

## **ANTIHYPERTENSIVE PROPERTIES OF SOME SELECTED MEDICINAL PLANT**

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### **ABSTRACT**

Traditional medicine is a comprehensive term for ancient, culture-bound health care practices that existed before the use of science in health matters and has been used for centuries. Medicinal plants are used to treat patients with hypertension diseases, hypertension, and heart failure. Hypertension causes difficulty in the functioning of the heart and is involved in atherosclerosis, raising the risk of heart attack and stroke. Many drugs are available for managing these diseases, though common antihypertensive drugs are generally accompanied by many side effects. Medicinal herbs have several active substances with pharmacological and prophylactic properties that can be used in the treatment of hypertension. This review presents an overview of some medicinal plants that have been shown to have hypotensive or antihypertensive properties.

**Keywords:** Traditional medicine, Hypertension, medicinal plants,

### **1. INTRODUCTION**

Phytomedicine can be defined as the herbal medicine with therapeutic and healing properties. It came into existence since the advent of human civilization. Sheng Nongs Herbal Book is known as one of the preliminary sources of traditional folk knowledge based on the use of herbs in China and dates back to around 3000 BC. It encompasses the details of almost 365 plants, animals, and minerals that find a place in medication. Our Earth houses approximately 420,000 species of plants; however, there is a lack of appropriate knowledge about them and their varied uses. There are three major areas, namely, food (foodstuffs), medicine (folk and traditional medicines), and research (phytochemical analysis), that predominantly find an immense use of herbal preparations and products and hence can be explored further. Gaining experience from random trials and careful observations from animal studies, people belonging to ancient periods started employing herbs as a therapeutic method against several illnesses. Based on this, the ever so popular Chinese herbal medicine (CHM) as well as Indian herbal medicine, native to and prominently developed in ancient China, Japan, Korea, and India, continue to rule and influence the modern health-care even today. As per the estimate of World Health Organization (WHO), herbal medicines are one of the most sought after primary health-care for around 3.5–4 billion people across the world, and a major portion of traditional medicine involves the plant extract-derived medicines and decoction which may also be termed as the “modern herbal medicine”.

A herbal medicine or a phyto pharmaceutical preparation can be defined as a medicine derived exclusively from a whole plant or parts of plants and manufactured in a crude form or as a purified pharmaceutical formulation. Although with the setting in of the industrial revolution and the advancements in organic chemistry, there was an equivalent increase in the preference for synthetic products as well.

Hypertension, or high blood pressure, is a prevalent and significant public health concern globally, often associated with an increased risk of cardiovascular diseases and other related complications. While conventional pharmaceutical interventions are commonly employed to manage hypertension, there is growing interest in exploring alternative and complementary approaches, including the use of Phytomedicine medicines derived from plants.

Hypertension is a major public health problem due to its high prevalence all around the globe. Around 7.5 million deaths or 12.8% of the total of all annual deaths worldwide occur due to high blood pressure. It is predicted to be increased to 1.56 billion adults with hypertension in 2025.

Raised blood pressure is a major risk factor for chronic heart disease, stroke, and coronary heart disease. Elevated BP is positively correlated to the risk of stroke and coronary heart disease. Other than coronary heart disease and stroke, its complications include heart failure, peripheral vascular disease, renal impairment, retinal hemorrhage, and visual impairment.

Hypertension (or HTN) or high blood pressure is defined as abnormally high arterial blood pressure. According to the Joint National Committee 7 (JNC7), normal blood pressure is a systolic BP < 120 mmHg and diastolic BP < 80 mm Hg. Hypertension is defined as systolic BP level of  $\geq 140$  mmHg and/or diastolic BP level  $\geq 90$  mmHg. The

grey area falling between 120–139 mmHg systolic BP and 80–89 mmHg diastolic BP is defined as “prehypertension”. Although prehypertension is not a medical condition in itself, prehypertensive subjects are at more risk of developing HTN.

It is a silent killer as very rarely any symptom can be seen in its early stages until a severe medical crisis takes place like heart attack, stroke, or chronic kidney disease. Since people are unaware of excessive blood pressure, it is only through measurements that detection can be done. Although majority of patients with hypertension remain asymptomatic, some people with HTN report headaches, lightheadedness, vertigo, altered vision, or fainting episode.

## **2. MEDICINAL PLANTS USED IN PREVENTION OF HYPERTENSION**

### **Allium sativum (garlic)**

Allium sativum is a plant that belongs to the family Liliaceae. The biological source of garlic is the bulb, which is the underground storage organ of the plant. The bulb is composed of multiple cloves enclosed in a papery sheath.



#### **Chemical constituents**

Organosulfur compounds in garlic such as allicin and s-allyl cysteine are thought to be the main bioactive compounds responsible for the management of blood pressure and dyslipidemia. These compounds have been shown to inhibit transcription factor NF- $\kappa$ B and angiotensin converting enzyme, whilst enhancing the production of the vasodilatory compounds hydrogen sulphide and nitric oxide, mechanisms by which the herb is thought to reduce blood pressure and oxidative stress.

**Allicin:** Allicin is a sulfur-containing compound that is released when garlic is crushed or chopped. It has antimicrobial properties and is considered one of the major bioactive compounds in garlic. **S-allyl cysteine:** This is a water-soluble compound formed during the aging and processing of garlic. It is believed to contribute to some of the potential health benefits of garlic.

#### **Medicinal uses**

Garlic is used to treat a variety of diseases around the world, including high blood pressure, infections, and snakebites, and it has also been used to ward off evil spirits and has antimicrobial effects in some cultures. Garlic inhibits and destroys bacteria, fungus, and parasites, as well as lowers blood pressure, cholesterol, and sugar levels, preventing blood clotting and protecting the liver. It also has anticancer effects. Garlic can also help to improve the immune system, prevent sickness, and preserve good health. It can activate the lymphatic system, which aids in the evacuation of waste from the body. Furthermore, it is a powerful antioxidant and can help protect cells from free radical damage. In particular, the heart, stomach, circulation, and lungs are also aided and supported by it. Garlic is an efficient natural agent in the treatment of wound infections caused by the common cold, malaria, cough, and pulmonary TB, as well as high blood pressure, sexually transmitted diseases, mental disorders, kidney and liver problems, asthma, and diabetes.

#### **Antihypertensive activity**

A recent meta-analysis on the effects of garlic supplements on blood pressure, including 20 trials and >900 participants, revealed a significant effect of garlic on blood pressure, with an average decrease in SBP of 8.6 mm and 6.1 mm in DBP in hypertensive subjects (n=14 trial arms, n=468 participants). Our first clinical trial including a prehypertensive group of adults (SBP  $\geq$ 130 mmHg) revealed that Kyolic garlic significantly reduced blood pressure in the hypertensive subgroup (SBP  $\geq$ 140 mmHg), but not in the normotensive subgroup (SBP <140 mmHg). This suggests that Kyolic aged garlic extract normalises blood pressure, in contrast to standard blood pressure medications, including angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), beta blockers (BBs), calcium channel blockers (CCBs), diuretics (Ds), which may sometimes lead to hypotension.

Our second dose-response trial revealed that a dose of 2 capsules/day of Kyolic aged garlic extract was sufficient to achieve an average blood pressure-lowering effect of 10 mmHg systolic and 5 mmHg diastolic, within 2–3 months. By contrast, 1 capsule per day was insufficient, whereas 4 capsules/day were not superior to 2 capsules/day. Two capsules of the High Potency Formula of Kyolic (Wagner/Nutrlife available in Australia/New Zealand) contains 480 mg of concentrated aged garlic extract powder and 1.2 mg S-allyl cysteine (SAC) and are equivalent to 2 capsules of the

Reserve Formula of Kyolic (Wakunaga of America available in the USA), containing 1.2 g of aged garlic extract powder and 1.2 mg of SAC. In our third 'AGE at Heart' trial we found Kyolic to be effective in reducing peripheral blood pressure, as well as central blood pressure, central pulse pressure, pulse wave velocity and arterial stiffness.

### **Curcuma longa (turmeric)**

Turmeric, Curcuma longa, a rhizomatous herbaceous perennial plant belonging to the family Zingiberaceae,



### **Chemical constituents**

Turmeric, and its active compound curcumin, has been studied for its potential health benefits, including its effects on hypertension (high blood pressure). Curcumin, the primary active compound in turmeric, has been investigated for its potential antihypertensive (blood pressure-lowering) effects. While the research is ongoing and not conclusive, there is some evidence to suggest that curcumin may influence factors related to blood pressure regulation.

Turmeric is a medicinal plant that belongs to the ginger family (Zingiberaceae) that is distributed throughout subtropical and tropical regions of the world and that is broadly growing in Asian countries such as China and India. This plant contains mainly fats (5.1%), protein (6.3%), carbohydrates (69.4%), minerals (3.5%), and moisture content. Curcumin also includes three curcuminoids (bisdemethoxycurcumin, 10% up to 15%; demethoxycurcumin, 20% up to 27%; and curcumin, 60% up to 70%). Curcumin (1,7-bis (4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) or diferuloylmethane is an important bioactive constituent and hydrophobic polyphenol that isolated from the rhizome of the turmeric plant.

### **Medicinal uses**

In folk medicine, turmeric has been used in therapeutic preparations over the centuries in different parts of the world. In Ayurvedic practices, turmeric is thought to have many medicinal properties including strengthening the overall energy of the body, relieving gas, dispelling worms, improving digestion, regulating menstruation, dissolving gallstones, and relieving arthritis. Many South Asian countries use it as an antiseptic for cuts, burns, and bruises, and as an antibacterial agent. In Pakistan, it is used as an anti-inflammatory agent, and as a remedy for gastrointestinal discomfort associated with irritable bowel syndrome and other digestive disorders. In Pakistan and Afghanistan, turmeric is used to cleanse wounds and stimulate their recovery by applying it on a piece of burnt cloth that is placed over a wound. Indians use turmeric, in addition to its Ayurvedic applications, to purify blood and remedy skin conditions. Turmeric paste is used by women in some parts of India to remove superfluous hair. Turmeric paste is applied to the skin of the bride and groom before marriage in some parts of India, Bangladesh, and Pakistan, where it is believed to make the skin glow and keep harmful bacteria away from the body. Turmeric is currently used in the formulation of several sunscreens. Several multinational companies are involved in making face creams based on turmeric.

In Ayurvedic medicine, turmeric is a well-documented treatment for various respiratory conditions (e.g., asthma, bronchial hyperactivity, and allergy), as well as for liver disorders, anorexia, rheumatism, diabetic wounds, runny nose, cough, and sinusitis. In traditional Chinese medicine, it is used to treat diseases associated with abdominal pain. From ancient times, as prescribed by Ayurveda, turmeric has been used to treat sprains and swelling. In both Ayurvedic and traditional Chinese medicine, turmeric is considered a bitter digestive and a carminative. Unani practitioners also use turmeric to expel phlegm or kapha, as well as to open blood vessels in order to improve blood circulation. It can be incorporated into foods, including rice and bean dishes, to improve digestion and reduce gas and bloating.

### **Antihypertensive activity**

To investigate the physiological significance of the regulation of curcumin on AT<sub>1</sub>R expression, we established an Ang II-induced hypertension model in C57Bl/6J mice. Eight-week-old mice (weight 20 g ± 0.89) were divided into three groups: control, Ang II (490 ng/min/kg), and Ang II (490 ng/min/kg) + curcumin (300 mg/kg/d). Ang II was administered subcutaneously via an osmotic minipump (Model 1004, ALZET Osmotic Pumps, CA) for one week. Curcumin was suspended in normal saline, and the mice were given the suspension by oral gavage once per day; normal saline was used as a control. After one week, the blood pressure and heart rate were measured using the tail-cuff method. The blood pressures of the Ang II-treated mice (SBP: 150 ± 6.24 mmHg, DBP: 86 ± 17.61 mmHg) were

significantly higher than the Ang II + curcumin group (SBP:  $91 \pm 7.55$  mmHg, DBP:  $47 \pm 2.64$  mmHg). However, the heart rate was not significantly different between the individual groups.

#### **Zingiber officinalis (ginger)**

Ginger is a flowering plant that belongs to the Zingiberaceae family. It is native to Southeast Asia but is now cultivated in many tropical and subtropical regions around the world. The rhizome of the ginger plant is characterized by its knobby appearance, pale yellow color, and a strong, distinctive aroma and flavor.



#### **Chemical constituents**

Ginger contains several bioactive compounds. Certain components in ginger may contribute to potential blood pressure-lowering properties. Some of the bioactive compounds in ginger include: Gingerol is the main bioactive compound in fresh ginger. It has antioxidant and anti-inflammatory properties. Some studies suggest that Gingerol may contribute to the vasodilatory effects of ginger, helping to relax and widen blood vessels. Shogaol, is a compound that forms when Gingerol is dried or cooked. While it's less abundant in fresh ginger, it may still play a role in the potential health benefits of ginger, including its effects on blood pressure. Zingerone is another compound found in ginger with antioxidant properties. It may contribute to the overall cardiovascular benefits of ginger.

#### **Medicinal uses**

It is used as stomachic, carminative, aromatic, stimulant and flavouring agent. Its oil is used in mouth washes, beverages and liquor preparation. Ginger has molluscicidal effects and controls parasitic infections. It also blocks the gastro intestinal reactions and nausea feeling. It causes adsorption of toxins and increases the gastric motility. It is also effective in the control of nausea and vomiting in Hyperemesis gravidarum as well as postoperative nausea and vomiting. Ginger also possess cardiovascular activity, antiplatelet aggregation property, analgesic, antipyretic, antitussive, antibacterial, anthelmintic, fungicidal and antiulcer activity. Limed ginger is the coated ginger with lime which improves its colour and quality. It is mainly done for long storage of ginger.

#### **Antihypertensive activity**

Initial searches yielded 60 articles. After analyzing full-text papers, 2 Randomized Controlled Trials (RCTs) met the inclusion criteria. A double blind RCT (n=70) compared the effect of ginger with placebo on cardiovascular risk factors in diabetic patients. There was no significant ( $p>0.05$ ) effect on systolic nor diastolic pressure (Mean arterial blood pressure (MABP) changes was  $0.1\pm 1.1$ ). A randomized three armed safety trial (n=60) studied the effects of 50 and 100mg/kg ginger and placebo in healthy subjects. 100 mg/kg dose significantly ( $p<0.05$ ) lowered systolic BP from  $114.3\pm 3.22$  mm Hg to  $105.5\pm 3.13$  and diastolic BP from  $73.3\pm 3.35$  mm Hg to  $70.5\pm 3.39$  mm Hg within two hours.

#### **Thea sinensis (tea)**

It contains the prepared leaves and leaf buds of *Thea sinensis* (Linne) kuntz., belonging to family Theaceae. *Camellia sinensis* is an evergreen shrub or small tree native to East Asia, and it is the source of various types of tea, including green tea, black tea, white tea, oolong tea, and pu-erh tea



#### **Chemical constituents**

Tea, particularly green tea, contains various bioactive compounds that have been studied for their potential antihypertensive effects. One of the key groups of compounds responsible for these effects is polyphenols, and within polyphenols, a specific type known as catechins is often highlighted. Here are some of the important active

compounds in tea that are associated with antihypertensive properties. Catechins, are a type of flavonoid polyphenol found in tea, with epigallocatechin gallate (EGCG) being the most abundant and studied catechin. EGCG, in particular, has been linked to potential cardiovascular benefits, including vasodilation and blood pressure regulation. Theanine is an amino acid found in tea leaves, particularly in green tea. It has been suggested to have relaxing and stress-reducing properties, which may indirectly contribute to blood pressure regulation by promoting a sense of calm. Flavonoids: Besides catechins, tea contains other flavonoids, such as quercetin and kaempferol. These compounds also exhibit antioxidant and anti-inflammatory properties, which can contribute to overall cardiovascular health.

### **Medicinal uses**

The tea plant, *Camellia sinensis*, is primarily known for its role in producing the various types of tea consumed worldwide, such as green tea, black tea, white tea, oolong tea, and pu-erh tea. While the primary use of the tea plant is in the preparation of tea beverages, the consumption of tea has been associated with several potential health benefits. It's important to note that these potential benefits are often linked to the bioactive compounds found in tea leaves. Here are some medicinal uses and health benefits associated with the consumption of tea.

**Antioxidant Properties:** Tea, particularly green tea, is rich in polyphenols and catechins, which have antioxidant properties. Antioxidants help neutralize free radicals in the body and may contribute to overall health.

**Heart Health:** Some studies suggest that regular tea consumption may be associated with a lower risk of heart disease. The antioxidants in tea may contribute to improved cardiovascular health by reducing cholesterol levels and supporting blood vessel function.

**Weight Management:** Green tea, in particular, has been studied for its potential role in weight management. Some research suggests that the catechins in green tea may aid in fat burning and may help with weight loss when combined with a healthy diet and exercise.

**Mental Alertness and Focus:** Tea contains caffeine, a natural stimulant that can help improve alertness and cognitive function. The combination of caffeine and other compounds, such as L-theanine, may contribute to enhanced focus and concentration.

**Cancer Prevention:** Some studies have explored the potential anticancer properties of tea, attributing these effects to the presence of polyphenols. However, more research is needed to establish definitive conclusions.

**Bone Health:** Some studies suggest that regular tea consumption may be associated with improved bone density and a reduced risk of osteoporosis. The exact mechanisms are not fully understood and require further investigation.

**Type 2 Diabetes Management:** Some research suggests that compounds in tea may help improve insulin sensitivity and regulate blood sugar levels, potentially benefiting individuals with type 2 diabetes.

**Anti-Inflammatory Effects:** The polyphenols in tea have anti-inflammatory properties, which may be beneficial for reducing inflammation in the body.

### **Antihypertensive activity**

In a long-term follow-up study, Tong et al. recruited 1,109 Chinese men ( $n = 472$ ) and women ( $n = 637$ ) who had participated in the Jiangsu Nutrition Study (JIN). Blood pressure was measured in 2002 and 2007. Tea (green, black and total tea) consumption was quantitatively assessed at the follow-up survey in 2007. Their results showed that total tea and green tea consumption were inversely associated with five-year DBP but not SBP. In the multivariable analysis, those with a daily total tea consumption of at least 10 g had DBP readings 2.41 mmHg (Total) and 3.68 mmHg (green) lower than those who consumed no tea. There was a significant interaction between smoking and total tea/green tea consumption, and diastolic blood pressure change. Green tea consumption was inversely associated with DBP change only in non-smokers and those without central obesity. The authors concluded that the consumption of green tea is inversely associated with five-year blood pressure change in Chinese adults, an effect diminished by smoking. Yang et al. also examined the long-term effects of tea drinking on the risk of hypertension. The study was carefully designed and used a large number of people (1,507 subjects of 711 men and 796 women), and detailed information on tea consumption and other lifestyle and dietary factors associated with hypertension risk. The result showed that those who drank at least 120 mL/day (half a cup) of moderate-strength green or oolong tea for a year, had a 46% lower risk of developing hypertension than the non-tea drinkers. Amongst those who drank 120 to 599 mL/day (two and a half cups), the risk of high blood pressure was reduced by 65%. They concluded that habitual moderate strength green or oolong tea consumption of at least 120 mL/day for one year significantly reduces the risk of developing hypertension in the Chinese population. Additionally, in a double-blind trial of 111 healthy volunteers, Nantz et al. compared the effects of a standardized capsule containing 200 mg of decaffeinated catechin green tea extract with a placebo. The volunteers consumed a standardized capsule of *Camellia sinensis* compounds twice a day.

After three weeks, SBP and DBP was lowered by 5 and 4 mmHg, respectively. After three months, SBP remained significantly lower.

### **Crocus saffron (saffron)**

Saffron comes from the flower of *Crocus sativum*, commonly known as the saffron crocus. Saffron is a spice derived from the dried stigmas (the female reproductive parts) of the saffron crocus flower.



### **Chemical constituents**

Saffron contains several bioactive compounds that have been studied for their potential health benefits, including their effects on blood pressure. The key active compounds in saffron that are believed to contribute to its antihypertensive properties include:

**Crocins:** Crocins are water-soluble carotenoids that contribute to the color of saffron. These compounds have antioxidant properties and may play a role in vasodilation, potentially helping to lower blood pressure.

**Safranal:** Safranal is an aromatic compound responsible for the characteristic fragrance of saffron. It has been studied for its antioxidant and anti-inflammatory properties, which may contribute to cardiovascular health.

**Crocin and Crocetin:** These are carotenoid compounds found in saffron that have been investigated for their potential vasodilatory effects, which could help in reducing blood pressure.

**Potassium:** Saffron contains potassium, an essential mineral that plays a role in maintaining fluid balance and electrolyte levels in the body. Adequate potassium intake is associated with lower blood pressure.

**Flavonoids:** Saffron contains certain flavonoids, which are known for their antioxidant and anti-inflammatory properties. These compounds may contribute to saffron's potential cardiovascular benefits.

### **Medicinal uses**

Saffron extracts and tinctures have been used for centuries in traditional medicine for the treatment of different syndromes and diseases. Some of these uses have been antispasmodic, euphoric, sedative, carminative, diaphoretic, expectorant, stomachic, stimulant, aphrodisiac, emmenagogue and abortifacient. It was previously widely used in the treatment of genital diseases, and menstrual regulation and relief. The spice's abortive action was well known in the Middle Ages, during which it was also used by midwives in deliveries for the sedative and antispasmodic action of saffron. It has also been used to treat eye diseases, heal wounds, fractures, and joint pain and for many other uses, leading to Pliny the Elder describing it as a kind of panacea in his *Naturae Historiarum XXXVII*. The strong interest in the potential biomedical applications of these spices are precipitated by the great public health problems that currently result from the disorders saffron treats.

### **Antihypertensive activity**

Randomized clinical trials (RCTs), published between 2008 and 2020, that were conducted in Iran. The length of the intervention varied from 1 to 12 weeks, and the dosages of saffron supplementation were between 15 and 1000 mg. A cohort of 249 participants was collated in the intervention group, and 139 participants in the control group. The participants of these studies were classified as healthy volunteers, having type 2 diabetes, or with schizophrenia, asthma, or metabolic syndrome. All of the studies enrolled both sexes, and only one was exclusively conducted on men. Four studies used crocin, and the other seven studies used saffron. Two different studies that utilized multiple interventions (saffron and crocin) and dosages (200 and 400 mg) were considered as independent studies for the purposes of analysis. The results of the pooled data from ten effect sizes indicated that saffron supplementation reduced SBP (WMD:  $-0.65$  mg/dL; 95% CI:  $-1.12$  to  $-0.18$ ,  $p = 0.006$ ) compared with placebo, with moderate heterogeneity ( $I^2 = 46.9\%$ ,  $p = 0.049$ ). Moreover, subgroup analysis showed that the saffron supplementation reduced SBP in all of the subgroups, except in those who had elevated SBP ( $>120$  mmHg) (WMD:  $-0.47$  mmHg; 95% CI:  $-0.98$  to  $0.03$ ,  $p = 0.068$ ).

### **Allium cepa (onion)**

Onions (*Allium cepa*) are plants that belong to family Liliaceae. The onion is a bulbous plant with a characteristic pungent odor and a strong flavor. The edible part of the onion is the bulb, which is formed by layers of fleshy leaves.



### **Chemical constituents**

Onions contain various bioactive compounds that have been investigated for their potential health benefits, including their possible antihypertensive effects. Some of the key compounds in onions that may contribute to these effects include:

**Quercetin:** Quercetin is a flavonoid with antioxidant and anti-inflammatory properties. It is abundant in onions, especially red onions. Some studies suggest that quercetin may help relax blood vessels, leading to improved blood flow and potentially contributing to lower blood pressure.

**Sulfur Compounds:** Onions are rich in sulfur compounds, including allicin. Allicin is released when onions are chopped or crushed and has been associated with various cardiovascular benefits, including potential vasodilation and blood pressure reduction.

**Potassium:** Onions contain potassium, an essential mineral that plays a role in maintaining electrolyte balance and blood pressure regulation. Adequate potassium intake is associated with lower blood pressure.

**Flavonoids:** In addition to quercetin, onions contain other flavonoids with potential health benefits. These compounds may have antioxidant and anti-inflammatory effects that could contribute to cardiovascular health.

**Fiber:** Onions are a good source of dietary fiber, which is linked to heart health. Fiber intake is associated with lower blood pressure and improved overall cardiovascular health.

### **Medicinal uses**

Onion has been utilized for thousands of years for remedial purposes. For instance, it was used by athletes in ancient Greece for purifying their blood and rubbed down by Roman gladiators to firm up the muscles. Hippocrates, the Greek physician, prescribed onion for diuretic effect, healing wounds, and combating pneumonia. It was recommended by medieval doctors to alleviate cough, headache, snake bite, hair loss, and other diseases. In traditional medicine, onion has been used for a large variety of ailments such as headache, fever, toothache, cough, sore throat, flu, baldness, epilepsy, rash, jaundice, constipation, flatulence, intestinal worms, low sexual power, rheumatism, body pain and muscle cramps, high blood pressure, and diabetes.

### **Antihypertensive activity**

This study was designed to show the effects of onion on blood pressure in N(G)-nitro L-arginine methyl ester (L-NAME) induced-hypertensive rats and stroke prone spontaneously hypertensive rats (SHRSP) using dried onion at 5% in their diets. For the experiment with L-NAME induced-hypertensive rats, male 6-weeks-old Sprague Dawley rats were given tap water containing L-NAME to deliver 50 mg/kg BW/day. In this experiment, we found distinct antihypertensive effects of onion on the L-NAME induced-hypertensive rats and the SHRSP. Dietary onion decreased the Thio barbituric acid reactive substances (TBARS) in plasma in these hypertensive rats. Also, onion increased the nitrate/nitrite (products of nitric oxide (NO)) excreted in urine and the NO synthase (NOS) activity in the kidneys in SHRSP. These results suggested that the increased NO caused by the greater NOS activity, and additionally by the increased saving of NO by the antioxidative activity of onion, was one of the causes of the antihypertensive effect of onion in SHRSP. In the L-NAME induced hypertensive rats, onion did not significantly block the inhibition of NOS activity by L-NAME, and decreased nitrate/nitrite excretion in urine was not restored. The mechanism of the antihypertensive effect of onion probably involves increased saving of NO by antioxidative activity of onion in L-NAME induced-hypertensive rats.

### **Elettaria cardamom (cardamom)**

Cardamom, sometimes cardamom or cardamum, is a spice made from the seeds of several plants in the genera *Elettaria* and *Amomum* in the family Zingiberaceae. Both genera are native to the Indian subcontinent and Indonesia.



### **Chemical constituents**

Cardamom (*Elettaria cardamomum*) contains various bioactive compounds that contribute to its potential health benefits, including possible antihypertensive effects. While more research is needed to establish a direct link between cardamom and blood pressure regulation, some of its active compounds may play a role in cardiovascular health. Here are some key components of cardamom that have been studied:

**Essential Oils:** Cardamom contains essential oils, with the primary components being cineol, terpinene, limonene, sabinene, and terpinen-4-ol. These essential oils contribute to the characteristic flavor and aroma of cardamom.

**Terpenoids:** Terpenoids are a class of compounds found in cardamom that includes various phytochemicals. Some terpenoids have been associated with antioxidant and anti-inflammatory properties, which could potentially benefit cardiovascular health.

**Phenolic Compounds:** Cardamom contains phenolic compounds, including flavonoids. Phenolic compounds are known for their antioxidant activity, and antioxidants can help neutralize free radicals in the body, potentially reducing oxidative stress.

**Minerals:** Cardamom is a good source of minerals such as potassium. Potassium is important for blood pressure regulation, as it helps balance the effects of sodium and supports proper muscle and nerve function.

**Fiber:** While not a compound per se, cardamom does contain dietary fiber. Dietary fiber has been associated with various health benefits, including potential effects on cholesterol levels and overall cardiovascular health.

### **Medicinal uses**

Cardamom (*Elettaria cardamomum*) is a spice native to the Indian subcontinent and is well-known for its culinary uses, adding a distinct and aromatic flavor to both sweet and savory dishes. Additionally, cardamom has been traditionally used for its medicinal properties in various cultures. Some of the potential medicinal uses of cardamom include:

**Digestive Aid:** Cardamom has been traditionally used to help with digestion. It may help alleviate indigestion, bloating, and gas. Chewing on cardamom seeds or drinking cardamom tea is a common practice in some cultures to relieve digestive discomfort.

**Anti-inflammatory Properties:** Cardamom contains compounds with potential anti-inflammatory effects. These properties may contribute to its traditional use in soothing inflammation and irritation in the digestive tract.

**Antimicrobial Property:** Cardamom has demonstrated antimicrobial properties in some studies. It may possess antibacterial and antifungal effects, which could be beneficial for oral health and combating certain types of infections.

**Respiratory Health:** In traditional medicine, cardamom has been used to alleviate respiratory issues. It may help in clearing congestion, easing coughs, and promoting overall respiratory health.

**Antioxidant Effects:** Cardamom contains antioxidants, which can help neutralize free radicals in the body. Free radicals are molecules that can damage cells and contribute to aging and various diseases. The antioxidants in cardamom may contribute to its potential health benefits.

**Anti-spasmodic Properties:** Cardamom may have anti-spasmodic effects, which means it could help in relieving muscle spasms and cramps.

**Mood Enhancement:** Some studies suggest that the aroma of cardamom may have mood-enhancing properties. In aromatherapy, cardamom essential oil is sometimes used for its uplifting and calming effects.

### **Antihypertensive activity**

*Elettaria cardamomum* (L.) Maton. (Small cardamom) fruit powder was evaluated for its antihypertensive potential and its effect on some of the cardiovascular risk factors in individuals with stage 1 hypertension. Twenty, newly diagnosed individuals with primary hypertension of stage 1 were administered 3 g of cardamom powder in two divided doses for 12 weeks. Blood pressure was recorded initially and at 4 weeks interval for 3 months. Blood samples were also collected initially and at 4 weeks interval for estimation of lipid profile, fibrinogen and fibrinolysis. Total antioxidant status, however, was assessed initially and at the end of the study. Administration of 3 g cardamom powder significantly ( $p<0.001$ ) decreased systolic, diastolic and mean blood pressure and significantly ( $p<0.05$ ) increased fibrinolytic activity at the end of 12th week. Total antioxidant status was also significantly ( $p<0.05$ ) increased by 90% at the end of 3 months. However, fibrinogen and lipid levels were not significantly altered. All study subjects experienced a feeling of wellbeing without any side-effects. Thus, the present study demonstrates that small cardamom effectively reduces blood pressure, enhances fibrinolysis and improves antioxidant status, without significantly altering blood lipids and fibrinogen levels in stage 1 hypertensive individuals.

### ***Theobroma cacao* (cocoa bean)**

The cocoa bean (technically cocoa seed) or simply cocoa, also called cacao, is the dried and fully fermented seed of *Theobroma cacao*, from which cocoa solids (a mixture of nonfat substances) and cocoa butter (the fat) can be extracted. Cocoa beans native to the Ecuadorian Amazon rainforest are the basis of chocolate and Mesoamerican foods including tejate, an indigenous Mexican drink.



### **Chemical constituents**

Cocoa beans contain several bioactive compounds that have been studied for their potential antihypertensive effects. While more research is needed to fully understand the mechanisms involved, some key compounds in cocoa that may contribute to its potential blood pressure-lowering properties include:

**Flavanols:** Epicatechin and Catechin: These are specific types of flavanols found in cocoa. Flavanols have been associated with improved endothelial function and vasodilation, which can help lower blood pressure.

**Theobromine:** Theobromine is a natural compound found in cocoa that belongs to the methylxanthine class. It has vasodilatory effects, meaning it can widen blood vessels and potentially contribute to lower blood pressure.

**Arginine:** Cocoa contains the amino acid arginine, a precursor to nitric oxide. Nitric oxide is a signaling molecule that helps relax blood vessels, promoting vasodilation and potentially lowering blood pressure.

**Magnesium:** Cocoa is a source of magnesium, an essential mineral that plays a role in blood pressure regulation. Magnesium helps balance sodium levels and relax blood vessels.

**Polyphenols:** Cocoa is rich in polyphenolic compounds, including various flavonoids and procyandins. Polyphenols have antioxidant properties and may contribute to cardiovascular health, potentially impacting blood pressure.

**Oligomeric Procyandins:** These are specific types of polyphenols found in cocoa that have been studied for their potential cardiovascular benefits, including effects on blood pressure.

### **Medicinal uses**

Cocoa beans, the primary ingredient in chocolate, have been traditionally used for their medicinal properties, and some research suggests potential health benefits associated with their consumption. Here are some of the potential medicinal uses of cocoa beans:

**Antioxidant Properties:** Cocoa beans are rich in flavonoids, particularly epicatechin, which have antioxidant properties. Antioxidants help neutralize free radicals in the body, which may contribute to the prevention of various chronic diseases and aging.

**Cardiovascular Health:** Some studies suggest that regular consumption of cocoa may have positive effects on cardiovascular health. Flavanols found in cocoa may help improve blood vessel function, reduce blood pressure, and enhance blood flow.

**Mood Enhancement:** Cocoa contains compounds that may influence mood and emotions. It contains theobromine, a mild stimulant, and serotonin precursors that could contribute to a sense of well-being. Dark chocolate, in particular, is often associated with mood improvement.

**Brain Health:** The flavonoids in cocoa have been studied for their potential neuroprotective effects. Some research suggests that cocoa consumption may be associated with improved cognitive function and a reduced risk of neurodegenerative diseases.

**Anti-Inflammatory Effects:** Cocoa has been found to have anti-inflammatory properties. Chronic inflammation is associated with various diseases, and cocoa consumption may contribute to reducing inflammation in the body.

**Improved Blood Sugar Regulation:** Some studies suggest that cocoa may have a positive impact on insulin sensitivity and blood sugar regulation. This could be beneficial for individuals with or at risk of type 2 diabetes.

**Skin Health:** The antioxidants in cocoa may contribute to skin health by protecting against oxidative stress. Additionally, cocoa butter, derived from cocoa beans, is a common ingredient in skincare products due to its moisturizing properties.

### **Antihypertensive activity**

In this study, we evaluated the short-term effect of a cocoa polyphenol extract (CPE), in spontaneously hypertensive rats (SHR). Male 17-22-week-old SHR were administered by intragastric gavage water, 50 mg kg (-1) Captopril or CPE at different doses (13, 26, 80 and 160 mg kg (-1)). The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded by the tail cuff method before the administration and also 2, 4, 6, 8, 24, 48 and 72 h post-administration. Highly significant decreases in the SBP and in the DBP were observed when captopril or CPE was administered to SHR. The cocoa extract produced a dose dependent effect in the SBP of the SHR up to the dose of 80 mg kg (-1). Nevertheless this dose of CPE did not decrease the arterial blood pressure in the normotensive Wistar Kyoto rats. The decrease in the SBP caused by 80 mg kg (-1) of CPE in the SHR (-39.1 ± 3.7 mm Hg) was maximum 6 h post-administration, and the initial values of SBP were recovered 72 h post-administration of this extract. Paradoxically, 160 mg kg (-1) of the cocoa extract caused a decreased antihypertensive effect than lower doses of CPE. In addition, the decrease in DBP was always more accentuated when the dose of CPE administered was lower. Our results suggest that CPE may be used as a functional food ingredient with beneficial effects for controlling arterial blood pressure.

## **3. CONCLUSION**

The results of various studies confirm the use of some selected medicinal plants used in traditional system of medicine to manage hypertension and important role in prevention and treatment of hypertension and also for the further research especially with reference to development of potent Phytomedicine for the treatment of hypertension Advance comprehensive studies are needed to make clear the antihypertensive effect of medicinal herbs.

## **4. REFERENCE**

- [1] Al Disi SS, Anwar MA, Eid AH. Anti-hypertensive herbs and their mechanisms of action: part I. *Front Pharmacol.* 2015;6:323. doi: 10.3389/fphar.2015.00323.
- [2] Wang J, Xiong X. Control strategy on hypertension in Chinese medicine. *Evid Based Complement Alternat Med.* 2012;2012:284847. doi: 10.1155/2012/284847
- [3] Anwar MA, Al Disi SS, Eid AH. Anti-hypertensive herbs and their mechanisms of action: part II. *Front Pharmacol.* 2016;7:50. doi: 10.3389/fphar.2016.00050.
- [4] Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM. et al. Heart disease and stroke statistics--2011 update: a report from the American Heart Association. *Circulation.* 2011;123(4):e18–e209. doi: 10.1161/CIR.0b013e3182f831c7
- [5] Hashemi V, Dolati S, Hosseini A, Gharibi T, Danaii S, Yousefi M. Natural killer T cells in preeclampsia: an updated review. *Biomed Pharmacother.* 2017;95:412–8. doi: 10.1016/j.biopha.2017.08.077
- [6] Sinha AD, Agarwal R. Clinical pharmacology of antihypertensive therapy for the treatment of hypertension in CKD. *Clin J Am Soc Nephrol.* 2019;14(5):757–64. doi: 10.2215/cjn.04330418
- [7] Singh P, Mishra A, Singh P, Goswami S, Singh A, Tiwari KD. Hypertension and herbal plant for its treatment: a review. *Indian J Res Pharm Biotechnol.* 2015;3(5):358–66.
- [8] Rastogi S, Pandey MM, Rawat AK. Traditional herbs: a remedy for cardiovascular disorders. *Phytomedicine.* 2016;23(11):1082–9. doi: 10.1016/j.phymed.2015.10.012.
- [9] Agrawal M, Nandini D, Sharma V, Chauhan NS. Herbal remedies for treatment of hypertension. *Int J Pharm Sci Res.* 2010;1(5):1–21. doi: 10.13040/ijpsr.0975-8232.1(5).1-21.

- [10] Jacob B, Narendhirakannan RT. Role of medicinal plants in the management of diabetes mellitus: a review. *3 Biotech.* 2019;9(1):4. doi: 10.1007/s13205-018-1528-0.
- [11] Shayganni E, Bahmani M, Asgary S, Rafieian-Kopaei M. Inflammaging and cardiovascular disease: management by medicinal plants. *Phytomedicine.* 2016;23(11):1119–26. doi:10.1016/j.phymed.2015.11.004
- [12] Erem C., Hacihasanoglu A., Kocak M., Deger O., Topbas M. Prevalence of prehypertension and hypertension and associated risk factors among Turkish adults: trabzon hypertension study. *Journal of Public Health.* 2009;31(1):47–58. doi: 10.1093/pubmed/fdn078.
- [13] Ahmed A., Rahman M., Hasan R., et al. Hypertension and associated risk factors in some selected rural areas of Bangladesh. *International Journal of Research in Medical Sciences.* 2014;2(3): p. 925. doi: 10.5455/2320-6012.ijrms20140816.
- [14] Mishra C. P., Kumar S. Risk factors of hypertension in a rural area of Varanasi. *Indian Journal of Preventive and Social Medicine.* 2011;42(1):101–111.
- [15] Abebe S. M., Berhane Y., Worku A., Getachew A. Prevalence and associated factors of hypertension: a crosssectional community based study in Northwest Ethiopia. *PLoS ONE.* 2015;10(4) doi: 10.1371/journal.pone.0125210.e0125210
- [16] Tabrizi J. S., Sadeghi-Bazargani H., Farahbakhsh M., Nikniaz L., Nikniaz Z. Prevalence and associated factors of prehypertension and hypertension in Iranian population: the lifestyle promotion project (LPP) *PLoS ONE.* 2016;11(10) doi: 10.1371/journal.pone.0165264.e0165264
- [17] Kumar M. R., Shankar R., Singh S. Hypertension among the adults in rural Varanasi: a cross-sectional study on prevalence and health seeking behavior. *Indian Journal of Preventive and Social Medicine.* 2016;47(1-2):78–83.
- [18] Chobanian A. V., Bakris G. L., Black H. R., et al. Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension.* 2003;42(6):1206–1252.
- [19] Prabakaran J., Vijayalakshmi N., VenkataRao E. Prevalence of hypertension among urban adult population (25–64 years) of Nellore. *International Journal of Research & Development of Health.* 2013;1(2):42–49.
- [20] Fisher N. D., Williams G. H. Hypertensive vascular disease. In: Kasper D. L., Braunwald E., Fauci A. S., et al., editors. *Harrison's Principles of Internal Medicine.* 16th. New York, NY, USA: McGraw-Hill; 2005. pp. 1463–1481.
- [21] Ried K. Effect of garlic on blood pressure, serum cholesterol and immunity: Updated meta-analyses and review. *J Nutr.* 2016;146:3895–96S. doi: 10.3945/jn.114.202192.
- [22] Ried K, Frank OR, Stocks NP. Aged garlic extract lowers blood pressure in patients with treated but uncontrolled hypertension: A randomised controlled trial. *Maturitas.* 2010;67:144–150. doi: 10.1016/j.maturitas.2010.06.001.
- [23] Ried K, Frank OR, Stocks NP. Aged garlic extract reduces blood pressure in hypertensives: A dose-response trial. *Eur J Clin Nutr.* 2013;67:64–70. doi: 10.1038/ejcn.2012.178.
- [24] Ried K, Travica N, Sali A. The effect of aged garlic extract on blood pressure and other cardiovascular risk factors in uncontrolled hypertensives: The AGE at Heart trial. *Integr Blood Press Control.* 2016;9:9–21. doi: 10.2147/IBPC.S93335.
- [25] Ried K, Travica N, Sali A. The effect of kyolic aged garlic extract on gut microbiota, inflammation, and cardiovascular markers in hypertensives: The GarGIC Trial. *Front Nutr.* 2018;5:122. doi: 10.3389/fnut.2018.00122.
- [26] Centers for Disease Control and Prevention (CDC): Vital signs: Awareness and treatment of uncontrolled hypertension among adults - United States, 2003–2010. *MMWR Morb Mortal Wkly Rep.* 2012;61:703–709.
- [27] Olsen H, Klemetsrud T, Stokke HP, Tretli S, Westheim A. Adverse drug reactions in current antihypertensive therapy: A general practice survey of 2586 patients in Norway. *Blood Pressure.* 1999;8:94–101. doi: 10.1080/080370599438266.
- [28] Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, Pannier B, Vlachopoulos C, Wilkinson I, Struijker-Boudier H, European Network for Non-invasive Investigation of Large Arteries Expert consensus document on arterial stiffness: Methodological issues and clinical applications. *Eur Heart J.* 2006;27:2588–2605. doi: 10.1093/eurheartj/ehl254.
- [29] Larijani VN, Ahmadi N, Zeb I, Khan F, Flores F, Budoff M. Beneficial effects of aged garlic extract and coenzyme Q10 on vascular elasticity and endothelial function: The FAITH randomized clinical trial. *Nutrition.* 2013;29:71–75. doi: 10.1016/j.nut.2012.03.016.

- [30] Nunan D, Wassertheurer S, Lasserson D, Hametner B, Fleming S, Ward A, Heneghan C. Assessment of central haemodynamics from a brachial cuff in a community setting. *BMC Cardiovasc Disord.* 2012;12:48. doi: 10.1186/1471-2261-12-48.
- [31] Nunan D, Fleming S, Hametner B, Wassertheurer S. Performance of pulse wave velocity measured using a brachial cuff in a community setting. *Blood Press Monit.* 2014;19:315–319. doi: 10.1097/MBP.0000000000000066
- [32] O'Rourke M. Arterial stiffness, systolic blood pressure, and logical treatment of arterial hypertension. *Hypertension.* 1990;15:339–347.
- [33] Ohshiro M, Kuroyanagi M, Keno A. Structures of sesquiterpenes from *Curcuma longa*. *Phytochemistry.* 1990;29:2201–5.
- [34] Kirtikar K. R, Basu B. D. Blatter E, Caius J. F, Mhaskar K. S. Indian Medicinal Plants. 2nd Ed. Vol II. Lalit Mohan Basu, Allahabad, India: 1993. p. 1182.
- [35] Wolde T, Kuma H, Kassahun Trueha D. Anti-bacterial activity of garlic extract against human pathogenic bacteria. *Journal of Pharmacovigil.* 2018;6(253):2–8.
- [36] Singh R, Singh K. Garlic: a spice with wide medicinal actions. *Journal of Pharmacognosy and Phytochemistry.* 2019;8(1):1349–1355.
- [37] Cutler R. R., Wilson P. Antibacterial activity of a new, stable, aqueous extract of allicin against methicillin-resistant *Staphylococcus aureus*. *British Journal of Biomedical Science.* 2004;61(2):71–74. doi: 10.1080/09674845.2004.11732646.
- [38] Alam M. K., Hoq M. O., Uddin M. S. Medicinal plant *Allium sativum*—A review. *Journal of Medicinal Plant Studies.* 2016;4(6):72–79.
- [39] Velišek J., Kubec R., Davídek J. Chemical composition and classification of culinary and pharmaceutical garlic-based products. *Zeitschrift für Lebensmittel-Untersuchung und -Forschung A.* 1997;204(2):161–164.
- [40] Lobo V., Patil A., Phatak A., Chandra N. Free radicals, antioxidants and functional foods: impact on human health. *Pharmacognosy Reviews.* 2010;4(8):118–126. doi: 10.4103/0973-7847.70902.
- [41] Ruby A. J, Kuttan G, Babu K. D, Rajasekharan K. N, Kuttan R. Anti-tumour and antioxidant activity of natural curcuminoids. *Cancer Lett.* 1995;94:79–83.
- [42] Selvam R, Subramanian L, Gayathri R, Angayarkanni N. The anti-oxidant activity of turmeric (*Curcuma longa*). *J Ethnopharmacol.* 1995;47:59–67.
- [43] Araujo C. C, Leon L. L. Biological activities of *Curcuma longa* L. *Mem Inst Oswaldo Cruz.* 2001;96:723–8.
- [44] Aggarwal B. B, Takada Y, Oommen O. V. From chemoprevention to chemotherapy: Common targets and common goals. *Expert Opin Investig Drugs.* 2004; 3:1327–38.
- [45] Araujo C. C, Leon L. L. Biological activities of *Curcuma longa* L. *Mem Inst Oswaldo Cruz.* 2001;96:723–8.
- [46] Sutarno H, Hadad EA, Brink M (1999). "Zingiber officinale Roscoe". In De Guzman CC, Siemonsma JS (eds.). *Plant resources of South-East Asia: no.13: Spices.* Leiden (Netherlands): Backhuys Publishers. pp. 238–244.
- [47] Modaghegh M.-H., Shahabian M., Esmaeili H.-A., Rajbai O., Hosseinzadeh H. Safety evaluation of saffron (*Crocus sativus*) tablets in healthy volunteers. *Phytomedicine.* 2008;15:1032–1037.
- [48] Fadai F., Mousavi S.B., Ashtari Z., Beigi N.A., Farhang S., Hashempour S., Shahhamzei N., Bathaei S.Z. Saffron aqueous extract prevents metabolic syndrome in patients with schizophrenia on olanzapine treatment: A randomized triple blind placebo controlled study. *Pharmacopsychiatry.* 2014;47:156–161. doi: 10.1055/s-0034-1382001.
- [49] Kermani T., Zebarjadi M., Mehrad-Majd H., Mirhafez S.-R., Shemshian M., Ghasemi F., Mohammadzadeh E., Mousavi S.H., Norouzy A., Moghiman T., et al. Anti-inflammatory effect of *Crocus sativus* on serum cytokine levels in subjects with metabolic syndrome: A randomized, double-blind, placebo- controlled trial. *Curr. Clin. Pharmacol.* 2017; 12:122–126..
- [50] Kermani T., Kazemi T., Molki S., Ilkhani K., Sharifzadeh G., Rajabi O. The efficacy of crocin of saffron (*Crocus sativus* L.) on the components of metabolic syndrome: A randomized controlled clinical trial. *J. Res. Pharm. Pract.* 2017; 6:228–232. doi: 10.4103/jrpp.JRPP\_17\_26.
- [51] Ebrahimi F., Aryaeian N., Pahlavani N., Abbasi D., Hosseini A.F., Fallah S., Moradi N., Heydari I. The effect of saffron (*Crocus sativus* L.) supplementation on blood pressure, and renal and liver function in patients with type 2 diabetes mellitus: A double blinded, randomized clinical trial. *Avicenna J. Phytomed.* 2019; 9:322–333
- [52] Zilaee M., Hosseini S.A., Jafarirad S., Abolnezhadian F., Cheraghian B., Namjoyan F., Ghadiri A. An evaluation of the effects of saffron supplementation on the asthma clinical symptoms and asthma severity in patients with

- mild and moderate persistent allergic asthma: A double-blind, randomized placebo-controlled trial. *Respir. Res.* 2019;20:39. doi: 10.1186/s12931-019-0998-x.
- [53] Behrouz V., Dastkhosh A., Hedayati M., Sedaghat M., Sharafkhah M., Sohrab G. The Effect of Crocin Supplementation on Glycemic Control, Insulin Resistance and Active AMPK Levels in Patients with Type 2 Diabetes: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial. *Diabetol. Metab. Syndr.* 2020; 12:59. doi: 10.1186/s13098-020-00568-6.
- [54] Azimi P., Ghiasvand R., Feizi A., Hosseinzadeh J., Bahreynian M., Hariri M., Khosravi-Boroujeni H. Effect of cinnamon, cardamom, saffron and ginger consumption on blood pressure and a marker of endothelial function in patients with type 2 diabetes mellitus: A randomized controlled clinical trial. *Blood Press.* 2016;25:133–140. doi: 10.3109/08037051.2015.1111020.
- [55] Teshika JD, Zakariyyah AM, Zaynab T, Zengin G, Rengasamy KR, Pandian SK, et al. Traditional and modern uses of onion bulb (*Allium cepa L*): a systematic review. *Crit Rev Food Sci Nutr.* 2019;59: S39–S70.
- [56] Upadhyay RK. Nutraceutical, pharmaceutical and therapeutic uses of *Allium cepa*: a review. *Int J Green Pharm.* 2016;10: S46–S64.
- [57] Ahmed N, Mahmood A, Ashraf A, Bano A, Tahir SS, Mahmood A. Ethnopharmacological relevance of indigenous medicinal plants from district Bahawalnagar, Punjab, Pakistan. *J Ethnopharmacol.* 2015; 175:109–123.
- [58] Josabad Alonso-Castro A, Jose Maldonado-Miranda J, Zarate-Martinez A, Jacobo-Salcedo Mdel R, Fernandez-Galicia C, Alejandro Figueroa-Zuniga L, et al. Medicinal plants used in the Huasteca Potosina, Mexico. *J Ethnopharmacol.* 2012; 143:292–298.
- [59] Ayyanar M, Ignacimuthu S. Ethnobotanical survey of medicinal plants commonly used by Kani tribals in Tirunelveli hills of Western Ghats, India. *J Ethnopharmacol.* 2011; 134:851–864.