



Research Journal of Pharmaceutical, Biological and Chemical Sciences

REVIEW ARTICLE

Comparative Review on Harmless Herbs with Allopathic Remedies As Anti-Hypertensive

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ABSTRACT

The incidence and prevalence of systemic hypertension are reaching global epidemic proportions. Hypertension is the leading cause of cardiovascular disease worldwide. Despite a diversity of pharmacological agents to treat high blood pressure, suboptimal control remains a significant problem in as many as 43% of patients and this rate has not significantly improved over the past 2 decades. There are a variety of factors contributing to this including patient's non-adherence due to complex drug regimens and medications side effects, under-treatment and treatment resistance. There, thus, remains a need to find herbal treatment to antihypertensive therapy that facilitate attainment of optimal blood pressure levels. This monograph will review a number of pharmacological targets and interventions, herbal alternatives to achieve optimum hypertensive boundaries as well as novel approaches for the same. This review mainly focuses on better herbal alternative of current allopathic remedies as well as newer herbal approaches like *Hibiscus* tea to treat hypertension.

Key words: Anti-hypertensives, *Passiflora nepalensis*, *Elaeocarpus ganitrus*, *Syzygiumpolyanthum*, Garlic, Saffron, Rauwolfia etc.

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INTRODUCTION

Hypertension is the most common cardiovascular disease and is a major public health issue in developed as well as developing countries.

Scientifically, blood pressure (BP) = Cardiac output (CO) x Peripheral vascular resistance. So, increase in CO or peripheral vascular resistance will increase BP, known as hypertension.

Hypertension involves mainly two types, essential and secondary. [1] The pathogenesis of essential hypertension is multi factorial and highly complex which will be caused by increase in sympathetic nervous system activity, increase in production of sodium-retaining hormones and vasoconstrictors, deficiencies of vasodilators such as prostacycline and nitric oxide, inappropriate or increased renin secretion- resulting in increased production of angiotensin-II and genetic predisposition. [2]

Pathogenesis of Secondary Hypertension will be caused by chronic kidney disease, renovascular disease, cushing's syndrome, pheochromocytoma, drugs such as nonsteroidal antiinflammatory drugs and oral contraceptives.

These all factors will cause increase in preload, increase in contractility, functional constriction and structural hypertrophy, which result in increase in cardiac output and peripheral vascular resistance will leads to hypertension.

DISADVANTAGES OF RECENT PHARMACOLOGICAL THERAPY: [3]

Pharmacological agents available for treatment of hypertension: Thiazide, loop, and potassium-sparing diuretics, β -adrenergic and α 1/ β -adrenergic antagonists (Therapeutics), Central α 2-adrenergic agonists, Central/peripheral adrenergic neuronal-blocking agent, Peripheral α 1-adrenergic antagonists (Therapeutics), Peripheral adrenergic neuronal blocking agents, Direct-acting vasodilators (Therapeutics), Calcium antagonists (Therapeutics), Angiotensin-converting enzyme inhibitors (Therapeutics), Tyrosine hydroxylase inhibitor, Angiotensin II receptor antagonists (Therapeutics).

The first-line of treating hypertension is considered diuretics. Diuretics reduce blood pressure by inducing frequent urination. By urination, body is able to flush out the excess salt and water. And if this excess salt and water are not flushed out, these can cause an increase in blood pressure. When taking diuretics, there is the possibility that will experience some of its identified side effects like muscle cramps, dehydration, dizziness, extreme tiredness, skin rash, blurred vision, abnormal heart rate, and others.

Another type of anti-hypertensive medicine that doctor may prescribe is angiotensin converting enzyme inhibitors. Commonly known as ACE inhibitors, these medicines can cause dilation of the blood vessels which leads to an increase in the blood flow and a decrease in blood pressure. The following drugs are categorized as ACE inhibitors: fosinopril, benazepril, lisinopril, enalapril, captopril, and others. And like diuretics, ACE inhibitors also have certain

side effects. Some of the side effects caused by ACE inhibitors are cough, kidney failure, skin rash, vomiting, diarrhea, fever, sore throat, and others.

Another anti-hypertensive drug that your doctor may prescribe is calcium channel blockers. Calcium channel blockers can cause widening of the blood vessels by blocking the entry of calcium into the cells of the heart and blood vessels. Just like with the other anti-hypertensive drugs, when blood vessels are dilated, there is increased blood flow and decreased blood pressure. The following medications are categorized as calcium channel blockers: verapamil, diltiazem, nifedipine, nicradipine, isradipine, felodipine, and amlodipine. Certain side effects come with the use of calcium channel blockers and examples of these are fatigue, headache, skin rash, diarrhea, constipation, edema, and others.

The different side effects that come with the use of these medications are by far their biggest disadvantages. So, scientific studies suggest different lifestyle changes and use of appropriate herbal medicine in the treatment of hypertension. Included in these various lifestyle changes are stress reduction, proper diet, regular exercise, limited salt intake, smoking cessation, limited alcohol intake, and use of appropriate herbals.

BENEFITS OF HERBS AS ANTI-HYPERTENSIVE: [4]

Symptoms of high blood pressure are headaches, heart palpitations, catching your breath after exertion, fatigue, flushed face, blurry vision, nosebleeds, strong need to urinate often, ringing in ears and dizziness. These symptoms can be resolved by herbals.

Herbs do not cause side effect like weakness, tiredness, drowsiness, impotence, cold hands and feet, depression, insomnia, abnormal heartbeats, skin rash, dry mouth, dry cough, stuffy nose, headache, dizziness, swelling around eyes, constipation or diarrhea, fever or anemia alone and associated with pressure medicines. 100% natural herbs are completely safe.

Herbals won't interfere with medications including diuretics, blood thinners, β -blockers and calcium channel blockers.

PROVED HERBS AS ANTI-HYPERTENSIVES:

***Passiflora nepalensis* Wall [5]**

Antihypertensive effect of an aqueous extract of the whole plant of *Passiflora nepalensis* wall (APN) in renal hypertensive rats was investigated. Hypertension in experimental animals was induced by renal ischemia and reperfusion (IR). The blood pressure, pulse pressure and heart rate fell dose dependently in renal hypertensive and normotensive rats, suggesting that APN possesses antihypertensive, hypotensive and negative chronotropic effects.

***Vitis thunbergii* var. *taiwaniana*: [6]**

Vitis thunbergii var. *taiwaniana* (VTT), the wild grape, is an endemic plant in Taiwan which has long been used as a folk medicine. Each plant growth regulator-treated VTT tissue culture (TC) was used to test the angiotensin converting enzyme (ACE) inhibitory activities. It was found that VTT-TC plantlets exhibited ACE inhibitory activities. It was found that VTT showed antihypertensive activities and the highest lowering effects was reached at 4th-h with reductions of SBP and DBP.

***Elaeocarpus ganitrus* Roxb. seeds [7]**

Aqueous extract of *Elaeocarpus ganitrus* Roxb. seeds powder (Family: Elaeocarpaceae) was evaluated for its antihypertensive activity in renal artery occluded hypertensive rats. Elevated blood pressure of the animals was significantly decreased by the aqueous extract of *E. ganitrus*. So, the antihypertensive activity of aqueous extract of *E. ganitrus* may be due to the action on rennin-angiotensin system.

***Syzygiumpolyanthum* (Wight) Walp. leafs extract and combined with *Eucheuma cottoni* and *Cyclea barbata* [8]**

Bay leaves (*Syzygiumpolyanthum*(Wight)Walp.) is one of Indonesia's potential medicinal plants. Lately, people use *S.polyanthum* to treat hyperglycemia(diabetesmellitus), hypertension and gout. *S.polyanthum* as antihyperglycemic agents has been studied comprehensively in the pre-clinicalphase.

This study is done to get scientific support for the utilization of *S.polyanthum* leafs extract in hypertension treatment. Besides, this study is done to obtain a combination with other materials to overcome the side effects (constipation).

Laiju extract: [9]

Anti-hypertensive effect of laiju extract (LJE) in renal hypertensive rat (RHR) and spontaneous hypertensive rat (SHR) was evaluated. RHR and SHR models were prepared by standard methods. It was shown that blood pressure was significantly lowered at 6 and 5 hours in high and moderate LJE respectively in both RHR and SHR groups. It suggests that LJE has potential in the prevention management of hypertension.

Stevioside from *Stevia rebaudiana* in: [10]

Stevioside is a natural sweet-tasting glycoside isolated from the herb *Stevia rebaudiana*, composed of stevia, a diterpenic carboxylic alcohol with three glucose molecules, mainly used commercially as sugar substitute. Previous study has shown that it can lower blood pressure in anesthetized spontaneously hypertensive rats (SHR). This study was undertaken to evaluate the antihypertensive effect of stevioside in different strains of hypertensive rats and to observe whether there is difference in blood pressure lowering effect. Noninvasive tail-cuff method was

employed to measure blood pressure. This study reconfirmed stevioside has hypotensive effect and the effect is more prominent in hypertensive rats.

Flavone extracts of *Puerariae Radix* (FEPR): [11]

Acute and chronic antihypertensive effects of FEPR were examined in spontaneous hypertensive rats (SHRs) and reno-hypertensive rats (two kidneys one clip model, 2K1C). Anesthetized dogs were used to evaluate the hemodynamic effects of FEPR. The determination of angiotensin converting enzyme (ACE) activity *in vitro* and plasma renin activity (PRA) and endothelin (ET) *in vivo* were used to study the pilot mechanism of FEPR. Moreover, the toxicity study of FEPR was evaluated.

FEPR significantly inhibited the ACE activities *in vitro* dose dependently, and inhibited the PRA *in vivo*, thus FEPR shows significantly blood pressure lowering and cerebral vascular resistance (CVR) decreasing effect, which can partly be explained by the involvement of the Renin-Angiotensin-System (RAS).

Green Coffee Bean Extract: [12]

A water-soluble green coffee bean extract (GCE) has been shown to be effective against hypertension in both spontaneously hypertensive rats and humans. This multicenter, randomized, double-blind, placebo-controlled, parallel group study evaluated the dose-response relationship of GCE in 117 male volunteers with mild hypertension. Both SBP and DBP blood pressures were significantly reduced in a dose-related manner by GCE. Adverse effects caused by GCE were not observed. The results suggested that daily use of GCE has a blood pressure-lowering effect in patients with mild hypertension.

MEDICINALLY AVAILABLE ANTTI-HYPERTENSIVE HERBS:

Lime blossom (*Tilia europea*)

For treating hypertension associated with arteriosclerosis and anxiety, take an infusion. Pour one cup of boiling water onto one teaspoonful of the dried flowers; leave to infuse ten minutes, filter, and drink. [13]

Kudzu (*Pueraria lobata*)

Chinese studies suggest that kudzu helps normalize blood pressure. When a tea containing about eight teaspoons of kudzu root was given daily to 52 people for two to eight weeks, 17 people experienced marked decline in their blood pressure. Kudzu is a powerful antioxidant. It has 100 times the antioxidant activity of vitamin E. Hence it also helps prevent heart disease and cancer. [13]

Garlic (*Allium sativum*)

Garlic is a wonder drug for heart. It has beneficial effects in all cardiovascular system including blood pressure. In clinical studies, garlic has been shown to decrease the systolic pressure by 20-30 mm Hg and the diastolic by 10-20 mm Hg. When people with high blood pressure were given one clove of garlic a day for 12 weeks, their diastolic blood pressure and cholesterol levels were significantly reduced. Eating quantities as small as one clove of garlic a day was found to have beneficial effects in managing hypertension. The pharmaceutical mechanism of garlic's effect on blood pressure is believed to be related to its effect on the autonomic nervous system, lipid-lowering properties and perhaps its high content of sulphur-containing compounds. Patients with high blood pressure were found to have decreased levels of sulphur-containing amino acids in their plasma. Use garlic in your cooking, salad, soup, pickles, etc. It is very versatile. [14]

Saffron (*Crocus sativus*)

Saffron contains a chemical called crocetin that lowers the blood pressure. You can use saffron in your cooking. (It is a very popular spice in Arabic cooking.) You can also make a tea with it. Many Indians add a pinch of saffron in the brewed tea to give a heavenly flavour. Unfortunately, it is very expensive. [15]

Valerian (*Valeriana officinalis*)

Valerian is good for hypertension. It contains a chemical called valerenic acid that inhibits an enzyme that breaks down GABA. GABA (Gamma-amino butyric acid) is known to control blood pressure. Its effect on blood pressure may also be from its sedative action. [16]

Mistletoe (*Viscum album*)

Mistletoe is believed to function as a regulator of blood pressure, exerting a healing effect in both hypertension and hypotension. In Europe, mistletoe has often been combined with hawthorn (*crataegus*) in treating hypertension. [17]

Rauwolfia serpentine

It has ability to deplete catecholamines from peripheral sympathetic nerve endings, decrease in sympathetic tone so, used in hypertension especially in hypertensive emergencies. [18]

Newer herbs as anti-hypertensive

Several studies have found that **Hibiscus tea** has a substantial antihypertensive effect attributable to the flower's ACE-inhibiting anthocyanin content, and possibly to a diuretic effect. One study found that hibiscus conferred an antihypertensive effect comparable to 50 mg /day of the drug captopril. [19, 20, 21]

Another potential treatment is **Coenzyme Q10**, which a meta analysis of 12 studies found reductions in systolic pressure of 10–17 points and a reduction in diastolic pressure of 8–10 points with doses of roughly 200 mg/day. [22, 23]

FUTURE ASPECTS OF HERBAL TREATMENT IN MANAGEMENT OF HYPERTENSION:

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. Early Dutch settlers used buchu to make a brandy tincture, which is still used today to treat hypertension. [24]

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. [25]

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. 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 indicating that seeds of *A. graveolens* can be used as a safe and effective treatment of high BP. [24]

Aristolochia manshuriensis: (Family: Aristolochiaceae; Common name: Guan Mu Tong). 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. [26]

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%. [25]

Avena sativa: (Family: Poaceae/Gramineae; Common names: Dietary Fiber, Green Oat). A diet containing soluble fiber-rich whole oats can significantly reduce the need for antihypertensive medication and improve BP control. The addition of oat cereals to the normal diet of patients with HTN has been found to significantly reduce both systolic and diastolic BP. Soluble fiber-rich whole oats may be an effective dietary therapy in the prevention and adjunct treatment of HTN. [27, 28]

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. [27]

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.. [29]

Capparis cartilaginea: (Family: Capparaceae; Common name: Lasaf). It has been reported that crude extract of *C. cartilaginea* produces a dose-dependent decrease in BP and slight bradycardia in anesthetized rats. [30]

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). [31]

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. [32]

Cassia occidentalis: (Family: Caesalpiniaceae; Common name: Coffee weed). It is a small tree growing 5 to 8 m in height. The leaf of this plant is used in local folk medicine as an antihypertensive agent. In vitro studies of the leaf extract have shown a relaxant effect on the aortic rings. The studies revealed that cassia extract may be relaxing smooth muscle and reducing BP by inhibiting Ca²⁺ influx through receptor-operated channel and voltage-sensitive channel, showing its nonselectivity on these Ca²⁺ channels. [33]

Castanospermum australe: (Family: Fabaceae; Common name: Black bean). Crude extract of *C. australe* has been reported to cause a fall in systolic as well as diastolic BP in a dose-dependent manner (1-100 mg/kg). This fall in BP has been attributed to the saponin fraction and medicogenic acid glucoside present in the crude extract. [34]

Coleus forskohlii: (Family: Lamiaceae; Common name: Karpurvali). The pharmacological properties of coleonol, a diterpene, isolated from *C. forskohlii*, have been investigated. Its predominant effect has been to lower the BP of anesthetized cat and rat as well as of the spontaneously hypertensive rat due to relaxation of the vascular smooth muscle. [35]

Commelina virginica: (Family: Commelinaceae; Common name: Virginia dayflower). It is a perennial herbaceous plant in the dayflower family. It is native to the mideastern and

southeastern United States. Whole plant extract has been reported to decrease the tension of phenylephrine-stimulated isolated guinea pig aorta rings by 15 to 35%. [25]

Crataegus pinnatifida: (Family: Rosaceae; Common name: Chinese Hawthorn). It has been used in China as a decoction for treatment of HTN for thousands of years. Pharmacological and clinical trials have shown that it lowers BP. Rhynchophylline, an alkaloid in cat's claw, has demonstrated an ability to inhibit platelet aggregation and thrombosis, which suggests that it may be useful in preventing strokes and reducing the risk of heart attack by lowering BP, increasing circulation, and inhibiting both the formation of plaque on arterial walls and formation of blood clots in the brain, heart, and arteries. In experiments with anesthetized rabbits, intravenous administration of the extract preparation lowered the BP for up to 3 hours. [36, 37, 38, 39]

Crinum glaucum: (Family: Amaryllidaceae; Common name: River Lily, Swamp Lily). *C. glaucum* used traditionally in Western Nigeria for treatment of asthma was investigated for its effects on respiratory and cardiovascular functions. Increasing doses of the aqueous extract caused an increase in tidal volume (increase in ventilatory rate and depth) and a corresponding decrease in both systolic and diastolic pressures. [40]

Cuscuta reflexa: (Family: Cuscutaceae; Common name: Giant dodder). Crude extract of *C. reflexa* has been reported to cause a decrease in systolic and diastolic BP as well as HR in anesthetized rats. The antihypertensive activity and bradycardia produced were found to be dose-dependent, but the decrease in HR was observed at slightly higher doses. Pretreatment with atropine (1 mg/kg) did not abolish the cardiovascular responses to *C. reflexa*. [41]

Daucus carota: (Family: Umbelliferae; Common name: Carrot). It has been used in traditional medicine to treat HTN. Activity-directed fractionation of aerial parts of *D. carota* resulted in the isolation of two coumarin glycosides coded as DC-2 and DC-3. Intravenous administration of these compounds caused a dose-dependent (1-10 mg/kg) fall in arterial BP in NMT anesthetized rats. [42, 43]

Desmodium styracifolium: (Family: Leguminosae; Common name: Osbeck). Preparations from the dry leaves and stem of the plant injected intravenously into anesthetized dogs increased coronary circulation, lowered arterial BP, slowed HR, and decreased the oxygen consumption of the heart. [44]

Fuchsia magellanica: (Family: Onagraceae; Common name: Hardy Fuchsia, Chiko, Tilco). This plant is native to Southern Argentina and Chile. Infusion of the leaf extract reduces body temperature, acts as a diuretic, and lowers BP. [45, 46]

Glycine max: (Family: Fabaceae Common name: Soybean). Soybean has been found to be effective as a hypotensive agent. One study has shown a very modest reduction in BP, whereas other study shows no benefit. [47]

Gossypium barbadense: (Family: Malvaceae; Common name: Pima cotton). It is a tropical perennial plant that produces yellow flowers and has black seeds. 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%. In Suriname's traditional medicine, the leaves of the plant are used to treat HTN and delayed/irregular menstruation. [25]

Hibiscus sabdariffa: (Family: Malvaceae; Common name: Roselle). This happens to be one of the most extensively studied plants for antihypertensive properties. The leaves, calyx, and corolla of this plant are used traditionally in many West African countries for various medicinal purposes and as edibles. The antihypertensive effect of this plant extract has been variously studied. One study reported the antihypertensive effect of calyx of HS. [48, 49, 50, 51]

Lavandula stoechas: (Family: Lamiaceae; Common name: French Lavender). Crude extract of *L. stoechas* has been reported to produce a fall in BP and HR in anesthetized NMT rats. Pretreatment of atropine abolished the cardiovascular responses, suggesting that the antihypertensive and bradycardia effects of the crude extract may be mediated through mechanism(s) similar to that of acetylcholine. [52]

Lepidium latifolium: (Family: Cruciferae; Common name: Rompepiedra or Stone breaker). This plant has been used as a folk medicine in the Canary Islands for renal lithiasis. It has been found to have hypotensive effect due to its diuretic action in rat. [53]

Linum usitatissimum: (Family: Linaceae; Common name: Linseed, Flaxseed). It is an annual herb believed to have originated in Egypt. Linseed and its oil are rich in α -linolenic acid, an essential fatty acid that appears to be beneficial for the heart diseases, inflammatory bowel disease, arthritis, and other health problems. α -linolenic acid belongs to a group of substances called omega-3 fatty acids. Several studies suggest that diets rich in omega-3 fatty acids lower BP significantly in people with HTN. [54]

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. [55]

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 pressures. No side effects to treatment were recorded and the compliance with treatment was high. [56, 57]

Moringa oleifera: (Family: Moringaceae; Common name: Murungai). In anesthetized rats, the crude extract of the leaves of *M. oleifera* caused a fall in systolic, diastolic, and mean BP in a dose-dependent manner. The antihypertensive effect was brief, returning to normal within two minutes. HR was not affected significantly, except at high doses (3 and 10 mg/kg), which produced a small degree of bradycardia. It was also established that thiocarbamate and isothiocyanate fractions of the crude extract were responsible for the antihypertensive activity. [58]

Musanga cecropiodes: (Family: Cecropiaceae; Common name: Umbrella tree, Cork Wood). It is a rapidly growing plant ubiquitous to the tropical rain forests, particularly of West Africa. The ethanol extract of the plant stem bark has been reported to have antidiarrheal activity. Several workers have demonstrated the scientific efficacy of the latex and the leaf extract as a vasorelaxant, and therefore a hypotensive agent. [59]

Ocimum basilicum: (Family: Lamiaceae; Common name: Basil). It has been reported that a crude extract of *O. basilicum* causes a fall in systolic, diastolic, and mean BP in a dose-dependent manner with median effective dose of 30 mg/kg. The antihypertensive effect is brief and returns to normal within two minutes. This cardiovascular effect of the extract has been attributed to eugenol, which exerts its effect by blocking the calcium channels. [60]

Peganum harmala: (Family: Nitrariaceae; Common name: Harmal). The crude extract fraction and all pure compounds: harmine, harmaline, tetrahydroharmine, harmol, and harmaloi from *P. harmala* produced antihypertensive effects in anesthetized rats in a dose-dependent manner. [61]

Phyllanthus amarus: (Family: Euphorbiaceae; Common name: Nela nelli). This plant is used as a diuretic and to lower BP in traditional medicine practice. Amaechina and Omogbai reported that intravenous administration of the aqueous extract of the leaves of this plant (5-80 mg/kg) to anesthetized NMT male rabbits produced a significant fall in mean diastolic, systolic, and mean arterial pressures in a graded dose-response manner. [62]

Pinus pinaster: (Family: Pinaceae; Common name: Maritime Pine). Pycnogenol is an extract from French maritime pine bark. It is most commonly known as a treatment for venous insufficiency and other vascular conditions. But it is being studied for a long list of other conditions, including HTN. Preliminary clinical research shows that pycnogenol 200 mg/day can modestly lower BP in people with mild HTN. It has been reported to act by inhibiting angiotensin-converting enzymes. [63]

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%. 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. [64]

Raphanus sativus: (Family: Cruciferae; Common name: Radish): The plant has been found to have antihypertensive activity. 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. [65]

***Rhaptopetalum coriaceum* oliver**: (Family: Scytopetalaceae). A decoction of the plant stem bark is traditionally prepared or soaked in locally distilled gin and taken as a remedy for HTN. Preliminary studies carried out on the plant stem bark extract showed its BP-lowering effects on NMT rats. *In vitro* studies of its vasodilatory mechanism revealed its action to be through calcium channel blockade, at a concentration of 0.2 mg/ml of *R. coriaceum* extract. This was done through inhibition of Ca²⁺ release and blockade of potential sensitive channels and receptor-operated channels by inhibiting noradrenaline and KCl-induced Ca²⁺ influx. Results from the *in vitro* studies suggest that ethanol extract of *R. coriaceum* may be more potent as calcium channel blocker than nifedipine. [66]

Sesamum indicum: (Family: Pedaliaceae; Common name: Sesame). Alcoholic extract of seeds (1-30 mg/kg) caused hypotension in anesthetized rats. A fall in systolic as well as diastolic BP in dose-dependent manner was observed. HR was found to decrease at slightly higher doses (10-30 mg/kg). A study in hypertensive patients indicated that sesame oil consumption remarkably reduced oxidative stress and simultaneously increased glutathione peroxidase, superoxidase dismutase, and catalase activities. These results support the hypothesis that sesame oil consumption may help to enhance antioxidant defense system in human beings. The investigators suggested that sesamin is a useful prophylactic treatment in HTN and cardiovascular hypertrophy. [67]

Solanum sisymbriifolium: (Family: Solanaceae; Common Name: Sticky Nightshade, Wild Tomato). The root of *S. sisymbriifolium* Lam., a perennial herb, has been used as a traditional medicine possessing diuretic and antihypertensive properties in Paraguay. The hypotensive effect of the crude hydroalcoholic extract from root was investigated both in NMT and hypertensive rats. The intravenous administration of the extract (50 and 100 mg/kg) produced a significant decrease in BP in anesthetized hypertensive (adrenal regeneration HTN + deoxycorticosterone acetate) rats. [68]

Theobroma cacao: (Family: Malvaceae; Common names: Chocolate, Cocoa Bean, Cocoa Butter). Cocoa powder, enriched with flavonoid constituents, is used for preventing cardiovascular disease. Flavonoids, contained in chocolate, stimulate formation of nitric oxide, increase vasodilatation, and reduce endothelial dysfunction. A growing body of clinical research also shows that daily consumption of dark or milk chocolate (*T. cacao*), 46 to 105 g daily,

providing 213 to 500 mg of cocoa polyphenols, can lower systolic BP by about 5 mmHg and diastolic by about 3 mmHg. [69]

Triticum aestivum: (Family: Poaceae/Gramineae; Common names: Bran, Wheat bran). It has been reported that increasing dietary wheat bran intake by 3 to 6 g/day modestly reduces systolic and diastolic BP. [70]

Uncaria rhynchophylla: (Family: Rubiaceae; Common name: Cat's Claw herb). In traditional oriental medicine, *U. rhynchophylla* has been used to lower BP and to relieve various neurological symptoms. The hypotensive activity has been attributed to an indole alkaloid called hirsutine, which has been found to act at the Ca²⁺ channels. Application of hirsutine after the increases in [Ca²⁺]_{cyt} induced by noradrenaline and high K⁺ notably decreased [Ca²⁺]_{cyt}, suggesting that hirsutine inhibits Ca²⁺ influx mainly through a voltage-dependent Ca²⁺ channel. [71]

Vitex doniana: (Family: Verbenaceae; Common name: Black plum). Ladeji et al. investigated the effect of oral administration of the extract of this plant on BP of rats. The extract was found to exert hypotensive effect. Both the systolic and diastolic BPs were significantly reduced within 45 min after oral administration of the extract. The BP began to return to normal after 2 hours. [72]

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. Thus, natural plants and herbs can be our source of drugs, with fewer side effects and better bioavailability for treatment of HTN in future. [73]

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