are curative in skin disorders and useful for treating snake and insect bites. Antihypertensive action has been reported for the aqueous acetone extract of the plant.

The antihypertensive activity of eleven hydrolysable tannins contained in the leaves of *L. racemosa* has been investigated. From the screening in spontaneously hypertensive rats, corilagin, castalagin, and chebulinic acid were identified as the major active substances. []

Plant	Chemical constituents	structure
<i>Ephedra sinica/Ephedra intermedia</i>	Ephedrine	
Hawthorn	ProcyanadinB-3 R=H prodelfinidinB-3 R=OH	 <p>Procyanidin B-3 (R = H) Prodelphinidin B-3 (R = OH)</p>

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

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