

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 Ascii 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

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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 139/89 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

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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 pressure⁶.

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 Asian'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 worldwide⁷ 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 women⁸. 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 Lanka⁹. 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)¹⁰. 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%¹¹. 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 hypertension¹². PMRC¹³, 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. Aziz¹⁴ 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 transition¹⁵, a recent review of prevalence surveys conducted in Bangladesh indicated that the prevalence of hypertension has increased from <3% to 9% since 1976¹⁶.

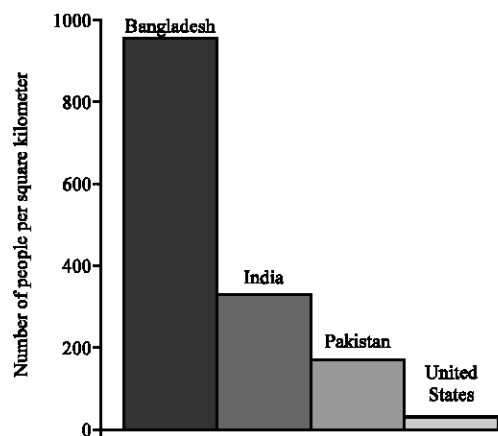


Fig. 1: Number of peoples living per square kilometer (<http://www.cotf.edu/earthinfo/sasia/SAeco.html>)

In Sri Lankan population, one in every four adults with age over 20 years has hypertension and this rate increases positively with age¹⁷.

All of the south Asian countries has over increasing population which have placed terrific sprain 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>; ¹⁸).

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 2011¹⁹. 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 2012²⁰.

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 to²¹ "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 countries^{22,23,24,25}. Medicines based on herbal formulations usually have lesser side effects and better compatibility with human body than modern medicines²⁶. Less side effects, better compatibility and only available treatment for some diseases makes the herbal medicines an ideal remedy for treatment of these diseases^{27,28,29,30}.

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 has not been completely proven to be effective against hypertension. According to Wright³¹ 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 function³⁶. 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.

***Achyranthes aspera*:** *Achyranthes 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 India³⁷. Leaves of this plant are thick, opposite and softly pubescent on both sides³⁸ flowers are greenish white and fruits are easily disarticulating³⁹. Srivastav¹⁵² have found that the methanolic extract of the whole plant has a strong diuretic effect and this diuretic potential acts as powerful antihypertensive agent¹⁵³. Diuretics increases the urine flow rate⁴⁰, decreases the oxygen demand and plasma volume³⁹ which lowers the blood pressure that ultimately reduces the hypertension and anxiety like disorders⁴¹. *Achyranthes aspera* contains different types of saponins, protein, vitamins, enzymes and a lot of inorganic compounds⁴². This plant is locally known as Charchita and it hold a good position as a medicinal herb all over the Asia⁴³. Nadkarni⁴⁴ 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. Niranjani⁴⁵ has conducted a study on the aqueous and alcoholic leave 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 flamboyant cloves⁴⁶. 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. Fallon⁴⁸ and Pedraza-Chaverri⁴⁹ have proved in their studies that garlic possesses antihypertensive and anticoagulant effects as it synthesis the nitric oxide that reduces nitrite 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 aorta^{50,51}, reduces blood pressure⁵² and enhances the diameter of venules and arterioles^{53,54}. 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^{55,56}. In a four year clinical trial conducted by Siegel⁵⁷, 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, Sirilanka, India and China. It has thin, bean shaped leaves and usually grows in shallow water or moist areas^{58,59}. 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^{60,61}, Leprosy⁶², Scleroderma⁶³ and Liver cirrhosis⁶⁴. Chemical constituents of this plant are saponins (Asiatic acid, centelloside and medecassosides) flavonoid, aminoacids, tannins and sugar^{65,66}. Widgerow⁶⁶ have proved in their study that *C. asiatica* can be used to treat anxiety. In another study by Ahmad and Ismail⁶⁷ has used this 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^{68,69}. Cesarone⁷⁰ in their study 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* (TTFCA) reduces the resting flux and increase the venoarterial response. So, TTFCA improves microcirculation in the vanes of the hypertensive patients.

***Crataegus oxyantha*:** *C. oxyantha* 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^{71,72}. 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 importance for its medicinal use⁷³. This plant is used as cardiogenic for heart disease^{74,75}, helps to dilate blood vessels⁷² 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 disease⁷⁵, another compound of this plant, citrin bioflavonoid that contains vitamin P, promotes the capillary resistance to hemorrhage (<http://www.thefreedictionary.com/vitamin+P>). Quercetin, triterpene saponins and Vitamin C are also present in *C. oxyantha* as its active chemical ingredients^{76,77}. A limited number of previous studies have

proven that Hawthorn exerts a mild blood pressure lowering activity⁷⁷ as it inhibits Angiotensin-converting enzyme (ACE) activity⁷⁸ and possesses mild diuretic action⁷¹. Walker⁷⁹ has conducted a study on 36 mildly hypertensive individuals. All individuals were given a dose of 500 mg of the *C. oxyantha* 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 tree⁸⁰. Its seeds and leaves are used to cure Asthma, sputum and cough and leucorrhoea^{81,82}. 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 alkylphenols etc.^{83,84}. These extracts possess antioxidant and anti-ischemic properties^{83,82}. Ginkgo leaves are also used to cure, headache, anxiety, depression, mood disturbances, thrombosis and memory loss^{84,85}. Another study conducted by Umegaki⁸⁶ 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 Brinkley¹⁵⁴ has conducted a study on 3069 individuals by giving a dose of 240mg/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"⁸⁷. It is usually found in the warm regions of the world but is rare in Asia⁸⁸. Though this plant is not common in Asia, it is still used for medicinal purposes in India and other neighboring countries⁸⁹. *P. nepalensis* is a herbal plant mostly climbs over the trees with its tendrils⁹⁰. Chemical constituents of this plant include alkaloids, glycosyl flavonoids and phenols etc.⁹¹; glycosyl flavonoids of *P. nepalensis* possesses a strong antioxidant activity⁹². This plant is also used as an antihypertensive agent⁹¹ and helps in the treatment of inflammation⁹². A study has been conducted by Patel⁹³ 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 property⁹⁴.

***Zingiber officinalis*:** *Zingiber officinalis* is a chunky underground stem that supports the other plant parts⁹⁷.

It can grow up to 3 feet only and can be harvested all the year round^{95,96}. Its rhizome is usually added to different foods as a flavor and is also being used for medicinal purposes. Rhizomes of ginger exhibit antimicrobial, antibacterial, antioxidant as well as antihypertensive properties^{97,98,81}. Different chemical constituents like, Volatile oil and sesquiterpenes (bisabolone, zingiberene and zingiberol) are used as antihypertensive agents⁸¹. It is documented that Gingerol prevents metastasis⁹⁹, inhibits hepatotoxicity¹⁰⁰ and tocopherol protects kidneys from acute renal failure¹⁰¹. Ghayur¹⁰² has reported that the crude extract of ginger induces the Ca^{2+} 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 increase the side effects of antihypertensives that usually cause dizziness, blurred vision, heart rate irregularities and hypotensive disorder¹⁰³. So the patients who are using any sort of antihypertensive medicines, must reduce the use of ginger to avoid hypotensive disorder¹⁰⁴.

***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 soils⁵⁵. It is a good refrigerant and used to make jams, jellies and beverages¹⁰⁶. In India, *H. sabdariffa* is recommended for the treatment of various diseases like hypertension, pyrexia and liver mayhem^{106,107}. 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 -sitosterol, cyaniding-3-rutinoside, stearic acid, galactose, pectin and alkaloids¹⁰⁸. McKay¹⁰⁹ 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 lower the blood pressure in pre and mildly hypertensive adults. A few more studies conducted by Herrera-Arellano¹¹⁰ and Ajay¹¹¹ 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^{112,113}. It is popular for its colorful flowers, blue berry stone fruits and has an important place in ancient medicinal system^{114,115}. Almost all part of *Rudraksha* tree are being used for the treatment

of cough, bronchitis, neuralgia, cephalgia, brain disorders, anxiety, depression, palpitation, nerve pain, epilepsy, migraine and liver disorders^{113,115}. It also possesses sedative¹¹⁶, antidepressant¹¹⁷, smooth muscle relaxant¹¹⁸, antihypertensive¹¹⁹, anti-inflammatory¹²⁰ and anticonvulsant¹²¹ activities. A few studies like; Bhattacharya¹¹⁸ and Ray¹²² has proved that the ethanolic extract of the fruits and leaves of the *E. ganitrus* produces quercetin, rudrakine, gallic acid and ellagic acids that exhibit hypertensive and a lot of other pharmacological properties. Sakat¹²³ 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 Asia¹²⁴. *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^{125,126}. 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 diuretic¹²⁷. Chemical constituents of this plant include flavonoids and sesquiterpene lactones that are useful to lower the blood pressure as well as hypertension¹²⁸. A few studies have been conducted to determine the anti-hypertensive properties of this plant. In a study conducted by Asgary¹²⁸ 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 pressure¹²⁹, 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 "rennin" that enters the blood through the renal artery and reacts with hypertensiogen that disturb the urination process and cause hypertension¹³⁰. High diastolic blood pressure or hypertension rose with increasing age, obesity, consumption of alcohol¹³¹ 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)¹³². In another study by Banday¹³³, 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 relaxation¹³⁴. Use of antioxidants contributes in lowering oxidative stress and improving hypertension¹³⁵. Herbal plants like *Ginkgo biloba*, *Passiflora nepalensis* and *Zingiber officinalis* have strong antioxidant properties to reverse hypertension complication. The herbal plants have different mechanisms for lowering blood pressure. For example *Achyranthes aspera* have diuretic effect and lowers elevated blood pressure by increasing urine output and enhancing excretion of electrolytes like Na⁺, K⁺ and Cl⁻³⁹. While garlic reduces blood pressures by gaseous signaling molecules H₂S which relax vascular smooth muscles and induce vasodilatation of isolated blood vessels. *C. asiatica* can reduce capillary permeability and increases venoarterial response that reduces hypertension⁷⁰. Hawthorn lowers the blood pressure by inhibiting Angiotensin-converting enzyme (ACE) activity⁷⁸. *E. ganitrus* exhibits Captopril and angiotensin converting enzyme inhibitor (ACE-I) that lowers the elevated blood pressure¹²³.

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^{136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151} 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 nepalensis* 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 Echium have the highest potential to be used in oxidant-related diseases and thus test of them in hypertension is proposed^{136,137}.

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.

REFERENCES

1. Carretero, O.A. and S. Oparil, 2000. Essential hypertension. Part I: Definition and etiology. *Circulation*, 101 (3): 329-35.
2. Beevers, D.G., G.Y.H. Lip, Y.H. Gregory and E. O'Brien, 2007. ABC of Hypertension. BMJ Books, London, Pages: 88.
3. Sen, S., R. Nesse, L. Sheng, S.F. Stoltenberg, L. Gleiberman, M. Burmeister and A.B. Weder, 2005. Association between a dopamine-4 receptor polymorphism and blood pressure. *Am. J. Hypertens.*, 18: 1206-1210.
4. Sato, M., M. Soma, T. Nakayama and K. Kanmatsuse, 2004. Dopamine D1 receptor gene polymorphism is associated with essential hypertension. *Hypertension*, 36: 183-186.
5. Hussain, T. and M.F. Lokhandwala, 1998. Renal dopamine receptor function in hypertension. *Hypertension*, 32: 187-197.
6. WHO, 2002. World health report: Reducing risks, promoting healthy life. World Health Organization, Geneva.
7. Cressman, M.D. and R.W. Gifford, 1983. Hypertension and stroke FREE. *J. Am. Coll. Cardiol.*, 1: 521-527.
8. Koupil, I., D.B. Shestov, P. Sparen, S. Plavinskaja, N. Parfenova and D. Vagero, 2007. Blood pressure, hypertension and mortality from circulatory disease in men and women who survived the siege of Leningrad. *Eur. J. Epidemiol.*, 22:223-234.
9. UNG, 2011. Millenniumindicators. United Nations Geoscheme, <http://millenniumindicators.un.org/unsd/methods/m49/m49regin.htm>.
10. Sahni, A., 2006. Preventing Chronic Disease in India: A Vital Investment. World Health Organization, Geneva.
11. Gupta, R., 2004. Trends in hypertension epidemiology in India. *J. Hum. Hypertens.*, 18:73-78.
12. Jafar, T.H., A.S. Levey, F.H. Jafary, F. White and A. Gul *et al.*, 2003. Ethnic subgroup differences in hypertension in Pakistan. *J. Hypertens.*, 21: 905-912.

13. PMRC, 1998. Pakistan National Health Survey 1990-1994. Pakistan Medical Research Council Publication, Islamabad, Pakistan.
14. Aziz, K., A.M. Faruqui, M. Teri, C.E. Davis and J. Abenathy, 2005. Blood pressure and hypertension distribution in a lower middle class urban community in Pakistan. J. Pak. Med. Assoc., 55: 333-338.
15. Yusuf, S., S. Reddy, S. Ounpuu and S. Anand, 2001. Global burden of cardiovascular diseases. Part I: General considerations, the epidemiologic transition, risk factors and impact of urbanization. Circulation, 104: 2746 -2753.
16. Zaman, M.M. and M.A. Rouf, 1999. Prevalence of hypertension in a Bangladeshi adult population. J. Hum. Hypertens, 13: 547-549
17. Katulanda, P., A.N.P. DeVasGunawardena, G.R. Constantine, M.H.R. Sheriff and D.R. Matthews, 2009. Prevalence and correlates of hypertension in Sri Lanka. Ceylon College of Physicians - 42nd Annual Academic Sessions, pp: 43.
18. OECD, 2010. Southeast Asian economic outlook 2010.
19. BBVA, 2012. Economic outlook: Asia. Third Quarter 2012. Economic Analysis. August 8, 2012, Pages: 22.
20. GOP, 2012. Highlights: Pakistan economic survey 2011-12. Economic Adviser's Wing, Finance Division, Government of Pakistan, Islamabad.
21. WHO, 1977. Resolution-promotion and development of training and research in traditional medicine. WHO Document No. WHA 30, pp: 49.
22. De Smet, P.A.G.M., 1997. The role of plant-derived drugs and herbal medicines in health care. Drugs, 54: 801-840.
23. Blumenthal, M., 1999. Harvard study estimates consumers spend \$5.1 billion on herbal products? Herbalgram, 45: 68-68.
24. Grunwald, J., 1995. The European phytomedicines market: Figures, trends, analysis. Herbalgram, 34: 60-65.
25. Blumenthal, M., 1998. The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines. The American Botanical Council, Austin, TX., USA., ISBN: 9780965555500, Pages: 685.
26. Kamboj, V.P., 2000. Herbal medicine. Curr. Sci., 78: 35-39.
27. Karim, A., M.N. Sohail, S. Munir and S. Sattar, 2011. Pharmacology and Phytochemistry of Pakistani Herbs and Herbal Drugs Used for Treatment of Diabetes. Int. J. Pharmacol., 7: 419-439.
28. Sohail, M.N., F. Rasul, A. Karim, U. Kanwal and I.H. Attitalla, 2011. Plant as a source of natural antiviral agents. Asian J. Anim. Vet. Adv., 6: 1125 -1152.
29. Sohail, M.N., A. Karim, M. Sarwar and A.M. Alhasin, 2011. Onion (*Allium cepa* L.): An alternate medicine for Pakistani population. Int. J. Pharmacol., 7: 736-744.
30. Sohail, F. and M.N. Sohail, 2011. Despite of its weedy nature is an important medicinal plant of NWFP, Pakistan. Int. J. Pharmacol., 7: 747 -748.
31. Wright, J.M. and V.M. Musini, 2009. First-line drugs for hypertension. Cochrane Data Syst. Rev.
32. Brown, M.J., 2009. Success and failure of vaccines against renin-angiotensin system components. Nat. Rev. Cardiol., 6: 639-47.
33. Zillich, A.J., J. Garg, S. Basu, G.L. Bakris and B.L. Carter, 2006. Thiazide diuretics, potassium and the development of diabetes: A quantitative review. Hypertension, 48: 219-224.
34. Edward, D. and M.D. Freis, 1954. Adverse effects of antihypertensive drugs. GP., 10: 32-33
35. Goodman, L.S., A. Gilman, L.L. Brunton, J.S. Lazo and K.L. Parker, 2006. Goodman and Gilman's the Pharmacological Basis of Therapeutics. McGraw-Hill, New York.
36. Katzung, B.G., 2004. Basic and Clinical Pharmacology. McGraw-Hill, New York.
37. Londonkar, R., V. Chinnappa Reddy and K. Abhay Kumar, 2011. Potential antibacterial and antifungal activity of *Achyranthes aspera* L. Recent Res. Sci. Technol., 3: 53-57.
38. Srivastav, S., P. Singh, G. Mishra, K.K. Jha and R.L. Khosa, 2011. *Achyranthes aspera*-An important medicinal plant: A review. J. Nat. Prod. Plant Resour., 1: 1-14.
39. Vetrivelan T. and M. Jagadeesan, 2003. Effect of alcoholic extract of *Achyranthes aspera* on acute and subacute inflammation. Phytother. Res., 17: 77-79.
40. Gupta V.K. and V. Arya, 2011. A review on potential diuretics of Indian medicinal plants. J. chem. Pharm. Res., 3: 613-620.
41. Hoeland, R.D. and M.J. Mycek, 2010. Lippincott Illustrated Reviews: Pharmacology. Lippincott Williams and Wilkins, Philadelphia, PA., USA., pp: 240-241.
42. Hariharan, V. and S. Rangaswami, 1970. Structure of saponines. A and B from the seeds of *Achyranthes aspera*. Phytochemistry, 9: 409-414.
43. Dwivedi, S., 2007. Relivance of medicinal herbs used in traditional system of medicine.
44. Nadkarni, K.M., 2005. Indian Materia Medica. Vol - 1, Bombay Popular Prakashan, Mumbai, pp: 21-22.
45. Niranjana S., D.K. Alok, M.K. Somya, G. Piriyanka and M.S. Susri, 2012. Diuretic activity of *Achyranthes aspera* leaves extracts. Int. Res. J. Pharm., 3: 216-218.
46. Block, E., 2010. Garlic and Other Alliums: The Lore and the Science. Royal Society of Chemistry, Cambridge, UK., ISBN-13: 9780854041909.

47. Newall, C.A., L.A. Anderson and J.D. Phillipson, 1996. Herbal Medicines: A Guide for Health-Care Professionals. Pharmaceutical Press, London, ISBN: 9780853692898, Pages: 296.
48. Fallon, M., G. Abrams, T. Abdel-Razek, J. Dai and S. Chen et al., 1998. Garlic prevents hypoxic pulmonary hypertension in rats. *Am. J. Physiol.*, 275: L283-287.
49. Pedraza-Chaverri, J., E. Tapia, O.N. Medina-Campos, M. de los Angeles Granados and M. Franco, 1998. Garlic prevents hypertension induced by chronic inhibition of nitric oxide synthesis. *Life Sci.*, 62: 71-77.
50. Lash, J.P., L.R. Cardoso, P.M. Mesler, D.A. Walczak and R. Pollak, 1998. The effect of garlic on hypercholesterolemia in renal transplant patients. *Transplant. Proc.*, 30: 189-191.
51. Schulz, V., R. Hansel and V.E. Tyler, 1979. Rational Phytotherapy: A Physicians Guide to Herbal Medicine. Springer, Berlin, Germany, Pages: 306.
52. Korotkov, V.M., 1966. The effect of garlic juice on blood pressure. *Vrach. Delo.*, 6: 123.
53. Martin, N., L. Bardisa, C. Pantoja, R. Roman and M. Vargas, 1992. Experimental cardiovascular depressant effects of garlic (*Allium sativum*) dialysate. *J. Ethnopharmacol.*, 37: 145-149.
54. Wolf, S., M. Reim and F. Jung, 1990. Effect of garlic on conjunctival vessels: A randomised, placebo-controlled, double-blind trial. *Br. J. Clin. Pract. Suppl.*, 69: 36-39.
55. Lakshmi, T., A. Roy, K.D. Manjusha, 2011. Coping with hypertension using safer herbal medicine: A therapeutic review. *Int. J. Drug. Dev. Res.*, 3: 31-57.
56. Silagy, C.A. and H.A. Neil, 1994. A meta-analysis of the effect of garlic on blood pressure. *J. Hypertens.*, 12: 463-468.
57. Siegel, G., A. Walter, S. Engel, A. Walper and F. Michel, 1999. Pleiotropic effects of garlic. *Wien Med. Wochenschr.*, 149: 217-224.
58. Bhavan, B.V., 1992. Selected Medicinal Plants of India. Tata Press, Bombay, India, Pages: 387.
59. Gohil, K.J., J.A. Patel and A.K. Gajjar, 2010. Pharmacological review on *Centella asiatica*: A potential herbal cure-all. *Indian J. Pharm. Sci.*, 72: 546-556.
60. Sairam, K., C.V. Rao and R.K. Goel, 2001. Effect of *Centella asiatica* Linn on physical and chemical factors induced gastric ulceration and secretion in rats. *Indian J. Exp. Biol.*, 39: 137-142.
61. Cheng, C.L. and M.W.L. Koo, 2000 Effects of *Centella asiatica* on ethanol induced gastric mucosal lesions in rats. *Life Sci.*, 67: 2647-2653.
62. Chaudhury, S., S. Hazra, G.C. Podder, S. Poddar and S. Sarkar et al., 1987. New multidrug regimen with indigenous drugs and dapsone in the treatment of lepromatous leprosy (preliminary report). *Indian J. Dermatol.*, 32: 63-67.
63. Sasaki, S., H. Shinkai, Y. Akashi and Y. Kishihara, 1972. Studies on the mechanism of action of asiaticoside (Madecassol) on experimental granulation tissue and cultured fibroblasts and its clinical application in systemic scleroderma. *Acta Derm. Venereol.*, 52: 141-150.
64. Darnis, F., Orce, P.P. de Saint-Maur and P. Mamou, 1979. Use of a titrated extract of *Centella asiatica* in chronic hepatic disorders. *Sem. Hop.*, 55: 1749-1750.
65. Leung, A.Y. and S. Foster, 1998. Encyclopedia of Common Natural Ingredients Used in Food, Drugs and Cosmetics. 2nd Edn. John Wiley and Son, New York, Pages: 284.
66. Widgerow, A.D., L.A. Chait, R. Stals and P.J. Stals, 2000. New innovations in scar management. *Aesth. Plast. Surg.*, 24:227-234.
67. Ahmad, B.F. and G. Ismail, 2003. Medicinal plants used by Kadazandusun communities around crocker range. ASEAN Review of Biodiversity and Environmental Conservation (ARBEC). <http://www.arbec.com.my/pdf/art1janmar03.pdf>.
68. Belcaro, G.V., R. Grimaldi and G. Guidi, 1990. Improvement of capillary permeability in patients with venous hypertension after treatment with TTFCA. *Angiology*, 41:533-540.
69. Taguchi, S., 2007. Hypoglycemic and antihypertensive activities of *Centella asiatica*. Associate J. Jpn. Soc. Med. Funct. Foods, 4: 109-114.
70. Cesarone, M.R., G. Belcaro, A. Rulo, M. Griffin and A. Ricci et al, 2001. Microcirculatory effects of total triterpenic fraction of *Centella asiatica* in chronic venous hypertension: Measurement by laser Doppler, TcPO₂-CO₂ and leg volumetry. *Angiology*, 52:S45-S48.
71. Weihmayr, T. and E. Ernst, 1996. Therapeutic effectiveness of crataegus. *Fortscher Med.*, 114: 27-29.
72. Blumenthal, M., A. Goldberg and J. Brinckmann, 2000. Herbal Medicine Integrative Medicine Communications. American Botanical Council, USA., pp: 182-192.
73. Daniele, C., G. Mazzanti, M.H. Pittler and E. Ernst, 2006. Adverse-event profile of *Crataegus* sp.: A systematic review. *Drug Saf.*, 29: 523-535.
74. Duke, J.A., 1985. Hand Book of Medicinal Herbs. CRC Press, Boca Raton, Florida, pp: 146-147.
75. Mills, S. and K. Bone, 2000. Principles and Practices of Phytotherapy: Modern Herbal Medicine. Churchill livingstone, Edinburg, UK., ISBN-13: 9780443060168, pp: 439-447.
76. Lakshmi, T., R.V. Geetha and A. Roy, 2012. *Crataegus oxyacantha* Linn. commonly known as Hawthorn: A scientific review. *Int. J. PharmTech. Res.*, 4: 458-465.
77. Schussler, M., J. Holzl and U. Fricke, 1995. Myocardial effects of flavonoids from *Crataegus* species. *Arzneimittelforschung*, 45: 842-845.

78. Uchida, S., N. Ikari, H. Ohta, M. Niwa, G. Nonaka, I. Nishioka and M. Ozaki, 1987. Inhibitory effects of condensed tannins on angiotensin converting enzymes. *Jpn. J. Pharmacol.*, 43: 242-246.
79. Walker F.A., G. Marakis, A.P. Morris and P.A. Robinson, 2002. Promising hypotensive effect of hawthorn extract: A randomized double blind pilot study of mild, essential hypertension. *Phytother. Res.*, 16: 48-54.
80. Drieu, K. and H. Jaggy, 2000. History, Development and Constituents of EGb 761. In: *Medicinal and Aromatic Plants-Industrial Profiles: Ginkgo Biloba*, Beek, van T.A. (Ed.). Harwood Academic Publishers, Amsterdam, pp: 267-277.
81. Agrawal, M., D. Nandini, V. Sharma and N.S. Chauhan, 2010. Herbal remedies for treatment of hypertension. *Int. J. Pharma. Sci. Res.*, 1: 1-21.
82. Yan, L.J., M.T. Droy-Lefaix and L. Packer, 1995. *Ginkgo biloba* extract (EGb 761) protects human low density lipoproteins against oxidative modification mediated by copper. *Biochem. Biophys. Res. Commun.*, 212: 360-366.
83. Rong, Y., Z. Geng and B.H. Lau, 1996 *Ginkgo biloba* attenuates oxidative stress in macrophages and endothelial cells. *Free Radic. Biol. Med.*, 20:121-127.
84. Le Bars, P.L., M.M. Ketz, N. Bermann, A.M. Freedman and A.F. Schatzberg, 1997. A placebo-controlled, double-blind, randomized trial of an extract of *Ginkgo biloba* for dementia: North American EGb Study Group. *JAMA*, 278:1327-1332.
85. Jung, F., C. Mrowietz, H. Kiesewetter and E. Wenzel, 1990. Effect of *Ginkgo biloba* on fluidity of blood and peripheral microcirculation in volunteers. *Arzneimittelforschung*, 40: 589-593.
86. Umegaki, K., K. Shinozuka, K. Watarai, H. Takenaka, M. Yoshimura, P. Daohua and T. Esashi, 2000. *Ginkgo biloba* extract attenuates the development of hypertension in deoxycorticosterone acetate-salt hypertensive rats. *Clin. Exp. Pharmacol. Physiol.*, 27: 277-282.
87. Dhawan, K., S. Dhawan and A. Sharma, 2004. *Passiflora*: A review update. *J. Ethnopharmacol.*, 94:1-23.
88. Beninca, J.P., A.B. Montanher, S.M. Zucolotto, E.P. Schenkel and T.S. Frode, 2007. Evaluation of the anti-inflammatory efficacy of *Passiflora edulis*. *Food Chem.*, 104: 1097-1105.
89. Joshi, U.H., T.H. Ganatra, P.N. Bhalodiya, T.R. Desai and P.R. Tigar, 2012. Comparative review on harmless herbs with allopathic remedies as Anti-hypertensive. *Res. J. Pharm. Biol. Chem. Sci.*, Vol. 3.
90. Kinghorn, G.R., 2001. Passion, stigma and STI. *Sex Transm. Inf.*, 77: 370-75.
91. Patel, S.S., 2009. Morphology and pharmacology of *Passiflora Edulis*: A review. *J. Herbal Med. Toxicol.*, 3: 175-181.
92. Patel, S.S., N.K. Verma and K. Gauthaman, 2009. *Passiflora Incarnata* Linn: A review on morphology, phytochemistry and pharmacological aspects. *Pharmacogn. Rev.*, 3: 186-192.
93. Patel, S.S., N.K. Verma, V.Ravi, K. Gauthaman and N. Soni, 2010. Antihypertensive effect of an aqueous extract of *passiflora nepalensis* wall. *Int. J. Applied Res. Nat. Prod.*, 3: 22-27.
94. Patel, S.S., N.K. Verma, B. Shrestha and K. Gauthaman, 2011. Antihypertensive effect of methanolic extract of *Passiflora nepalensis*. *Rev. Bras. Farmacogn.*, Vol.21.
95. Marwat, S.K., M.A. Khan, A. Khan, M. Ahmad, M. Zafar, F.U. Rehman and S. Sultana, 2009. Vegetables mentioned in the Holy Quran and Ahadith and their ethnomedicinal studies in Dera Ismail Khan, N.W.F.P., Pakistan. *Pak. J. Nutr.*, 8: 530-538.
96. Akram, M., M.I. Shah, K. Usmanghan, E. Mohiuddin and A. Sami *et al.*, 2011. *Zingiber officinale roscoe* (A medicinal plant). *Pak. J. Nutr.*, 10: 399-400.
97. Adebolu, T.T., P.T. Adeboye and N.B. Adegbola, 2007. Evaluation of a traditional decoction made from *Psidium guajava* and *Zingiber officinale* for anti bacterial activity. *Res. J. Microbiol.*, 2: 954-959.
98. Stoilova, I., A. Krastanor, A. Stoyanova, P. Denev and S. Gargova, 2007. Antioxidant activity of a ginger extract (*Zingiber officinale*). *Food Chem.*, 102:764-770.
99. Lee, H.S., E.Y. Seo, N.E. Kang and W.K. Kim, 2008. [6]-Gingerol inhibits metastasis of MDA-MB-231 human breast cancer cells. *J. Nutr. Biochem.*, 19: 313-319.
100. Ajith, T.A., U. Hema and M.S. Ashwathy, 2007. *Zingiber officinale* Roscoe Prevents acetaminophen-induced acute hepatotoxicity by enhancing hepatic antioxidant status. *Food Chem. Toxicol.*, 45: 2267-2272.
101. Ajith, T.A., V. Nivitha and S. Usha, 2007. *Zingiber officinale* Roscoe alone and in combination with β -tocopherol protect the kidney against cisplatin-induced acute renal failure. *Food Chem. Toxicol.*, 45: 921-927.
102. Ghayur, M.N. and A.H. Gilani, 2005. Ginger lowers blood pressure through blockade of voltage-dependent calcium channels. *J. Cardiovasc. Pharmacol.*, 45: 74-80.
103. Uddin R., 2011. Drug and herb interactions with ginger for rheumatoid arthritis. <http://www.livestrong.com/article/408697-drug-herb-interactions-with-ginger-for-rheumatoid-arthritis/>
104. Suekawa, M., A. Ishige, K. Yuasa, K. Sudo, M. Aburada and E. Hosoya, 1984. Pharmacological studies on ginger. I. Pharmacological actions of pungent constituents, (6)-gingerol and (6)-shogaol. *J. Pharmacobiodyn.*, 7: 836-848.

105. Leung, A.Y. and S. Foster, 1996. Encyclopedia of Common Natural Ingredients Used in Food, Drugs and Cosmetics.. 2nd Edn., John Wiley and Sons, Inc., New York, USA.
106. Chopra, R.N., S.L. Nayar and I.C. Chopra, 1986, Glossary of Indian Medicinal Plants, Council of Scientific and Industrial Research, New Delhi, 1986
107. Manandhar, N.P. and S. Manandhar, 2002 Plants and People of Nepal. Timber Press, Oregon, ISBN: 13-9780881925272, Pages: 599.
108. Muller, B.M. and G. Franz, 1992. Chemical structure and biological activity of polysaccharides from *Hibiscus sabdariffa*. Plant Med., 58:60-67
109. McKay, D.L., C.Y. Chen, E. Saltzman and J.B. Blumberg, 2010. *Hibiscus sabdariffa* L. tea (tisane) lowers blood pressure in prehypertensive and mildly hypertensive adults. J. Nutr., 140:298-303
110. Herrera-Arellano, A., S. Flores-Romero, M.A. Chavez-Soto and J. Tortorie-Ilo., 2004. Effectiveness and tolerability of a standardized extract from *Hibiscus sabdariffa* in patients with mild to moderate hypertension: A controlled and randomized clinical trial. Phytomedicine, 11: 375-82.
111. Ajay, M., H.J. Chai, A.M. Mustafa, A.H. Gilani and M.R. Mustafa, 2007. Mechanisms of the anti-hypertensive effect of *Hibiscus sabdariffa* L. calyces. J. Ethnopharmacol., 109: 388-93.
112. Pandey, G., 2004. Dravyaguna-Vijnana: Materia Medica-Vegetable Drugs. Krishnadas Ayurveda Series. 48, Part III, Krishnadas Academy, Varanasi, pp: 261-262
113. Khare, C.P., 2004. Encyclopedia of Medicinal Plants. Spring Publication, New York, Pages: 198.
114. Asolkar, L.V., K.K. Kakkar and O.J. Chakre, 1992. Second Supplement to Glossary of Indian Medicinal Plant with Active Principles. Vol. 1, Publication and Information Directorate, CSIR, New Delhi, Pages: 177.
115. Dasgupta, A., S.S. Agrawal and D.K. Basu, 1984. Anticonvulsant activity of the mixed fatty acids of the *Elaeocarpus ganitrus* Roxb. Indian J. Phyiol. Pharmacol., 28: 245-286.
116. Satyavati, G.V., M.K. Raina and M. Sharma, 1976. Medicinal Plants of India. Vol. 1, Indian Council of Medical Research, New Delhi, pp: 370-71.
117. Singh, R.K., S.B. Acharya and S.K. Bhattacharya, 2000. Pharmacological activity of *Elaeocarpus sphaericus*. Phytother Res., 14: 36-39.
118. Bhattacharya, S.K., P.K. Debnath, V.B. Pandey and A.K. Sanyal, 1975. Pharmacological investigations on *Elaeocarpus ganitrus*. Planta Medica, 28: 174-177.
119. Sarkar, P.K., S.S. Sengupta and S.S. Bhattacharya, 1972. Effect of *Elaeocarpus ganitrus* Roxb. seeds on blood pressure. Indian J. Pharma., 4: 128-135.
120. Singh, R.K. and B.L. Pandey, 1999. Anti-inflammatory activity of *Elaeocarpus sphaericus* fruit extract in rats. J. Med. Arom. Plant Sci., 21: 1030-1032.
121. Pandey, V.B. and S.K. Bhattacharya, 1985. Scientific appraisal of rudraksha (*Elaeocarpus ganitrus*): Chemical and pharmacological studies. J. Res. Educ. Indian Med., 1985, Jan-June, 47-50.
122. Ray, A.B., L. Chand and V.B. Pandey, 1979. Rudrakine: A new alkaloid from *Elaeocarpus ganitrus*, Phytochemistry, 18: 700-701.
123. Sakat, S.S., S.S. Wankhede, A.R. Juvekar, V.R. Mali and S.L. Bodhankar, 2009. Antihypertensive effect of aqueous extract of *Elaeocarpus ganitrus* Roxb. seeds in renal artery occluded hypertensive rats. Int. J. PharmTech. Res., 1: 779-782.
124. Niazmand, S., M. Esparham, S.A. Rezaee and F. Harandizadeh, 2011. Hypotensive effect of *Achillea wilhelmsii* aqueous-ethanolic extract in rabbit. Avicenna J. Phytomed., 1: 51-56
125. Trivedi, P.C., 2009. Indian Medicinal Plants. Avishkar Publisher, India.
126. Choudhary, M.I., S. Jalil, M. Todorova, A. Trendafilova, B. Mikhova, H. Duddeck and Attatur-Rahman, 2007. Inhibitory effect of lactone fractions and individual components from three species of the *Achillea millefolium* complex of Bulgarian origin on the human neutrophils respiratory burst activity. Nat. Prod. Res., 21: 1032-1036.
127. Skwarek, T., 1979. Effects of Herbal Preparations on the propagation of influenza viruses. Acta Polon. Pharm., 36: 1-7.
128. Asgary, S., G.H. Naderi, N. Sarrafzadegan, N. Mohammadifard, S. Mostafavi and R. Vakili, 2000. Antihypertensive and antihyperlipidemic effects of *Achillea wilhelmsii*. Drugs Exp. Clin. Res., 26: 89-93.
129. Komai, R., T. Obara, T. Ohkubo, T. Kato and M. Kikuya *et al.*, 2007. Factors affecting heart rate as measured at home among treated hypertensive patients: The Japan home versus office blood pressure measurement evaluation (J-HOME) study. *Hypertens. Res.*, 30: 1051-1057.
130. Burroughs, A.K., 2011. The Hepatic Artery, Portal Venous System and Portal Hypertension: the Hepatic Veins and Liver in Circulatory Failure. In: Sherlock's Diseases of the Liver and Biliary System, Dooley, J.S., A. Lok, A. Burroughs and J. Heathcote (Eds.). 12th Edn., John Wiley and Sons, New York, pp: 152-209.
131. Buck, C.W. and A.P. Donner, 1987. Factors affecting the incidence of hypertension. CMAJ, 136: 357-360.

132. Banday, A.A. and M.F. Lokhandwala, 2011. Oxidative stress causes renal angiotensin II type 1 receptor upregulation, Na⁺/H⁺ exchanger 3 overstimulation and hypertension. *Hypertension*, 57: 452-459.
133. Banday, A.A., F.R. Fazili and M.F. Lokhandwala, 2007. Oxidative stress causes renal dopamine D1 receptor dysfunction and hypertension via mechanisms that involve nuclear factor- κ B and protein kinase C. 18: 1446-1457
134. Khullar, M., V. Relan and B.S. Sherawat, 2004. Antioxidant activities and oxidative stress byproducts in human hypertension. *Hypertension*, 43: e7-e8
135. Kitiyakara, C. and C.S. Wilcox, 1998. Antioxidants for hypertension. *Curr. Opin. Nephrol. Hypertens.*, 7: 531-538.
136. Hasani-Ranjbar, S., B. Larijani and M. Abdollahi, 2009a. A systematic review of the potential herbal sources of future drugs effective in oxidant-related diseases. *Inflamm. Allergy Drug Targets*, 8: 2-10.
137. Hasani-Ranjbar, S., N. Nayeibi, B. Larijani and M. Abdollahi, 2009b. A systematic review of the efficacy and safety of herbal medicines used in the treatment of obesity. *World J. Gastroenterol.*, 15: 3073-3085.
138. Hasani-Ranjbar, S., N. Nayeibi, B. Larijani and M. Abdollahi, 2010a. A systematic review of the efficacy and safety of *Teucrium* Species; from anti-oxidant to anti-diabetic effects. *Int. J. Pharmacol.*, 6: 315-325.
139. Hasani-Ranjbar, S., N. Nayeibi, L. Moradi, A. Mehri, B. Larijani and M. Abdollahi, 2010b. The efficacy and safety of herbal medicines used in the treatment of hyperlipidemia: A systematic review. *Curr. Pharm. Des.*, 16: 2935-2947.
140. Hasani-Ranjbar, S., H. Vahidi, S. Taslimi, N. Karimi, B. Larijani and M. Abdollahi, 2010c. A systematic review on the efficacy of herbal medicines in the management of human drug-induced hyperprolactinemia; Potential sources for the development of novel drugs. *Int. J. Pharmacol.*, 6: 691-695.
141. Hasani-Ranjbar, S., S. Khosravi, N. Nayeibi, B. Larijani and M. Abdollahi, 2012. A systematic review of the efficacy and safety of anti-aging herbs in animals and human. *Asian J. Anim. Vet. Adv.*, 7: 621-640.
142. Hosseini, A., M. Abdollahi, 2012. It is time to formulate an antioxidant mixture for management of diabetes and its complications: Notice for pharmaceutical industries. *Int. J. Pharmacol.*, 8: 60-61.
143. Mehri, A., S. Hasani-Ranjbar, B. Larijani and M. Abdollahi, 2011. A systematic review of efficacy and safety of *urtica dioica* in the treatment of diabetes. *Int. J. Pharmacol.*, 7: 161-170.
144. Momtaz, S. and M. Abdollahi, 2010. An update on pharmacology of *Satureja* species; from antioxidant, antimicrobial, antidiabetes and anti-hyperlipidemic to reproductive stimulation. *Int. J. Pharmacol.*, 6: 346-353.
145. Momtaz, S. and M. Abdollahi, 2012. A comprehensive review of biochemical and molecular evidences from animal and human studies on the role of oxidative stress in aging: An epiphenomenon or the cause. *Asian J. Anim. Vet. Adv.*, 7: 1-19.
146. Rahimi, R., M.R. Shams-Ardekani and M. Abdollahi, 2010. A review of the efficacy of traditional Iranian medicine for inflammatory bowel disease. *World J. Gastroenterol.*, 16: 4504-4514.
147. Rahimi, R., S. Mozaffari and M. Abdollahi, 2009. On the use of herbal medicines in management of inflammatory bowel diseases: A systematic review of animal and human studies. *Digest. Dis. Sci.*, 54: 471-480.
148. Rahimi, R. and M. Abdollahi, 2012. Herbal medicines for the management of irritable bowel syndrome: A comprehensive review. *World J. Gastroenterol.*, 18: 589-600.
149. Rezaie, A., R.D. Parker and M. Abdollahi, 2007. Oxidative stress and pathogenesis of inflammatory bowel disease: An epiphenomenon or the cause? *Digest. Dis. Sci.*, 52: 2015-2021.
150. Sarwar, M., I.H. Attitalla and M. Abdollahi, 2011. A review on the recent advances in pharmacological studies on medicinal plants; animal studies are done but clinical studies needs completing. *Asian J. Anim. Vet. Adv.*, 6: 867-883.
151. Salari, P. and M. Abdollahi, 2011. A comprehensive review of the shared roles of inflammatory cytokines in osteoporosis and cardiovascular diseases as two common old people problem; actions toward development of new drugs. *Int. J. Pharmacol.*, 7: 552-567.
152. Srivastav, S., P. Singh, K.K. Jha, G. Mishra, S. Srivastava, M.S. Karchuli and R.L. Khosa, 2011. Diuretic activity of whole plant extract of *Achyranthes aspera* Linn. *Europ. J. Exp. Biol.*, 1: 97-102.
153. Dubey, S., V.K. Verma, A.K. Sahu and A.K. Jain, 2010. Evaluation of diuretic activity of aqueous and alcoholic rhizomes extracts of *Costus speciosus* linn in wister albino rats. *Int. J. Res. Ayurveda Pharmacy*, 1: 648-652.
154. Brinkley, T.E., J.F. Lovato, A.M. Arnold, C.D. Furberg and L.H. Kuller *et al.*, 2010. Effect of Ginkgo biloba on blood pressure and incidence of hypertension in elderly men and women. *Am. J. Hypertens.*, 23 (5): 528-533.