Overview on Indian Medicinal Plants as Potential Anti-hypertensive agents

Sunny Bhardwaj*[1], Amar deep Ankalgi[1], Arti Devi[1], Mahendra Singh Ashawat[2]

[1]Department of Pharmaceutical Analysis and Quality Assurance, Laureate Institute of Pharmacy Kathog, Jawalamukhi, Himachal Pradesh-176031, India.
[2]Department of Pharmaceutics, Laureate Institute of Pharmacy Kathog, Jawalamukhi, Himachal Pradesh-176031, India.

Corresponding author
Mr. Sunny Bhardwaj
M.Pharmacy , 4th Semester
Department of Pharmaceutical analysis and Quality Assurance
Laureate institute of Pharmacy, Kathog-HP

Abstract: Hypertension is one of the most common cardiovascular ailments that leads to weakness and precipitating factors for several other diseases. Medicinal Plants are beneficial in management of heart attacks, cerebrovascular conditions, hypertension, atherosclerosis and heart failure. Traditional plant-based medicines are used in management of Hypertension. Apium graveolens, Cinnamon Cinnamomum zeylanicum, Rauwolfia serpentina are few medicinal plants with blood pressure lowering effects. The popularity of natural products is increasing day by day due to their lower side effect and cost effectiveness. This review explains seventeen medicinal plants which are used by pastoral and ethnical and tribal peoples of India for cure and management of hypertension. The data was collected through extensive literature reviews. This review has been arranging in a systemic way such as vernacular name, botanical name, family, different part used with their mechanism of action.

Keywords: Hypertension, Cardiovascular diseases, Herbal medicine, Blood pressure, Antihypertensive herbs, Indian Medicinal plants.

Introduction:

Heart and peripheral blood vessels help in transportation of oxygen and nutrients to the different part of the body and metabolic waste to the excretory organs such as lungs and kidney. Abnormalities in heart and blood vessels lead to different cardiovascular ailments such as hypertension, heart failure, cardiovascular disorders etc. The most common aetiology of heart dysfunctions are alcohol consumption, fatty diets and malnutrition. [1,2]

Blood pressure (BP) can be defined as the pressure exercise by blood inside the vessel walls. It has two types, SBP (systolic blood pressure< 120 mmHg) and DBP (diastolic blood pressure< 80 mmHg). In Hypertension case SBP increase upper than 140 mmHg or DBP elevate upper than 90 mmHg. Hypertension (HTN) is the most common threat factor in acute myocardial infarction and is accountable for about16.5 deaths annually across the world. [3] It's classified as either primary (essential) or secondary (Fig. 1). About 90 to 95 of cases are named primary HTN, which refers to high BP for which no medical cause can be found. [4] The remaining 5 to 10 of cases, called secondary HTN, are precipitated by other diseases like diabetes, eclampsia, pheochromocytoma, etc. [5]

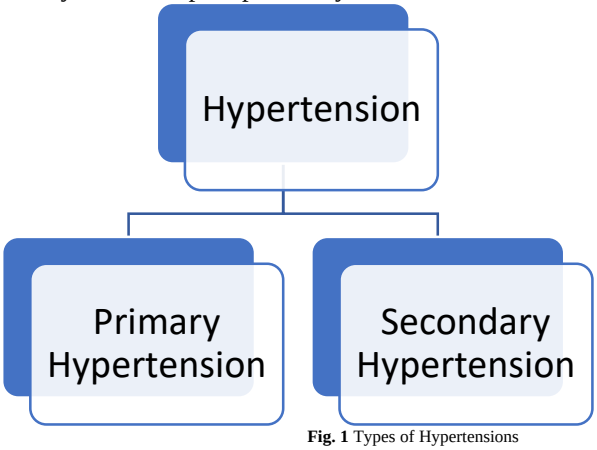


Fig. 1 Types of Hypertensions

Hypertension (HTN) associated myocardial infarction is responsible for about16.5 deaths annually across the world. [6] It has been predicted that by the era 2025, 29 of the world's adults, or nearly1.56 billion people, will suffer from HTN. [7] Seventy-five to eighty percentage of the world's population in developing countries rely on herbal products for diseases management due to the compatibilities of herbal products with the human body, lower costs and minimal side effects. [8] Whereas synthetic derivatives such as diuretics, sympatholytic agents, renin inhibitors, angiotensin converting enzyme (ACE) inhibitors, calcium channel blockers, β-

adrenergic and α1/ β-adrenergic antagonists, and vasodilators have various side effects, including muscle cramps, abnormal heart rate, blurred vision, skin rash, vomiting, kidney failure, extreme fatigue, headache, and edema. [9,10] In this review article, a review of the different plants that have antihypertensive effects for use in the control of HTN is presented.

Pathophysiology of Hypertension:

Hypertension is a chronic rise of blood pressure that, in the long- term, causes organ damage and results in increased morbidity and mortality. Blood pressure is result of cardiac output. It follows that case with arterial hypertension may have an increase in cardiac output, an increase in systemic vascular resistance, or both. [11,12] The autonomic nervous system plays an important part in the control of blood pressure. In hypertensive cases, both increased release of, and enhanced peripheral sensitivity to, norepinephrine can be found. In human essential hypertension, and experimental hypertension, volume regulation and the relationship between blood pressure and sodium excretion (pressure natriuresis) are abnormal. [13]

The pathophysiological mechanisms implicated in the progress of HTN comprise raised vascular resistance, generally distinguished through reduced vascular radius because of enhanced vascular constriction and arterial remodelling. [14] multiple factors contribute to the pathophysiology of HTN, including increases in the renin angiotensin-aldosterone system (RAAS), stimulation of the sympathetic nervous system, vasopressin, disturbed G protein- coupled receptor signalling, inflammation, different T- cell parts, and the diversity of vasoactive peptides secreted by other endothelial cells and smooth muscle cells. [15] Various genetic factors and effect of insulin resistance on hypertension is depicted in Figure 2.

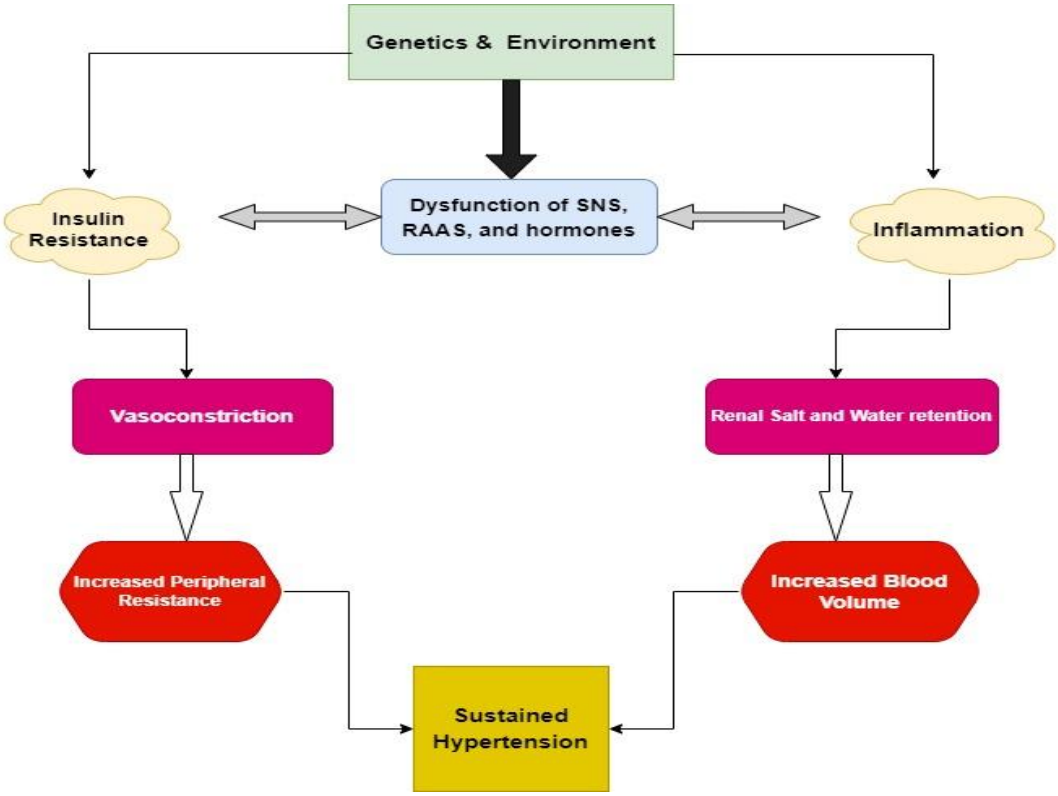


Fig 2. Effect of genetic factors, RAAS and insulin resistance on hypertension

Different Physiological effectors like Potassium channels (Fig. 3), Nitric oxide (NO) (Fig. 4), renin angiotensin system (Fig. 5), and Calcium ions (Fig. 6) modulate the vascular tone and any imbalance in these factors may lead to hypertension.[16]

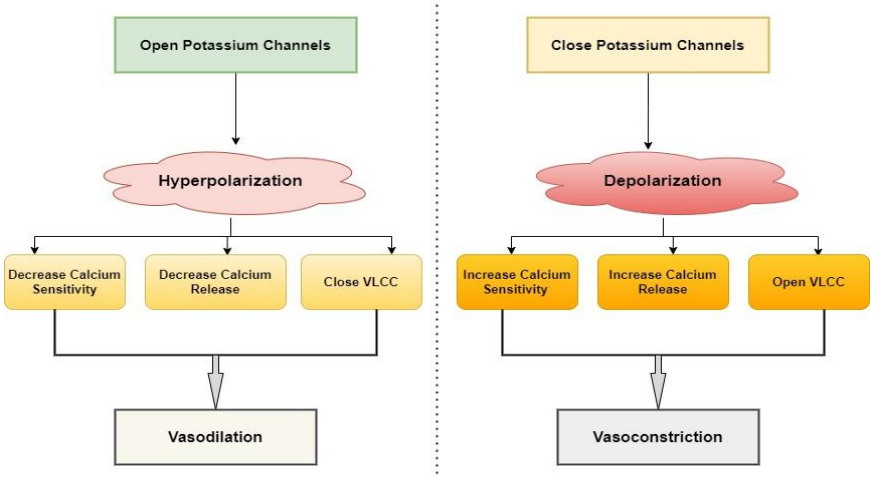


Fig. 3 Effect of potassium channels blood vascular system.

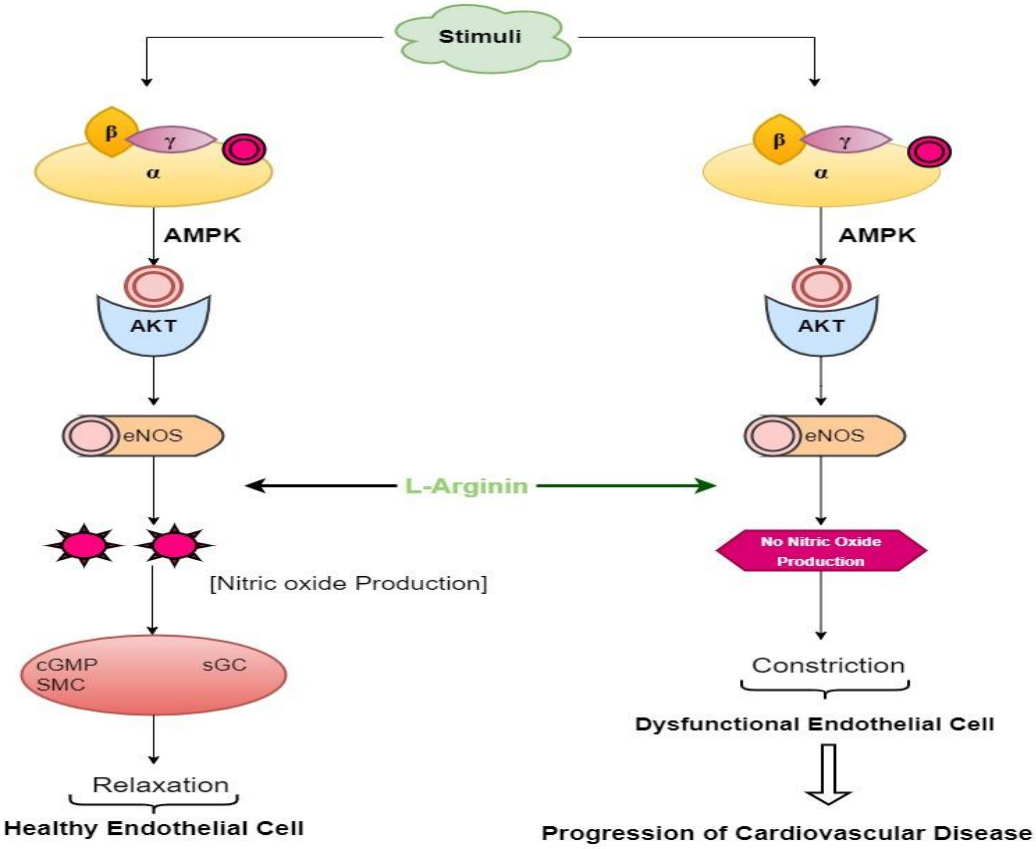


Fig. 4 Role of NOS on blood vascular system.

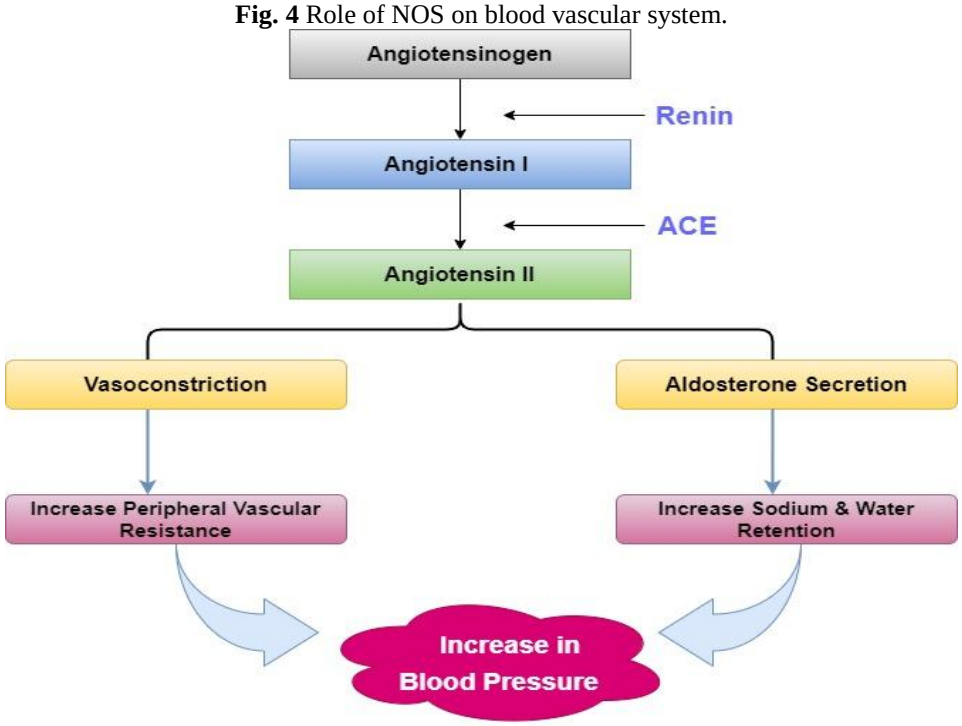


Fig. 5 Role of ACE (Angiotensin-Converting Enzyme) in blood pressure regulation.

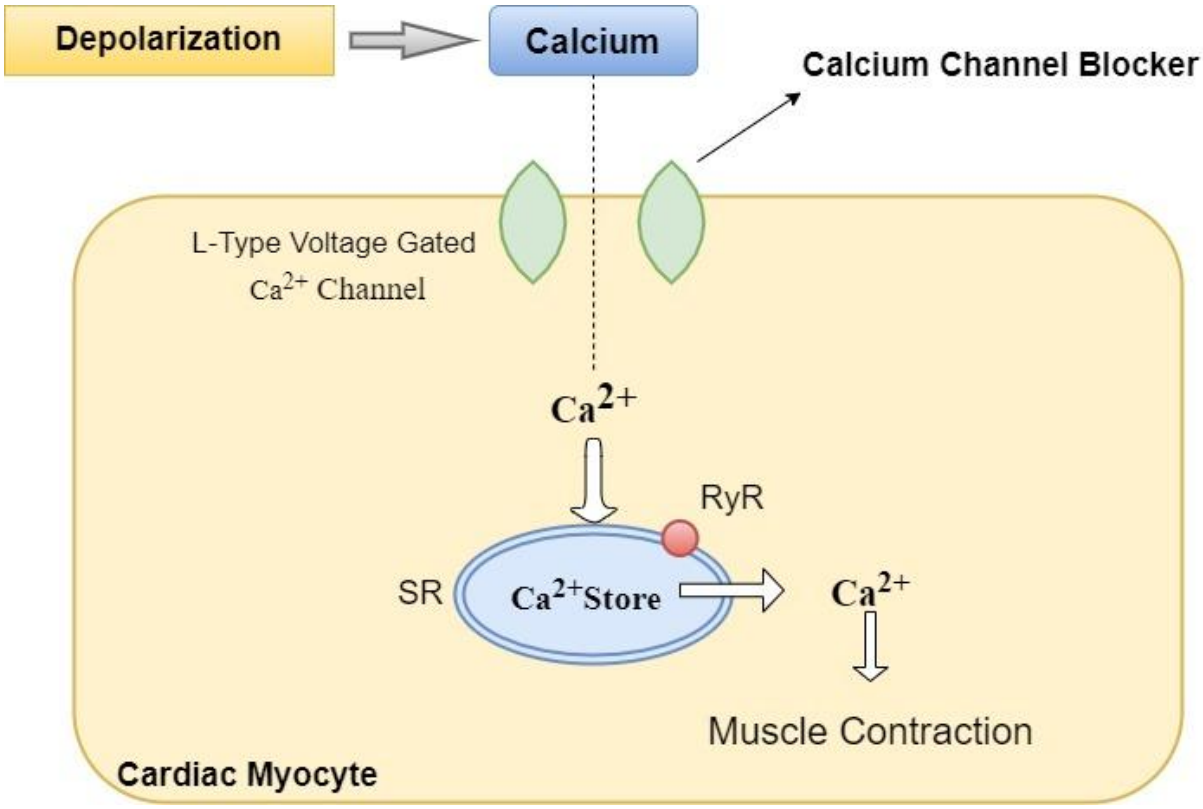


Fig. 6 Mechanism of calcium channel mediated vasoconstriction.

Summary of some medicinal plants used for hypertension with a brief description

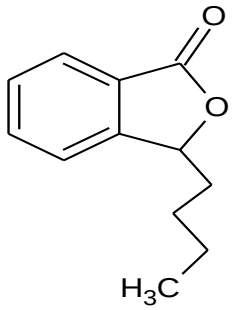
Literature review and scientific studies revealed and recommended different plant-based medicines for the treatment and management of hypertension. [17] Utmost herbal drugs control and ameliorate HTN through various molecular mechanisms such as antioxidant, anti-inflammatory, anti-apoptosis properties, stimulating the eNOS-NO signalling pathway, suppressing endothelial permeability, and activating angiogenesis. [18] Following is the brief discussion of medicinal plants with its therapeutic benefits:

1) Apiumgraveolens, Family: Umbelliferaeor Apiaceae.

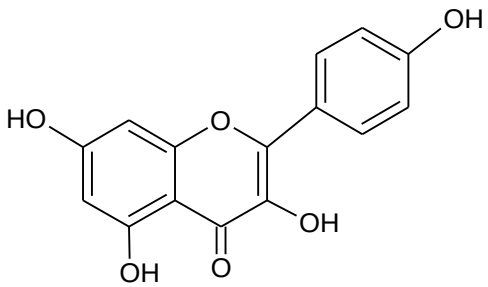
(Common Name: Celery, Ajmod).

It is generally found in tropical and temperate zone of Asia and Africa. Different parts of Apium graveolens are used for the medication different medicinal formulations because of its anti-inflammatory, anti-hypertensive, anti-microbial, bactericidal, fungicidal, anti-cancer, anti-virus, gastro-intestinal, anti-spasmodic and anti-oxidant properties. [19]

According to Moghadam et al. its hexane extracts of celery seed has been shown to have a BP- reducing effect in deoxycorticosterone acetate (DOCA) – induced hypertensive rats. [20] because of better preservation of n-butylphthalide, which is responsible for the flavour and aromatic odour of celery. This effect of n-butylphthalide was also supported by SHRs. [21] According to Ko et al. apigenin flavone extracted form effect voltage and receptor gated channels via blocking of Calcium inflow which in result block aortic ring contracting in the isolated aorta of rat. [22] Fazal et al. reported that day-to-day use of seed extract for 4 weeks can reduce blood pressure by 12. [23] Also, Popovic et al. reported that the flavonoid content of this herb reduces oxidative stress which can potentiate antioxidant mechanisms [24]. Moghadam et al. verified that celery seeds have a hypotensive effect due to some hydrophobic factors, similar as n-butylphthalide (NBP). [25]



n-butylphthalide



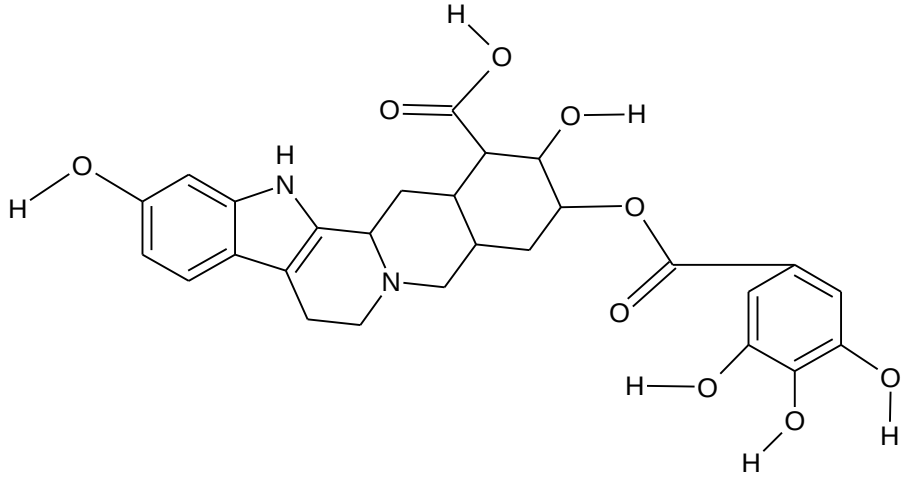
Apigenin

2) Rauwolfia Serpentina, (Family: Apocynaceae/ Dogbane).

Common Name: Devil Pepper, Indian Snakeroot, Serpentine Wood.

Rauwolfia serpentina is a tropical woody plant used for the treatment of HTN by reducing the levels of dopamine and epinephrine and by promoting vasodilation.[26] Rauwolfia consists of indole alkaloids as major phytochemical with others including fatty acids, alcohols, sugars and glycosides, steroids, phytosterols, flavonoids, oleoresins and tannins, indole alkaloids are present in all parts of the plant but major source is root's bark.[27] Reserpine is the major one and has antihypertensive activity as can reduce both

systolic and diastolic blood pressure.[28] Reserpine has the irreversible binding capacity to VMAT2 results in biogenic amines depletion e.g. serotonin, nor-adrenaline and dopamine level in VTA (ventral tegmental area), hypothalamus.[29]



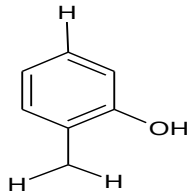
Reserpine

3) Nigella sativa (Family: Ranunculaceae)

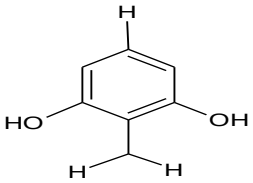
Common Name: Seed of Blessing, Black Cumin.

The Nigella sativa plant, also known as the seed of blessing, has been used in the Middle East, Europe, and Africa for years. It has broad range of pharmacological activities and used to treat many ailments and disorders like diabetes, inflammation, hypertension, cardiovascular complications, hepatic disorder, cancer, kidney disorder and arthritis. N. sativa has a decreasing effect on blood pressure.[30] Black cumin also lowers BP through vasorelaxation by means of its ability to block Ca^{2+} channels. The black seed oil has four significant, pharmacologically active compounds: thymol (THY), thymoquinone (TQ), thymohydroquinone (THQ), dithymoquinone (DTQ) and α-hederin, essential oils, flavonoids, antioxidants, alkaloids, saponin, proteins, fatty acids etc.

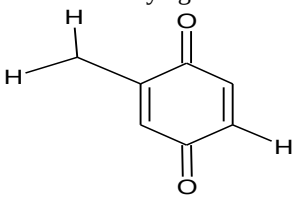
Wong reported that daily use of the extract of N. sativa twice daily for eight weeks in mild hypertension results in a significant decrease in blood pressure.[31] Huseini et al. concluded that the oil of N. sativa can considerably decreases both DBP and SBP.[32] Besides, Ahmad et al. explained that TQ cause vasodilation by reducing synthesis and release of metabolites of COX-1 and COX-2.[33] Black cumin has an inhibiting effect on NF-kB and TNF-a to act as an anti-inflammatory agent.[34]



Thymol



Thymohydroquinone



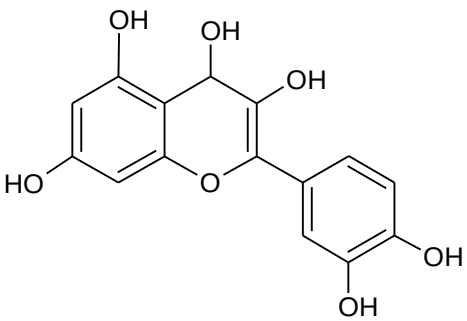
Thymoquinone

4) Bidenspilosa L., (Family Asteraceae)

Common Names: Broom Stick, Beggar 'stick and Black-Jack.

Black Jack is annual plant that grows in South America and also found in tropical and subtropical regions around the world. The whole plant of B. Pilosa plant are used as components in folk medicines in different form as a tincture, dry powder, maceration or decoction.[35] Different parts of Bidens Pilosa contain numerous useful chemical constituents with at least 60 flavonoids. So, normally extracts of this plant are used as medicine to treat around 40 categories of illnesses by different expected mechanism like vasodilatation, lipid profile improving, free radicals scavenging insulin sensibility, calcium blocker etc. [36-39]

Previous studies have authenticated that quercetin increases the NO production and bioavailability which help in better endothelium function. Additionally, Bilanda et al. supported it that quercetin can reduce and prevent hypertension [40]. Bidens Pilosa's methylene chloride and aqueous extracts reverse the hypertriglyceridemia. High blood pressure produced by fructose feeding, but does not affect plasma levels of glucose and insulin but a few experiments showing effect on insulin sensitivity.[41]

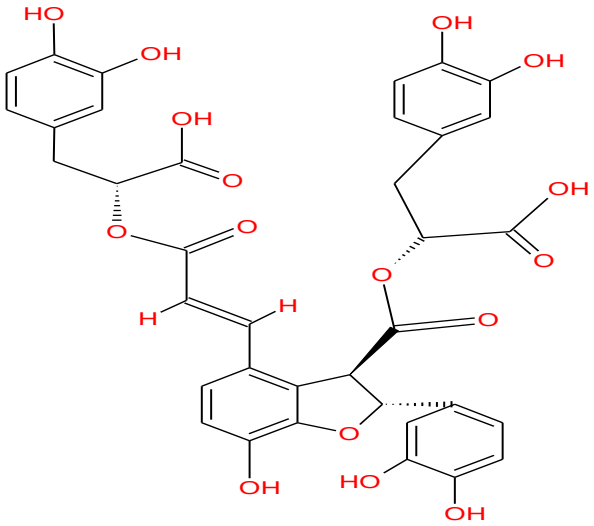


Quercetin

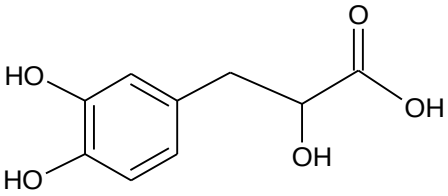
5) Salviae miltiorrhizae, (Family: Labiatae)
Common Name: Danshen, Red/Chinese Sage.

A traditional Chinese herb, Salvia miltiorrhiza, has been disclose to have cardioprotective effects on humans. Its major phytochemicals are danshensu, tanshinones (tanshinone I &tanshinone II) salvianolic acids with other compounds as minor. Mainly root extracts, hold beneficial pharmacological behaviour like anti-microbial, antiviral, anti-oxidant, anti-cancer, anti-inflammatory activity and cardiovascular diseases.[42] Danshen's roots extract diminish pulse rate and systolic blood pressure, moderately via enhancing the synthesis of eNOS signalling and amplify NO production to produce vasodilation. Tanshinone IIA causes vasodilation without involvement of endothelium cells mechanism.[43]

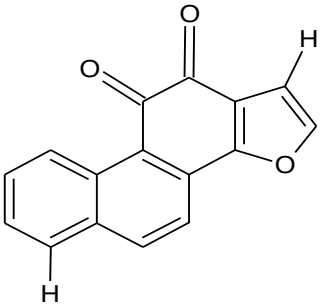
Danshen also inhibits ACEs to cause reduction in blood pressure results in scientific antihypertensive effects documented that danshen also affects other parameters involved in hypertension such as ROS production, oxidation, inflammation and proliferation. [44,45]



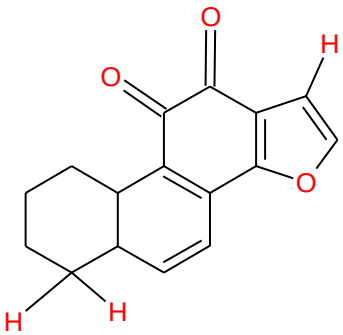
Salvianolic acid



Danshensu



Tashinone I



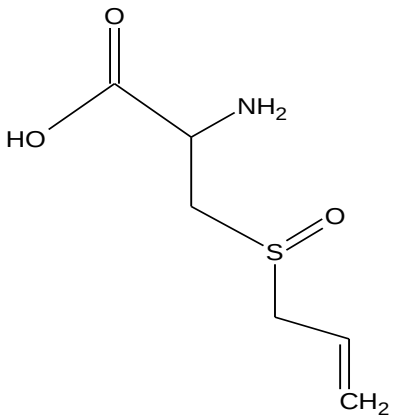
Tashinone IIA

6) Allium Sativum, (Family: Alliaceae or Liliaceae).
Common Name: Garlic.

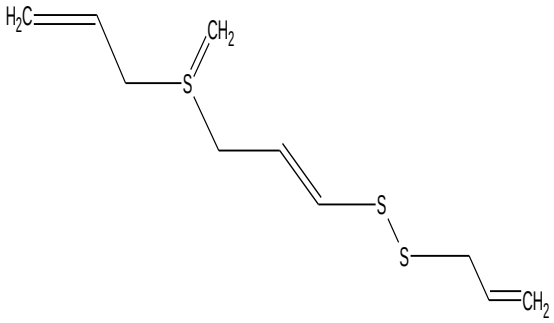
The bulb of A. Sativum is a multipurpose spice or herb popularly used for thousands of years as a vegetable because of its strong flavour and taste worldwide. Garlic supplements have disclosed their effectiveness in the treatment of HTN, decreasing BP by about 10 mm Hg systolic and 8 mm Hg diastolic. Allium Sativum is known for its antibacterial, antioxidant, anti-inflammatory, anti-cancer, and hypocholesteraemia effects.[46]

Aged garlic extract (AGE) begets a steady decrease in BP compared to with other forms of garlic. Furthermore, garlic supplements prompt a major decrease in both SBP and DBP by 3.75- and 3.39-mm Hg, respectively.[47] The presence of organosulfur constituents like allicin (major active constituent), ajoene, S-allyl-l-cysteine, diallyl disulfides (DADS), methyl thiosulfonate and diallyl

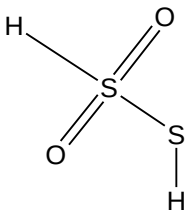
trisulfides are responsible for these pharmacological activities. Moreover, AGE has superoxide foraging abilities in human neutrophils, and regular use of 150 or 400 mg/kg of garlic extract lead to an increase in eNOS activity and a decrease in nicotinamide adenine dinucleotide phosphate (NADPH)-oxidase in the aortas of fructose-fed rats.[48] The components of garlic inhibit ACE activity, diminish Ang II-induced vasoconstrictor responses, prevent VSMCs proliferation in smooth muscles.[49]



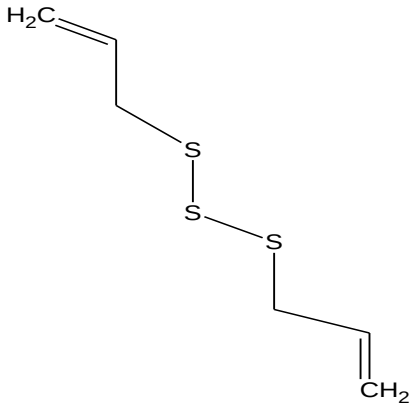
Allicin



ajoene



methyl thiosulfonate

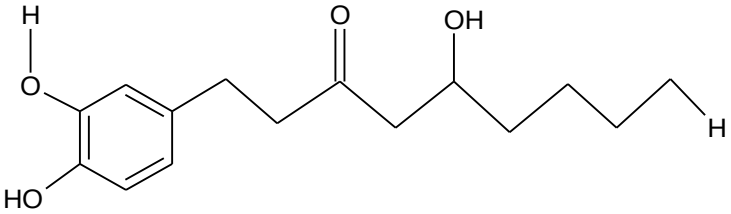


diallyl trisulfides

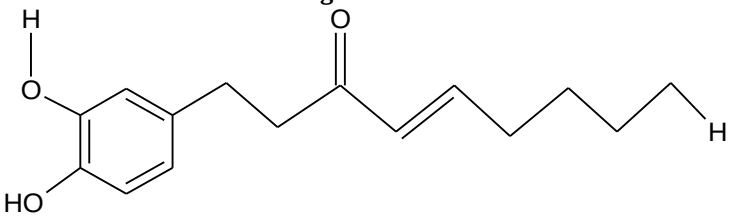
7) Zingiber officinale, (Family: Zingiberaceae)

Common Name: Ginger.

Ginger contains a large amount of potassium, which help in the regulation of Blood pressure and heart rhythm. Administration of two bioactive components of ginger, (6)-gingerol and (6)-shogaol, orally (70– 140 mg/ kg) or intravenously (1.75–3.5 mg/kg) creates tri-phasic BP profiles: first a rapid drop, then an intermediate rise, and lastly, a delayed decline in Blood Pressure. [50] Currently, (6)-gingerol is considered to be a new Ang II type 1 receptor antagonist.[51] Zingiber officinale has a long history of traditional use. It includes numerous components name as beta-carotene, gingerdiol, gingerol, gingerdione, caffeic acid, capsaicin and curcumin. The literature survey confirmed that ginger has multiple biological activities, counting blood pressure-lowering, antioxidant, cholesterol lowering, anti-inflammatory, antimicrobial, anticancer, antiplatelet aggregation, hypoglycaemic, cardiovascular protective, neuroprotective, respiratory protective, antidiabetic, chemo preventive, antiobesity, antiemetic, angina.[52] Some studies proved that ginger can be used with antihypertensive drugs for the treatment of hypertension to provide an addition effect.[53]



Gingerol



Shogoal

8) Panax (Panax ginseng, Panaxquinquefolius, Panax japonicas, Panaxnotoginseng), family: Araliaceae.
Common Name: Japanese Ginseng, Asian or Korean Ginseng, Chinese ginseng, American Ginseng.

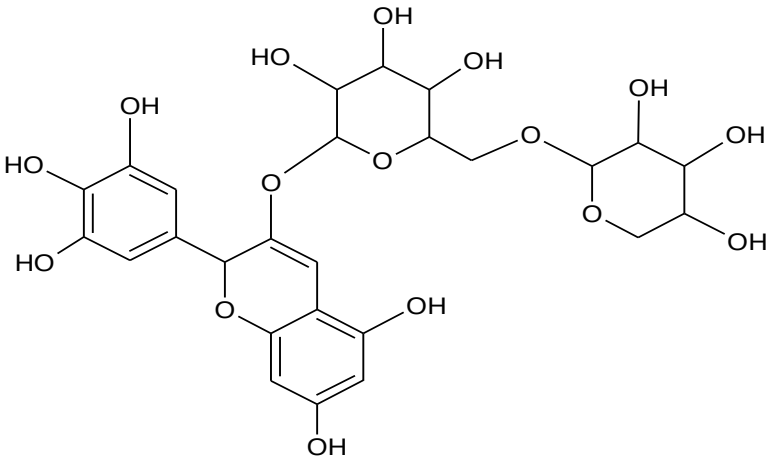
The Panax "all healing" has self-confidence traditionally to heal all ill health problems of the human body.[54]Roots of Panax mainly used in folk medicine for ample variety of pharmacological and therapeutic purposes for centuries either in solid form or in liquid.[55] Till date, some of 40 ginsenosides have been discovered most active and useful.[56] Ginseng regulates BP levels in hypotensive patients probably through vascular function change, controlling the autonomic nervous system, or adjusting the arterial baroreflex.[57] The panax ginseng extract in mild hypertensive patients induces a considerable decline of 3.1 mm Hg in SBP and mm Hg in 2.3 DBP.[58]

Ginsenoside Rg3(red ginseng) stimulates eNOS, enhances NO and cGMP levels, and stimulates Ca^{2+} - gated K^{+} channels. Moreover, ginseng has an anti-proliferative influence on VSMCs, and it has antihypertensive and anti-atherosclerotic abilities.[59] Red ginseng also reduces Ang II-induced VSMC growth. Also, ginseng also inhibits adrenal catecholamines emission, which has an additional effect on antihypertensive character.[60]

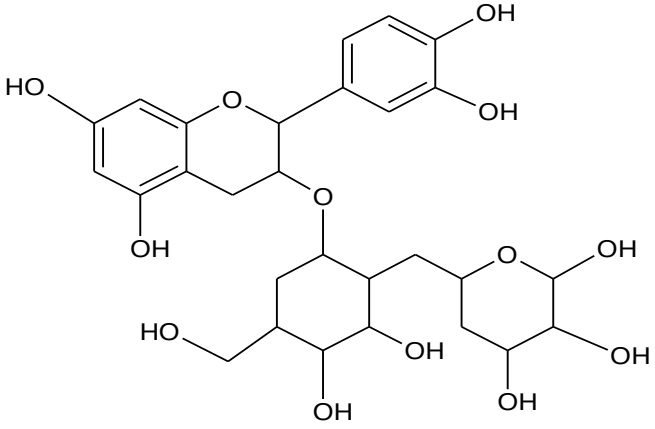
9) Hibiscus Sabdarifa (HS), (Family: Malvacae).
Common Name: Rosella, Hibiscus, Jamaica Sorrel, Red Sorrel.

The various part of this plant like flower, leaves and calyx are used for the treatment of various medicinal problems in many West African countries.[61] Due to its pleasing taste, decorative appearance, medicinal and culinary effect, HS is used worldwide to produce many types of modern cold and hot drinks. In patients with HTN, treatment with the dried extract of the calyx (250 mg) for 4 weeks has displayed remarkable antihypertensive effects.[62] After four weeks of ingesting 10 g/d of hibiscus calyx, the SBP and DBP of hypertensive patients was decreased significantly by 15.32- and 11.29-mm Hg, respectively.

In mild and pre-hypertensive patients, using hibiscus tea (240 ml) 3 times daily for six weeks decreased SBP, DBP, and MAP considerably by 7.2, 3.1-, and 4.5-mm Hg, respectively.[63] Previous studies showed that on treatment with HS the SBP and DBP level declined dose dependently in salt induced hypertensive and in the normotensive group.[64] When comparing to ACE-inhibitors, it was equally effective to captopril but less effective than lisinopril.[65]Its effects were facilitated through the elevated production of NO, blocking of Ca^{2+} channels, and opening of KATP channels. The water-soluble active constituents of HS, anthocyanins, predominantlycyanidin-3-sambubiosideand delphinidin-3-sambubioside, are responsible for the hypocholesterolaemia, antioxidant & antihypertensive effect.[66]



Delphinidin-3-sambubioside



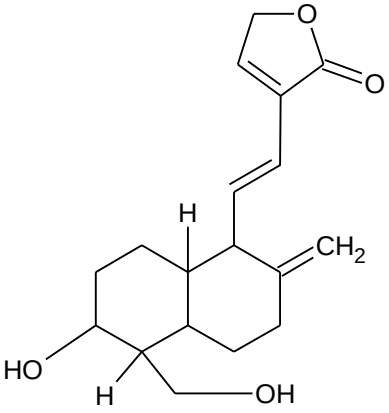
Cyanidin-3-sambubioside

10) Andrographis paniculata, (Family: Acanthaceae).
Common Name: Kalmegh, Kirayat, Bhunimba, King of Bitter.

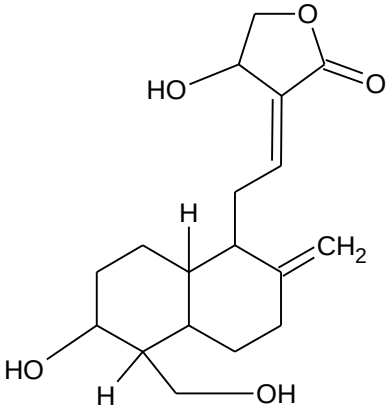
This is a traditional medicinal plant of eastern and south-eastern Asia commonly used for treating cold, fever, upper respiratory and gastrointestinal tract infections, hepatitis, herpes and CVDs.[67] Andrographis paniculate acts by inhibiting the activity of β-adrenoceptors, autonomic ganglion receptor and angiotensin converting enzyme (ACE).[68]Crude extract containing a high

concentration of 14-deoxy-11,12-didehydroandrographolide produce remarkable hypotensive property via increased NO release which is responsible for vasodilation.

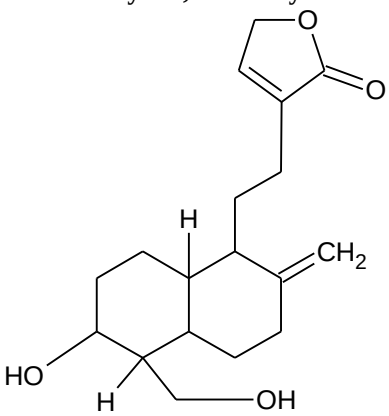
14-deoxy 11,12-didehydroandrographolide, andrographolide and 14-deoxyandrographolide responsible for anti-inflammatory, bactericidal, antioxidant and hypotensive effects.[69] Its chloroform extract can activate NO synthesis and finally stimulate NO production in endothelial cells which ultimately cause relaxation in smooth muscles by inhibiting Ach action.[70] A. paniculata decrease BP by decreasing reactive oxygen species and ACE activities in impulsively hypertensive rats (SHR).[71]Moreover, 14-deoxy-11,12- didehydroandrographolide decrease the level of $Ca2^+$ inside cell by voltage-gated $Ca2^+$ channels. The chloroform extract of Andrographis paniculata blocks the L-type $Ca2^+$ current and high K^+ activation pathways produced endothelial protective effects to relax the smooth muscle and the results were comparable to verapamil.[72]



Andrographolide



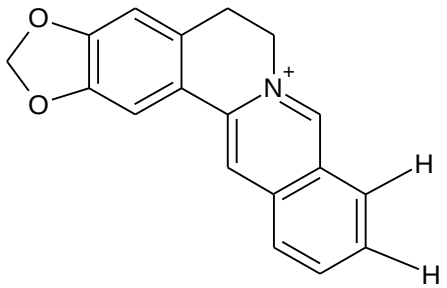
14-deoxy- 11,12-didehydroandrographolide



14-deoxyandrographolide

11) Coptis chinensis, (Family: Ranunculaceae).
Common Name: Chinese Gold Thread).

It is utilized in Chinese folk medicine. Main chemical constituent of Coptis chinensis is berberine which is responsible for its major pharmacological activities such as sedative, immunostimulatory, hypotensive, antimicrobial, choleretic, anticonvulsant, uterotonic, anthelminthic, anticancer and carminative activities. Moreover, it also affects lipid and carbohydrate metabolism, cardio tonicity and endothelial function.[73] Coptis chinensis can block Ca^{2+}channels and inhibit cardiac hypertrophy. BBR can cause a significant decline in SBP (by an average of 4.91 mm Hg) and DBP (2 mm Hg).[74] BBR (150 mg/kg) can also scavenge ROS, prevent NADPH oxidase, and increase the antioxidant enzymes and superoxide dismutase (SOD).[75] BBR increases the expression of eNOS with a simultaneous increase in NO release that causes increased vasodilation. Furthermore, BBR prevents endothelial injury and controls inflammatory pathways by inhibiting NF-κB, VCAM-1expression and VSMC proliferation.[75]



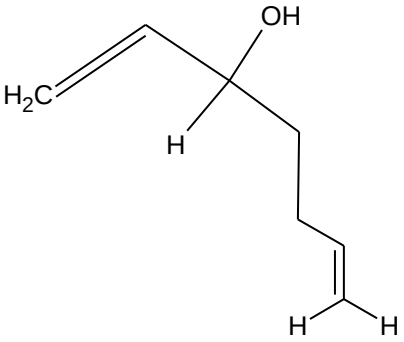
Berberine

12) Coriandrum sativum, (Family: Umbelliferae/Apiaceae),
Common Name: Kasbour, Coriander, Cilantro.

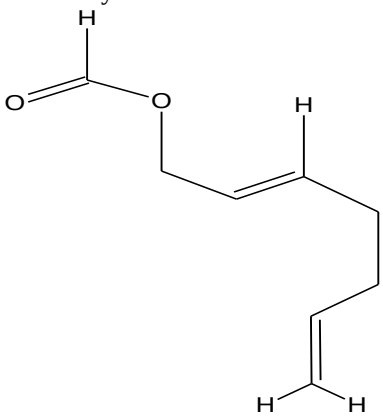
Coriandrum sativum is a traditional medicine use for the treatment of cardiovascular and gastrointestinal diseases. It has been shown to display antioxidant effects.[76] Its oil is used in many cosmetics' formulation. The main active constituents of coriander are

linalool, geranyl acetate and gamma-terpinene. It also has other chemical constituents like a-cedrene (3.87%), citronellal (1.96%), geraniol (1.87%), b-pinene (1.82%), b-sesquiphellandrene (1.56%), citral and Citronellyl acetate (1.36% each), citronellol (1.31%), m-cymene (1.27%) and a-farnesence (1.22%) as minor.

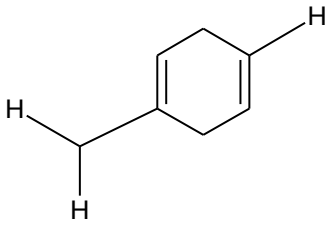
Till date coriander have been not tested in clinical trials to evaluate its result on BP but, it is reported in many studies that coriander shows antioxidant activities and inhibits ROS production by b-adrenoceptor. Intravenous use of the aqueous methanolic extract of the seeds (1–30 mg/mL) causes a reduction in SBP, DBP, and MABP, possibly through the Ca^{2+} antagonist. Additionally, this extract exhibits diuretic affects.[77] The active constituents act synergistically to balance vasoactive constituent for management and treatment of hypertension. Also, coriandrum sativum extract has an inhibitory effect on NF-kB and Inos.[78]



Linolool



Geranyl acetate

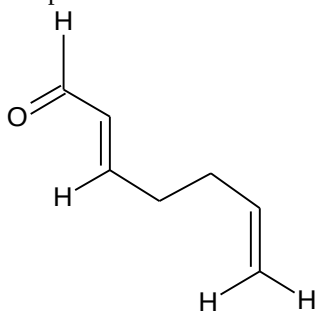


gama-terpinone

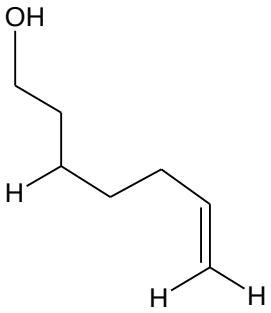
13) Cymbopogon citrates (Family: Gramineae),
Common Name: Lemongrass, Citronella, Squinant).

Lemongrass is widely used in Southern Asia, China, and Brazil. Its antihypertensive effects have been ascribed to Citral, its active phytochemical compound.[79] Extract of shoot and leaves of C. citrates has been widely used for its nutritional, cosmetic and medicinal applications, globally for the high content of essential oil. Various studies acknowledged the occurrence of its phytoconstituents such as flavonoids, alkaloids, essential oil, phenols, tannins, deoxy sugars, saponins, anthraquinones in the leaves and stem of herb.[80]

The major constituent of C. citrates is citral which is alone or in combination with other components has been used as antimicrobial, antioxidant, chemo-protective and antispasmodic properties. Citral effects synthesis and release of NO to produce vasorelaxation by inhibiting the attenuation caused by L-NAME. Moreover, leaves extract may affect synthesis of prostacyclin to induce relaxation. Furthermore, the relaxant effect of the combination of the extract of root, stems and leaves may be due to the blockage of Ca^{2+} ion channels (endothelium-independent).[81] Fresh leaf extract of Cymbopogon citrates in combination with other herbal medicines like fruits 'extract of Citrus medica and fresh leaf extract of Persea Americana can reduce hypertension in rats induced by sucrose and ethanol. This mixture can be used to protect kidney, liver and vascular endothelium damaged by chronic utilization of sucrose and ethanol.[82] Lemongrass oil can capability to suppress the activity of ROS. Interestingly, citral reduces iNOS and NF-kB activity and produce anti-inflammatory action.[83]



Citral



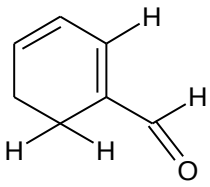
Citronelal

14) Crocus sativus (Family: Iridaceae),
Common Name: Safron.

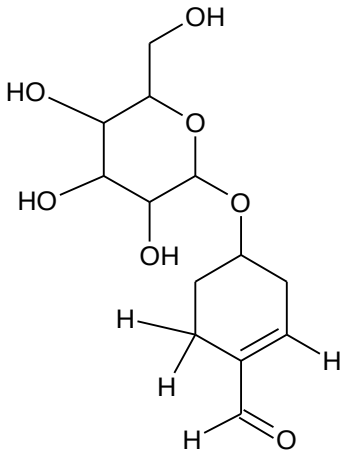
Tea is a beverage of cured leaves or leaf buds of the tea plant Camellia sinensis.[84] It is used for pleasant flavour and colour in different foods and in cosmetology also. It has chemical constituents such as flavanols (kaempferol) carotenoids (crocin and

crocetin), phenolic compounds, anthocyanins, terpenoids and alkaloids. the extract of saffron was used as an antispasmodic, aphrodisiac, expectorant, anti-depressant, antitussive, anticonvulsant, neuroprotective, hypolipidemic, anxiolytic, anticancer, cardiovascular protective and antioxidant.[85] main chemical constituents are crocin, safranal, picrocrocin and crocetin. These components show anti-hypertensive property by different mechanisms of action. Green tea decreases both SBP and DBP by 1.98 and 1.92, respectively.[86]

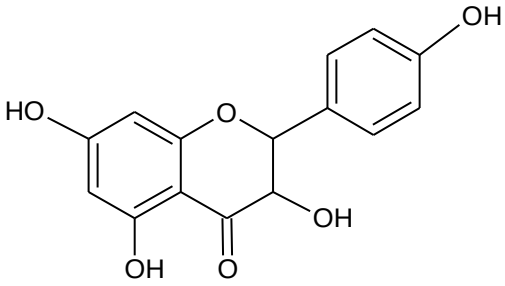
Remarkably, it has been stated that green tea induces a more potent hypotensive effect than black tea.[87] One study established that hypertensive patient who used up to 4479 mg of black tea for 24 weeks showed a substantial decrease by 2- and 2.1-mm Hg in SBP and DBP, respectively.[88] The mechanisms of oxidative stress reduction by tea which include increasing CAT antioxidant enzyme, inhibition of eNOS uncoupling, superoxide's scavenging capacity, and reducing NAPDH oxidase production, cause a reduction in BP besides TNF-α levels.[89] Safranal also affect protein kinase B phosphorylation/ GSK-3b, activation of iNOS, TNF-a expression and NF- kB activity.[90]



Safranal



Picrocrocin

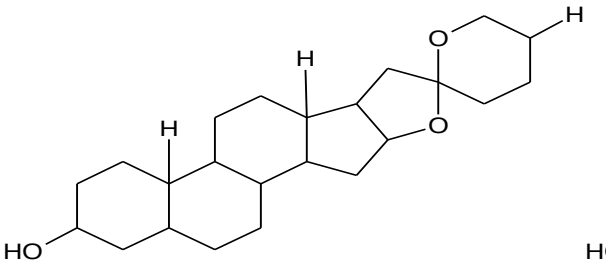


Kaemferol

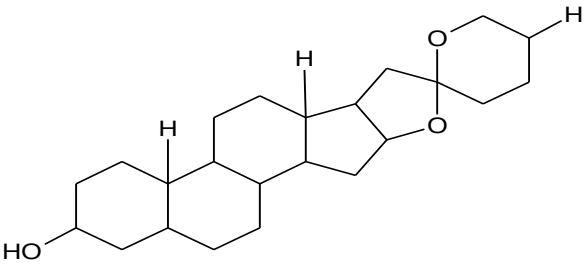
15) Tribulus terrestris (Family: Zygophyllaceae),
Common Name: Gokhru/Gokshura, Puncture Vine.

Tribulus terrestris has been used as medicine for a long time to treat various types of ailments such as antiurolithic, diuretic, hypolipidemic, antidiabetic, hepatoprotective, analgesic, absorption enhancing, cardiotonic, anti-inflammatory, antibacterial, antispasmodic, anticancer, anticariogenic, larvicidal and anthelmintic activities.[91] Different parts of shrub contain a range of medicinally important chemical constituents which as flavanol, spirostanol and furostanol saponins (tigogenin, neotigogenin, hecogenin, neohecogenin, gitogenin, neogitogenin, chlorogenin, Sars sapogenin, ruscogenin, and diosgenin), flavonoids, alkaloids and glycosides (quercetin 3-O-rutinoside, quercetin 3-O-glycoside and kaempferol 3-O-glycoside).[91]

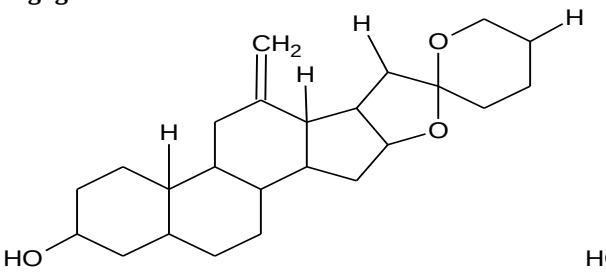
Aqueous and methanolic extracts of gokhru have an antihypertensive effect directly by membrane hyperpolarization and relaxation of arterial smooth muscle in hypertensive rats.[91] Adaikanet al. reported that useful effects for the treatment of different ailments are regarded to its capability to rise up the discharge of nitric oxide (NO) from the nitrergic nerve endings and endothelium.[92] Also, Sharif, et al. suggested that the antihypertensive effect of gokhru may be link with its angiotensin converting enzyme (ACE) inhibitor action.[93]



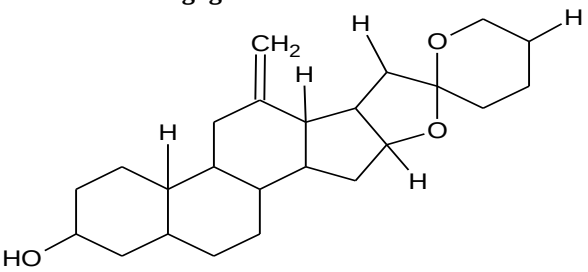
Tigogenin



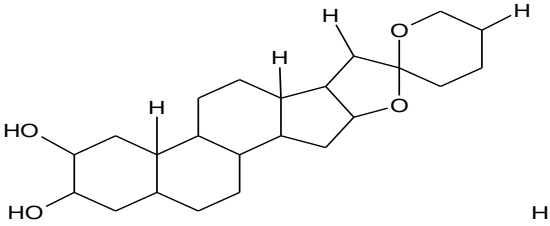
Neotigogenin



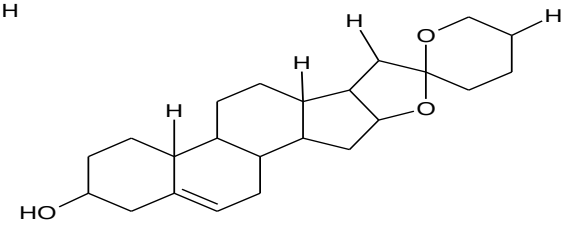
Hecogenin



Neohecogenin



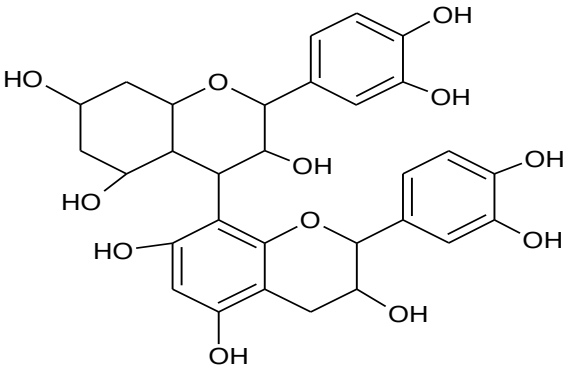
Gitogenin



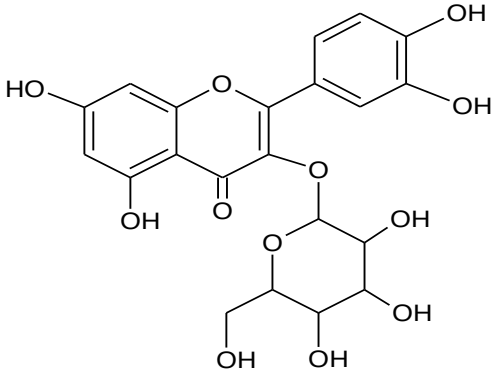
Diosgenin

16) Crataegus spp. (Genus: CrataeguscrenulataSyn., Pyracanthacrenulata, Family: Rose), Common Name: Hawthorns, Hawberry or Thorn Apple.

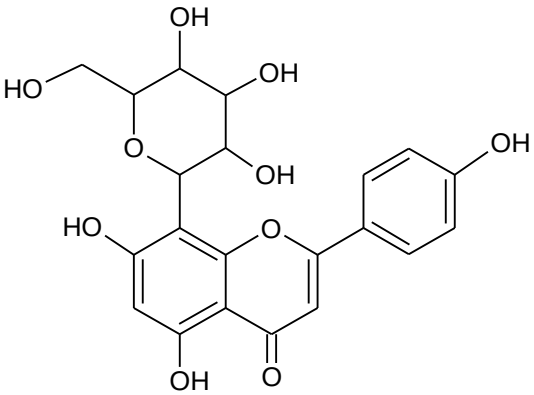
Hawthorn's shrubs are employed in conventional medicine for long years for the handling of CVDs. The major chemical constituent of Crataegustanacetifoliaisquercetin, a polyphenolic flavonoid, which is responsible for its major pharmacological functions a vasorelaxant, anti-inflammatory and anti-oxidant effects. Other multiple components of these plants are oligomeric proanthocyanidins i.e., procyanidin, procyanidin B-2, hyperoside etc. and flavonoids i.e., vitexin, rutin, etc. Moreover, extracts of hawthorn are effectual on both endothelial cells and VSMCs. Crataegustanacetifolia's extract cause vasodilation by increasing phosphorylation and activation of eNOS at serine1177 which in result enhances synthesis and release of NO in endothelial cells.[94] Walker et al. reported that hawthorns drug (500 mg for regular 10 weeks) can decreases in DBP in hypertensive patients.[95] According to Bone and Mills major reduction in BP occurs only after administration of drug in higher doses for longer duration of time.[96] Asgary et al. run a random, placebo-controlled, double-blind clinical trial by the administration of Crataegus curvisepala's hydro-alcoholic extracts of flowers for three months found that both DBP and SBP decreased by around 8 and 13 mmHg, respectively.



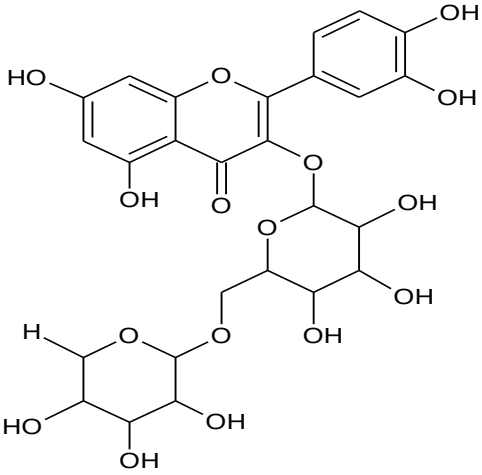
Procyanidin B2



Hyperoside



Vitexin



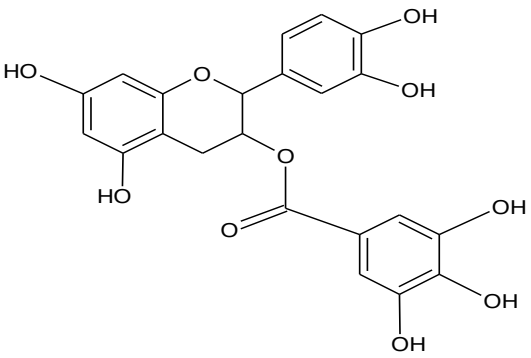
Rutin

17) Camellia sinensis (Common Name: Tea; Family: Theaceae)

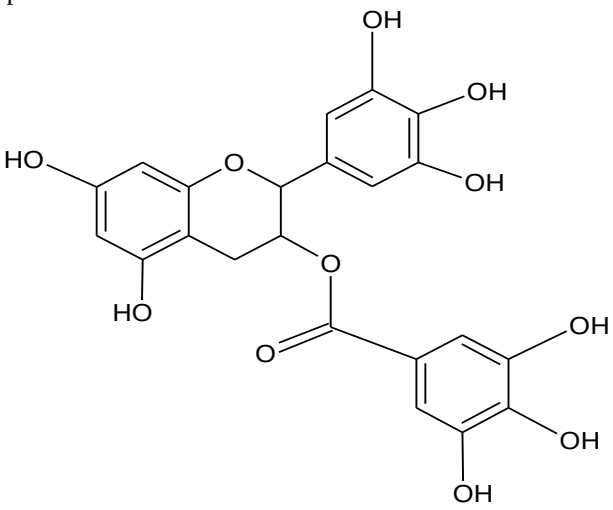
Tea is a beverage of cured leaves or leaf buds of the tea plant which is most frequently consumed beverages in worldwide next to the water.[97] 8 It has pleiotropic effects comprising antibacterial, anti-inflammatory, anti-cancer, and antidiabetic properties, accompanied by antihypertensive actions. Green tea decreases both SBP and DBP by 1.98 and 1.92, respectively.[98] Remarkably, it has been stated that green tea induces a more potent hypotensive effect than black tea.[99] One study established that hypertensive patient who used up to 4479 mg of black tea for 24 weeks showed a substantial decrease by 2- and 2.1-mm Hg in SBP and DBP, respectively.[100]

The major flavonoids of tea are catechins which include (−)-epicatechin-3-gallate (ECG), −)-epigallocatechin-3-gallate (EGCG), (−)- epicatechin (EC), (−)- epigallocatechin (EGC, primary component).[101] These catechins are converted to flavins and the arubigins, by effective vasodilators. These catechins are also responsible for major elevation in blood flow by increased liberation of NO through a simultaneous decline in intensities of oxidative stress and dimethylarginine.[102] Aqueous extract of Camellia

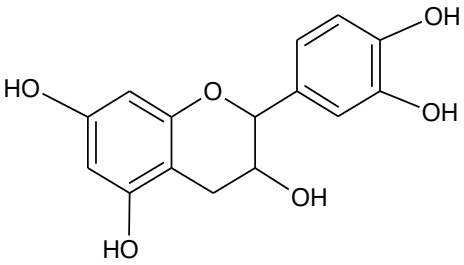
sinensis can produce pleiotropic effects as well as anti-diabetic, anti-inflammatory antibacterial, antihypertensive and anti-cancer activities.[103] The o-methylated EGCG content of tea can inhibit angiotensin-converting enzyme therefore consumption of black tea extract by daily 7 days has a decreasing effect on systolic blood pressure (SBP). Epigallocatechin gallate (EGCG), derived from tea, caused a decrease in VCAM-1 levels, prevented NFκB activation, and stimulated prevention of proliferation in human aortic VSMCs through the upregulation of HO-1 enzyme expression.[104]



Epicatechin-3-gallate



Epigallocatechin-3-gallate



Epicatechin

The botanical name, family, vernacular name, Phyto-active constituents and therapeutic uses of discussed seventeen plants are enlisted in Table-1.

Table 1: Medicinal Plants with their therapeutic values:

S.no	Botanical name	Family	Vernacular name	Phytoactive constituents	Therapeutic uses
01	Apiumgraveolens	Umbelliferae or Apiaceae	Celery, Ajmod	n-butylphthalide, Apigenin	Anti-inflammatory, Anti-hypertensive, Anti-microbial.
02	Allium Sativum	Alliaceae or Liliaceae	Garlic	Allicin,Ajoene, methyl thiosulfonate, diallyl trisulfides	Antibacterial, Antioxidant, Anti-hypertensive
03	Andrographis paniculata	Acanthaceae	Kalmegh, Kirayat, Bhunimba, King of Bitter	Andrographolide, 14-deoxy-11,12-didehydroandrographolide, 14-deoxyandrographolide	Cold, fever, Anti-hypertensive, hepatitis, herpes
04	Bidenspilosa L	Family Asteraceae	Black-Jack, Broom Stick	Quercetin	Antiseptic, Anti-inflammatory, Anti-hypertensive

05	Coptis chinensis	Ranunculaceae	Chinese Gold Thread	Berberine	antimicrobial, choleretic, anticonvulsant, Anti-hypertensive
06	Coriandrum sativum	Umbelliferae or Apiaceae	Kasbour, Coriander	Linalool, Geranyl acetate, gama-terpinone	Antioxidant, Anti-inflammatory, Antioxidant
07	Cymbopogon citrates	Gramineae	Lemongrass, Citronella	Citral, Citronelal	Vasorelaxant, Anti-hypertensive
08	Crocus sativus	Iridaceae	Safron	Safranal, Picrocrocin, Kaemferol	Antioxidant, Vasorelaxant
09	Camellia sinensis	Theaceae	Tea	Epicatechin-3-gallate, Epigallocatechin-3-gallate, Epicatechin	Vasorelaxant, Antioxidant
10	Crataegus spp.	Rose	Hawberry, Thorn Apple	ProcyanidinB2, Hyperoside, Vitexin, Rutin	Anti-inflammatory, Anti-hypertensive
11	Hibiscus Sabdarifa	Malvacae	Rosella, Hibiscus	Delphinidin-3-sambubioside, Cyanidin-3-sambubioside	Anti-proliferative, Antioxidant
12	Nigella sativa	Ranunculaceae	Black Cumin	Thymol, Thymohydroquinone, Thymoquinone	Vasorelaxant, antihypertensive
13	Panax ginseng	Araliaceae	Japanese Ginseng, Asian or Korean Ginseng	Ginsenosides	Antioxidant, Anti-inflammatory
14	Rauwolfia Serpentina	Apocynaceae/ Dogbane	Devil Pepper, Indian Snakeroot	Reserpine	Anti-hypertensive, Sedative
15	Salviae miltiorrhizae	Labiatae	Red/Chinese Sage	Salvianolic acid, Danshensu, Tashinone I, Tashinone IIA	Antioxidant, Anti-inflammatory
16	Tribulus terrestris	Zygophyllaceae	Gokhru/Gokshura	Tigogenin, Neotigogenin,Hecogenin, Neohecogenin,Gitogenin, Diosgenin	Anti-hypertensive
17	Zingiber officinale	Zingiberaceae	Ginger	Gingerol, Shogoal	Anti-hypertensive

Conclusion:

Plant derived products have greater contribution in the management of hypertension. Traditional healers use them for centuries in curing the ailments. In this review, we discussed seventeen Indian plants, their sources, active constituents, therapeutic uses and research work carried out by various researchers in the area of hypertension. The plant derivatives possess antihypertensive effects by various mechanism like modulation of endothelial function, free radical and nitric oxide inhibition, pro-inflammatory signalling, platelet activation, opening and ending of different ion channels, ACE and Ang-II inhibition, gene modulation etc. Hence, herbal remedies have potential as antihypertensive agents and preferences and rational approach should be adopted and priority must be given to discover antihypertensive products having Indian plant origins.

Abbreviations

BP	Blood Pressure
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
HTN	Hypertension
ACE	Acetyl-CO Enzyme
RAAS	Renin angiotensin-aldosterone system
NO	Nitric Oxide
DOCA	Deoxycorticosterone acetate
VTA	Ventral tegmental area
SHRs	Spontaneously hypertensive rats
NBP	n-butylphthalide
VMAT	Vesicular monoamine transporter
THY	Thymol
TQ	Thymoquinone
THQ	Thymohydroquinone
DTQ	Dithymoquinone
DAD'S	Diallyl disulfides
NADPH	Nicotinamide adenine dinucleotide phosphate
VSMC	Vascular smooth muscle cell
AGE	Acute gastroenteritis
KATP	ATP-sensitive potassium channel
CVD	Cardiovascular disease
BBR	Berberine
VCAM	Vascular cell adhesion protein
MABP	Mean artery blood pressure
iNOS	Nitric oxide synthases
NF-KB	Nuclear factor kappa B
ROS	Reactive oxygen species
EGCG	Epigallocatechin-3-gallate

Acknowledgement
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