South Asian Herbal Plants as Anti-hypertensive Agents- A Review

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ABSTRACT
Despite the fact that a variety of consistent guidelines are available for the treatment of hypertension, the problem of insufficient management of this condition still persists. The rate of its prevalence is increasing so rapidly that in 2025 one out of every three adults will be a victim of hypertension. In developing countries, adopting the preventive measures for this disease remains the only possible option for its management in the majority of the cases, because drug therapy is highly expensive. Moreover these drugs increase the risk of developing new diseases, making the situation more complicated. Keeping in mind the South Asian poverty condition, economic constraints and harmful effects of drugs, this review aims to investigate the commonly used herbs in South Asian countries for the treatment of hypertension. Different search engines were explored including Pubmed, Google and Asci database (up 10 August 2012) by using various keywords. Priority was given to research article and information presented by authentic organizations and federations. Ten herbal plants that are effectively used in South Asian countries were analyzed for their anti-hypertensive potential on the basis of previously published literature. Among studied herbs *Ginkgo biloba, Passiflora nepalensis* and *Zingiber officinalis* showed considerable results and in most of the cases their antioxidant capacity was found to be responsible for their anti-hypertensive properties. The only need is to discover the unexplored herbs so that they can be used as an alternate of synthetic expensive drugs.

Key words: Antihypertensive, herbal remedies, silent killer, harmful effects


INTRODUCTION
Hypertension is a chronic disease in which blood pressure in the arteries is elevated. The normal blood pressure of a person is 120/80 mmHg, where 120 and 80 represents systolic and diastolic measurements respectively. Blood pressure between 120/80 and 139/80 mmHg denote increased risk of hypertension called as pre-hypertension while blood pressure of 140/90 or above is considered hypertension (http://medicalnewstoday.com/articles/150109.php). There are basically two types of hypertension: primary and secondary hypertension. Primary hypertension is a condition with no medical causes like aldosteronism, renovascular disease, renal failure, and pheochromocytoma. This condition accounts for 95% of all hypertension patients and factors that lead towards the development of this disease, vary considerably from patient to patient1. In secondary hypertension the causes of high blood pressure are identifiable, like endocrine diseases, kidney diseases, glucose tolerance and obesity2. There is another type of hypertension known as uncomplicated hypertension that occurs without any obvious sign and symptoms, hence it is labeled as silent killer (http://www.medicinenet.com/high_blood_pressure/page4.htm). Though there are many identifiable and unidentifiable reasons but genetics plays an important role in the development of this condition. According to a research hypertension is more likely to rise with age and a new genetic link was discovered for hypertension. Findings revealed that dopamine receptor gene is associated with hypertension as cells use the DRD4 gene to make a chemical called as dopamine3. Dopamine is associated with hypertension as it controls sodium excretion by direct interaction with dopamine receptor4. Dopamine receptor is localized to proximal tubule of kidney and any defect in this receptor results in inhibition of sodium reabsorption in tubules by inhibition of Na, H-exchanger and Na,K-ATPase activity5. The increased Na concentration results in the development of elevated systolic and diastolic pressure.

Status of hypertension in South Asia: Hypertension is a silent killer, and is responsible for more than 7 million deaths every year, world-wide (http://www.macter.com/HTN.html). Hypertension is considered as the leading cause of death and one of the principal factors for heart diseases and strokes. According
to a survey the prevalence of hypertension is 972 Million worldwide and it keeps on increasing so rapidly that in 2025 this number may exceed 1.56 Billion with one in three adults worldwide has raised blood pressure.  
Six out of seven continents are permanently inhabited and among those Asia is the most populous one, representing 60% of the total world population with its 4.2 billion inhabitants. According to the World Bank, 70% of the South Asian population is suffering from poverty and about 75% of South Asia’s poor live in rural areas and most rely on agriculture for their livelihood (http://go.worldbank.org/1E8JVGXF30). Hypertension is the single most important cause of strokes worldwide and according to World Health Organization estimates, 5.5 million people died of stroke in 2002, and roughly 20% of these deaths occurred in South Asia. It has been proven that malnutrition affects the systolic blood pressure and circulatory disease in men and women. The economic condition of South Asia is poor, hence most of its population suffers with malnutrition and starvation due to which hypertension is at its climax in this region. According to the United Nations geographical region classification Southern Asia comprises the countries of Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, and Sri Lanka. In India, deaths due to chronic diseases were 3.78 million in 1990 (40.4% of all deaths) and are expected to reach 7.63 million in 2020 (66.7% of all deaths). Hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India. It has also been estimated that prevalence of hypertension is about 10% in rural areas and 250% among urban adults and the life time risk of developing hypertension is estimated to be 90%. Due to similar environmental and economical situation of Pakistan and India hypertension in Pakistan remains a major health problem. Pakistan is the However, no large scale epidemiological studies are available to determine the true incidence of stroke in Pakistan. Estimated annual incidence is 250/100,000, translating to 350,000 new cases every year (www.pakstroke.com). National health survey of Pakistan 1990-1994 revealed that one in every five people aged 15 or older in the country had hypertension.  
PMRC, conducted by Pakistan Medical Research Council, had shown significant prevalence of risk factors for the coronary heart disease (CHD) and further revealed that hypertension in urban population is higher than rural with more prevalence in males than females. Aziz showed that BMI is qualitatively linked with high blood pressure and people with higher BMI are at more risk of high blood pressure. Although Bangladesh was classified as being in the earliest stage of epidemiologic transition, a recent review of prevalence surveys conducted in Bangladesh indicated that the prevalence of hypertension has increased from <3% to 9% since 1976.

Fig. 1: Number of people living per square kilometer (http://www.carto.edu/earthinfo/asia/SAtco.html)

In Sri Lankan population, one in every four adults with age over 20 years has hypertension and this rate increases positively with age.

All of the south Asian countries has over increasing population which have placed terrific strain on available resources. Bangladesh’s situation is the most distressed and after Singapore it is the second most inhabited country in the world. Number of people per square kilometer in different countries is shown in Fig. 1.

Due to the varying as well as increasing population sizes and continuous decrease in scarce resources, South Asia has always provided highly divergent economic images. Poor economic conditions of this region is also due to the weak economic development caused by faulty government policies and corruption that has ultimately lowered industrial production and trade late in the year 2011. Due to the shortfall in the industrial production Gross domestic product (GDP) of this region fell from 9.1% in 2010 to about 6.6% in 2011 and Pakistan has shown the lowest growth rate in the region http://www.thenews.com.pk/Todays-News-3-88210-P-).

About 80% of the South Asia’s GDP growth is accounted for India, but it has been weakened to about 6.8% in 2012 then that of 8.5% in 2011. Reasons for the slow growth rate may be the rising borrowing costs, high input prices, slowing global growth and heightened uncertainty. Pakistan represents 15% of the South Asia’s GDP, has been worsened the economic activity due to safety measurements, political vagueness and a breakdown in policy implementation. GDP of Pakistan has also been lowered from 3% in 2010 to about 3.7% in 2012.

There is a lot of internal and external factor that is contributing to the lowered economic growth. Internal factors include the limiting macroeconomic policy.
stances, large fiscal deficits that have contributed to weaker domestic demand, higher borrowing costs, elevated inflation and deteriorating political and security conditions.

HERBAL REMEDIES

Do every plant is a medicinal plant? No, according to31 "a medicinal plant is any plant that can be used to synthesize valuable drugs as one or more of its organs contain substances that can be useful for medicinal purpose". About 65-80% of the world population depends fundamentally on herbal remedies for their primary health care. The majority of this population belongs to developing countries where they don’t have easy access to modern medicines due to the poverty. During the past decades, public interest in natural therapies, namely herbal medicine, has increased dramatically not only in developing countries but mainly in industrialized countries22,23,26. Medicines based on herbal formulations usually have lesser side effects and better compatibility with human body than modern medicines24. Less side effects, better compatibility and only available treatment for some diseases makes the herbal medicines an ideal remedy for treatment of these diseases24,26,28,30.

Need of herbal remedies for hypertension: On the basis of recent research, scientists and medicinal practitioners believe that change in life style could be helpful in reducing hypertension. Reduction of body weight, regular aerobic activity, consumption of diet rich in fruits, alcohol moderation and reduced sodium intake are some preventive measures for managing hypertension (http://www.clinpharm.medschl.cam.ac.uk/public/BP Guidelines.pdf). However, in some cases, diet and exercise are not enough on their own to treat hypertension; under such conditions there are two other ways to treat hypertension with varying degree of success like use of drugs31 and vaccines32. Vaccination according to Wright33 among commonly used hypertensive drugs first-line low-dose thiazides are most effective to reduce hypertension and mortality and morbidity (stroke, heart attack and heart failure). He has proved that first-line low-dose thiazides are the best choice for elevated blood pressure when compared with beta-blockers, calcium channel blockers, angiotensin converting enzyme (ACE) inhibitors, alpha-blockers, and angiotensin II receptor blockers (ARB). Besides the fact that antihypertensive drugs are used frequently for the treatment of hypertension some side effects are also associated with increased risk of developing diabetes by disturbing the glucose balance of body33. Apresoline is effective against high blood pressure but its daily usage more than 300 mg per day results in adverse effects like head ach, tachycardia and palpitation34. Hydrochlorothiazide may cause severe hyponatremia35. Angiotension-converting Enzyme Inhibitor can produce minor toxic effects including drug fever, skin rashes and altered sense of taste36, Angiotension II receptor blocker include adverse effects like hypotension, hyperkalemia, and reduced renal function37. Moreover these drugs are so expensive that treatment of hypertension with drugs is not feasible in developing countries. So exploration of herb that can be used for managing hypertension is of immense importance.

Achyrantes aspera: Achyrantes aspera is one of those plants that possess antihypertensive property. It is a subscandent annual herb found all over the Pakistan and in the hilly areas of India39. Leaves of this plant are thick, opposite and softly pubescent on both sides39 flowers are greenish white and fruits are easily disarticulating39. Srivastav102 have found that the methanolic extract of the whole plant has a strong diuretic effect and this diuretic potential acts as powerful antihypertensive agent95. Diuretics increases the urine flow rate56, decreases the oxygen demand and plasma volume59 which lowers the blood pressure that ultimately reduces the hypertension and anxiety like disorders56. Achyrantes aspera contains different types of saponins, protein, vitamins, enzymes and a lot of inorganic compounds92. This plant is locally known as Charchita and it hold a good position as a medicinal herb all over the Asia40. Nadkarni9 has proved that the water in which the whole plant has been boiled for 20-30 min. can be used as Diuretic in renal dropsies and general anasarca. Niranjani96 had conducted a study on the aquous and alcoholic leaf extracts of this plant and found that these extracts has great potential for diuretic therapy that reduces hypertension.

Allium sativum: Allium sativum (garlic) is being used for medicinal purposes since ancient times; it is a species of Allium genus with underground bulb made up of flambouyant claves41. It contains a lot of minerals, enzymes, amino acids and about 33 sulphur compounds47. Garlic is usually used to treat different diseases by lowering blood pressure and cholesterol level. Fallon46 and Pedraza-Chaverri47 have proved in their studies that garlic possesses antihypertensive and anticoagulant effects as it synthesis the nitric oxide that reduces nitrate accumulation in atherosclerotic plaques that is very much harmful for arterial blood pressure regulation. Garlic is being used as antihypertensive agent as it exerts vasodilating effects on the carotid arteries and aorta42, reduces blood pressure47 and enhances the diameter of venules and arterioles131,134. Various studies have proved that a dose of 2400 mg of dried garlic shows hypotensive
effect within 5 h of administration, which remains effective for about 14 h. In a four year clinical trial conducted by Siegel, the dose of 900 mg per day of a garlic powder was found to have antihypertensive effect by about 7%.

**Centella asiatica**: *C. asiatica* (Gotu Kola) is a perennial herb found in Pakistan, Sri Lanka, India and China. It has thin, bean shaped leaves and usually grows in shallow water or moist areas. Traditionally the whole plant of *C. asiatica* is used for the treatment of different diseases but its major use is to treat skin problems. *C. asiatica* is also used to cure gastric ulcers, leprosy, scleroderma and liver cirrhosis. Chemical constituents of this plant are saponins (Asiatic acid, centelloside and madecassoside), flavonoid, aminoacids, tannins and sugar. Widgerow et al. have proved in their study that *C. asiatica* can be used to treat anxiety. In another study by Ahmad and Ismail, it has been used as a herb in powered form and found that it has lowered the blood pressure and ultimately reduced the hypertension. Asiaticoside that is the major constituent of this plant when compared with the Captopril in an ACE activity test, showed low activity as compared to captopril, so the activity of Asiaticoside reduced the blood pressure as well as the sugar level. Cesarone et al. used the laser Doppler evaluation technique and proved that by taking 60 mg (twice a day) of the herbal extract (triterpenic fraction) of *Centella asiatica* (TTFA) reduces the resting flux and increase the venoarterial response. So, TTFA improves microcirculation in the vases of the hypertensive patients.

**Crateagus oxyacantha**: *C. oxyacantha* is a thorny deciduous tree and commonly known as hawthorn berry. It is called Hawthorn berry because of its thorny stems and berry shaped fruits. During spring it bears large bunches of pink flowers, which develop into red berry shaped fruits in autumn. Hawthorn has been used to treat a lot of diseases for a long time. Almost the whole plant of hawthorn is being used for medicinal purposes but the leaves and the flowers are more important for its medicinal use. This plant is used as cardiotonic for heart disease, helps to dilate blood vessels and improves blood flow. Flavonoids like, oligomeric proanthocyanidins (OPCs) present in the leaves and the flowers is an active constituent of this plant that helps to cure cardiovascular disease, another compound of this plant, citrin bioflavonoid that contains vitamin P, promotes the capillary resistance to hemorrhage. Quercetin, triterpene saponins and Vitamin C are also present in *C. oxyacantha* as its active chemical ingredients. A limited number of previous studies have proven that Hawthorn exerts a mild blood pressure lowering activity as it inhibits Angiotensin-converting enzyme (ACE) activity and possesses mild diuretic action. Walker has conducted a study on 36 mildly hypertensive individuals. All individuals were given a dose of 500 mg of the *C. oxyacantha* extract daily; they found that all the subjects have demonstrated a significant decrease in diastolic blood pressure, which ultimately showed a trend towards decrease in anxiety.

**Ginkgo biloba**: *Ginkgo biloba* is one of the oldest surviving tree species and is locally known as Maidenhair tree. Its seeds and leaves are used to cure Asthma, sputum and cough and leucorrhoea. Different extracts obtained from leaves indicate that it has a lot of useful constituents like, flavone glycosides, terpene lactones, different types of organic acids and alkyphenols etc. These extracts possess antioxidant and anti-ischemic properties. Ginkgo leaves are also used to cure, headache, anxiety, depression, mood disturbances, thrombosis and memory loss. Another study conducted by Umegaki has found that by feeding 2% GBE diet for 20 days lowered the 5-hydroxytryptamine content in platelets, that directly cause hypertension. Few studies are also found against the view that “Ginkgo biloba reduces the hypertension”, like Brinkley has conducted a study on 3069 individuals by giving a dose of 240 mg/day of *G. biloba* extract for a follow up period of 6.1 years. They found that *G. biloba* does not reduce the blood pressure of the individuals that is why the incidence of hypertension remained the same.

**Passiflora nepalensis**: The word Passiflora has been derived from a Latin word “Passio” which is a symbol for “Passion of Christ”. It is usually found in the warm regions of the world but is rare in Asia. Though this plant is not common in Asia, it is still used for medicinal purposes in India and other neighboring countries. *P. nepalensis* is a herbal plant mostly climbs over the trees with its tendrils. Chemical constituents of this plant include alkaloids, glycosyl flavonoids and phenols etc. Glycosyl flavonoids of *P. nepalensis* possesses a strong antioxidant activity. This plant is also used as an antihypertensive agent and helps in the treatment of inflammation. A study has been conducted by Patel in which they have demonstrated that the aqueous extract of the *P. nepalensis* possesses a strong antihypertensive as well as hypotensive activity. In another recent study researchers have found that the methanolic extract of the whole *P. nepalensis* plant lowered the blood pressure and heart rate of hypertensive rats, which clearly shows that this plant possesses strong antihypertensive property.

**Zingiber officinalis**: *Zingiber officinalis* is a chunky underground stem that supports the other plant parts.
Its can grow up to 3 feet only and can be harvested all the year round. Its rhizome is usually added to different foods as a flavor and is also being used for medicinal purposes. Rhizomes of ginger exhibits antimicrobial, antibacterial, antioxidant as well as antihypertensive properties. Different chemical constituents like Volatile oil and sesquiterpenes (bisabolone, zingiberene and zingiberol) are used as antihypertensive agents. It is documented that Gingerol prevents metastasis, inhibits hepatotoxicity and tocopherol protects kidneys from acute renal failure. Ghayur has reported that the crude extract of ginger induces the Na⁺ channel-blocking (CCB) activity that lowers the blood pressure which ultimately reduces the hypertension in the patients. It is also found that ginger may also increases the side effects of antihypertensives that usually cause dizziness, blurred vision, heart rate irregularities and hypotensive disorder. So the patients who are using any sort of antihypertensive medicines, must reduce the use of ginger to avoid hypotensive disorder.

**Hibiscus sabdariffa:** *H. sabdariffa* is an erect shrub commonly known as bottle brush and widely found in tropical areas native to Asia and Africa. This plant is usually grown in home gardens with well drained and moist soils. It is a good refrigerant and used to make jams, jellies and beverages. In India, *H. sabdariffa* is recommended for the treatment of various diseases like hypertension, pyrexia and liver mayhem. Most of the chemical ingredients of this plant are concentrated in leaves, which contain fat, carbohydrates, fiber, thiamine, β-carotene and ascorbic acid etc. The other parts of the plant contain β-sitostero, cyaniding-3-rutinose, stearic acid, glucose, pectin and alkaloids. McKay has conducted a clinical trial in 65 hypertensive adults by giving three servings (240 ML per day) of distilled *Hibiscus* extract. They have found that after 6 weeks, this treatment has significantly lowered the systolic blood pressure without any side effect. This study has suggested that incorporation of *Hibiscus* tea in your daily diet can lowers the blood pressure in pre and mildly hypertensive adults. A few more studies conducted by Herrera-Arelano and Ajay have also proved that crude extract of the calyces of *Hibiscus sabdariffa* can significantly reduce both the systolic as well as diastolic blood pressures that is why *Hibiscus sabdariffa* can be regarded as a strong antihypertensive agent.

**Elaeocarpus ganitrus:** *Elaeocarpus ganitrus* is a small tree that belongs to the family Elaeocarpaceae and usually found in India, Nepal and Indonesia. It is popular for its colorful flowers, blue berry stone fruits and has an important place in ancient medicinal system. Almost all part of *Rodrakasha* tree are being used for the treatment of cough, bronchitis, neuralgia, cephalalgia, brain disorders, anxiety, depression, palpitation, nerve pain, epilepsy, migraine and liver disorders. It also possesses sedative, antidepressant, smooth muscle relaxant, antihypertensive, anti-inflammatory and anticonvulsant activities. A few studies like; Bhattacharya and Roy has proved that the ethanolic extract of the fruits and leaves of the *E. ganitrus* produces quercetin, ractradin, gallic acid and ellagic acids that exhibits hypotensive and a lot of other pharmacological properties. Sakat has conducted a study on hypertensive male Wistar rats by treating with the aqueous extract *E. ganitrus* for 6 weeks and after 6 weeks they have found that a dose of 25-100 mg kg⁻¹ of the aqueous extract of *E. ganitrus* had significantly decreased the elevated blood pressure of the animals. The reason for this reduction in blood pressure was that it may be due to the activation of rennin-angiotensin system that possesses Captopril and angiotensin converting enzyme inhibitor (ACE-Ⅰ).

**Achillea wilhelmsii:** *Achillea* generally known as yarrow plant belongs to the family asteraceae. It is a woody perennial shrub widely found in temperate areas of Asia. *A. wilhelmsii* is an erect shrub ascending up to 35 cm tall and a large number of small flowers unite to form large flat clusters of flowers that can be of different colors. Aerial parts of this plant, like leaves and flowers have various medicinal uses like reduce sweating, improves digestion, stop bleeding and encourage clotting. Dark blue essential oils of this plant possess anti-inflammatory activity and other aerial parts of this plant are used as a tonic to increase bile flow and reduce high blood pressure and act as a diuretic. Chemical constituents of this plant include flavonoids and sesquiterpine lactones that are useful to lower the blood pressure as well as hypertension. A few studies have been conducted to determine the anti-hypertensive properties of this plant. In a study conducted by Asgary have given 15-20 drops of the hydroalcoholic extract of *Achillea wilhelmsii*, twice daily, for about 6 months. LDL-cholesterol were significantly decreased after 4 months and After 6 months it showed a significant decrease in triglycerides, total cholesterol. This study has proven that *Achillea wilhelmsii* is effective against elevated blood pressure.

**DISCUSSION**

Among the factors effecting heart rate are the lack of β-blocker or angiotensin-converting enzyme inhibitor, habitual smoking, diabetes mellitus, high diastolic blood pressure, unhealthy diet, harmful use of alcohol, raised blood lipid level, over weight and obesity. The main cause of the hypertension is the persistent rise in blood pressure that is mainly due to the resistance in the passage...
of blood through the arteries and arteriole. Constriction of the main renal artery of kidney causes renal disease, as kidney produces an enzyme "renin" that enters the blood through the renal artery and reacts with hypertensiogen that disturb the urination process and cause hypertension\(^\text{10}\). High diastolic blood pressure or hypertension rose with increasing age, obesity, consumption of alcohol\(^\text{11}\) and oxidative stress. The oxidative stress exaggerates Ang II signaling which contribute to high blood pressure by overstimulation of renal NHE3 (renal Na\(^+/\)H\(^+\) exchanger 3)\(^\text{12}\). In another study by Banday\(^\text{13}\), it was stated that oxidative stress increase blood pressure by induction of phosphorylation of D1 receptors. Oxidative stress elevates blood pressure by endothelial dysfunction by increasing Ca level and antioxidants reverse the effects of oxidants by improving endothelium-dependent relaxation\(^\text{14}\). Use of antioxidants contributes in lowering oxidative stress and improving hypertension\(^\text{15}\). Herbal plants like *Ginkgo biloba*, *Passiflora napelensis* and *Zingiber officinalis* have strong antioxidant properties to reverse hypertension complication. The herbal plants have different mechanisms for lowering blood pressure. For example *Adlayanthas aspersa* have diuretic effect and lowers elevated blood pressure by increasing urine output and enhancing excretion of electrolytes like Na\(^+\), K\(^+\) and Cl\(^-\). While garlic reduces blood pressures by gaseous signaling molecules H\(_2\)S which relax vascular smooth muscles and induce vasodilatation of isolated blood vessels. *C. asiatica* can reduce capillary permeability and increases venoarterial response that reduces hypertension\(^\text{16}\). Hawthorn lowers the blood pressure by inhibiting Angiotensin-converting enzyme (ACE) activity\(^\text{17}\). *E. ganitrus* exhibits Captopril and angiotensin converting enzyme inhibitor (ACE-I) that lowers the elevated blood pressure\(^\text{18}\).

In support of the present review on the positive effects of plants with antioxidant components in hypertension, very good systematic reviews have been published in the recent years\(^\text{19,20,21}\) that confirm the same positive effects of antioxidants in other most common diseases of the world such as diabetes, colitis, hormonal disease, osteoporosis and most interestingly aging. Therefore, further studies are still needed and it is crucial to present new formulations and mixtures to the world for various diseases and pharmaceutical companies have the major role in this respect.

**CONCLUSION**

All the herbs reviewed in this study can be applied to cure hypertensive disorder. Among studied herbs *Ginkgo biloba*, *Passiflora napelensis* and *Zingiber officinalis* showed considerable results and in most of the cases their antioxidant capacity was found to be responsible for their antihypertensive properties. In support of the present findings, a recent systematic review indicated that amongst useful herbs, some like Cinnamon, *Silybum marianum*. Garlic, Nigella, and Echinacea have the highest potential to be used in oxidant-related diseases and thus test of them in hypertension is proposed\(^\text{19,21}\).

Herbal medicines are getting more popularity because allopathic medicines has a lot of side effects. South Asian population is using traditional system of medicines to cure a number of diseases. So there is a need to conduct more research to explore the full potential of the alternative herbal medication.

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