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Review Article

An Overview of the Most Important Medicinal Plants that Affect Hypertension and their Antihypertensive Mechanism

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Abstract

Despite the increased awareness about high blood pressure, it remains a major cause of morbidity and mortality in the community. Medication and high blood pressure can be treated with medication and non-medication. The high prevalence of high blood pressure around the world and development of serious and dangerous complications this disease a major health problem in all societies and is a major cause of cardiovascular disease. Concerns about the side effects of chemical drugs lead to misuse of medications, intolerance to patients and consequently, impaired control of the disease. That's why today there is a new approach to medicinal plants and a lot of research is being done on medicinal plants. The purpose of the present study is investigation of plants and provides the mechanism of action of the most effective medicinal plants in the treatment of hypertension. This paper examines the use of electronic search in articles published in various Internet databases and reference books on the mechanism of action of various plants in the treatment of hypertension by affecting the molecular mechanisms involved in the disease. According to the results of some medicinal plants such as *Camellia sinensis* (L.) Kuntze, *Berberis vulgaris* L., *Rosa × damascena* Herrm., *Punica granatum* L., *Olea europaea* L., *Teucrium polium* L., *Lavandula angustifolia* Mill., *Urtica Dioica* L., *Cinnamomum zeylanicum* Blume, *Glycyrrhiza glabra* L., *Allium sativum* L. and *Juglans regia* L. are the most important medicinal plants affecting high blood pressure. Studies have shown that medicinal plants with various mechanisms such as vasodilation, production of nitric oxide (NO), calcium channel blockers, increased potassium, inhibition of renin-angiotensin pathway, and activation of intracellular CGMP and expansion of vasodilator effect to hypertension treatment.

Keywords: Hypertension, Medicinal Plants, Molecular Mechanisms, Drug

Introduction

Increase blood pressure is very important. This common disease is asymptomatic and can usually be treated. However, However, if blood pressure is not treated, it is usually treatable and can have fatal consequences if left untreated [1]. Blood pressure consists of two scales: systolic and diastolic, which depend on the contraction (systole) or relaxation (diastole) of the heart muscle between beats. At rest, normal systolic blood pressure (or maximum blood pressure between 100 and 140mm Hg) and normal diastolic blood pressure (or minimum blood pressure) are between 60 and 90 mm Hg. Hypertension refers to blood pressure above 140/190 mm Hg [2,3]. Nutrition and lifestyle play a central role in preventing hypertension. There is a constant search for oral compounds effective on blood pressure. Other effective ways to reduce and control high blood pressure include diet, exercise, stress management and use of herbal medicine. Because increase in blood pressure is usually asymptomatic in the first 15-20 years, it progressively damages the cardiovascular system during this period

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[4,5]. In people with high blood pressure, the incidence of myocardial infarction increases up to five times. The other consequence of high blood pressure is the development of atherosclerosis [5]. Systemic inflammation plays a role in the development of atherosclerosis and other cardiovascular diseases [6]. The high prevalence of high blood pressure and its dangerous complications on the organs of the body have made this disease a major health problem in all societies [7]. The global prevalence of high blood pressure is about one billion people, and about 7.1 million annual deaths can be attributed to high blood pressure [8]. The incidence of this disease is increasing in all countries, especially in Iran [9]. The prevalence of high blood pressure also depends on race composition and population. In whites living in urban areas, one-fifth of people have a blood pressure of more than 140.90 mm Hg. The prevalence in women is quite dependent on age and increases sharply after the age of 50. The blood pressure ratio in women is 60 to 70mm Hg in men over the age of 30 and 1.1 to 1.2 at the age of 65[10]. Adequate control of high blood pressure remains a problem, and the main cause is the asymptomatic nature of the first 15-20 years, which progressively damages the cardiovascular system during the course of the disease[11]. It also affects sexual function, social role, and many other aspects of a patient's life, such as his or her ability to sustain family life and daily activities [12]. Obesity, ringtone, diet and alcohol consumption, family history, various psychological factors, emotional factors, stress, anger, and hostility are the factors that affect blood pressure [13,14]. If blood pressure is not controlled properly in a timely manner, it will lead to unpleasant side effects [15]. Lifestyle modification and drug strategies help control the disease [16].

Due to the fact that hypertension cause the most common cardiovascular disease and has a high level of treatment and care, and since the use of drugs has side effects, researchers recommend non-pharmacological methods or the use of herbs instead of the usual medication regimen, depending on the pathological mechanisms of hypertension. This paper examines the mechanism of action of different plants in the treatment of hypertension by emphasizing the molecular mechanisms involved in this disease

Medicinal plants have two type of secondary metabolites that showed pharmacologic activity. The first one is essential oil and the other one is extraction. Essential oils have different compounds that have been used in herbal medicines. Because of the importance of natural products, many researchers are interested to know about the chemical compounds and the pharmacologic efficacies of them. In addition, essential oil composition could be effected by various factors, which have been reported by several researchers [17-21].

Material and Methods

To search for relevant articles indexed in Information Sciences Institute, PubMed, Scientific Information Database, Iran Medex, and Scopus from 1988 to 2017, with further emphasis on those indexed between 2004 and 2015, these search terms were used: Hypertension, Medicinal Plants, Molecular mechanisms. After the retrieved articles had been examined, eligible and relevant articles were included in the analysis.

Results

Studies have shown that medicinal plants help to treat hypertension with various mechanisms such as relaxation of blood vessels, production of nitric oxide (NO), blockage of calcium channels, increase in potassium, inhibition of renin-angiotensin pathway, and activation of intracellular cGMP and expansion of vasodilator effect.

Table 1 shows the most important medicinal plants and the effective compounds of plants and their mechanism of action on blood pressure. According to the result green tea, barberry, rosemary, pomegranate, olive, chloroprene, lavender, nettle, cinnamon, licorice, garlic, and walnut are the most important medicinal plants affecting high blood pressure.

Green tea

Green tea (*Camellia sinensis*) contains polyphenols (such as epithelium, epigallocatechin, and galaxies), catechins, tannins and coenone. Fresh green tea leaves contain phenolic acids such as gallic acid and the amino acid tinin. Most green tea polyphenols in solution to powder range from 10% to 45% caffeine. The plant also contains amino acids such as tyrosine, arginine and lysine, carbohydrates, proteins, and vitamins. Consumption of green tea lowers diastolic and systolic blood pressure. Also, consuming green tea has a significant reduction in systolic blood pressure and LDL cholesterol [22].

Barberry

Barberry is a thorny plant with the scientific name *Berberis vulgaris* from the Breberidacea family. A recent research has shown the analgesic, anti-inflammatory and anti-cancer effects of the plant's roots [23]. Examples of the plant alkaloids are Berberine, Klmbamyn, Zhatrvryzyn Palmatine, Brbamyn, and Akantyn [24]. Most of the alkaloid compounds in barberry fruit have therapeutic effects. One of these compounds is berberine. The effect of berberine on blood pressure is mainly through the central nervous system [25]. The vasodilator action of the plant is through the effect on the smooth muscles of the arteries and the release of EDRF from the vascular endothelium. Berberine increases intracellular cGMP and expands the vasodilatory effect of blood

vessels. Berberine also blocks calcium channels and lowers arterial blood pressure [26, 27].

Rose

Rose with the scientific name *Rosa* × *damascena* Herrm. belongs to the Rosaceae family [28]. Rose contains large amounts of volatile oil in the petals. Most essential oils include terpene alcohols such as geraniol and L-citrulline with a mild odor [29]. The scent of flowers is effective in treating postpartum depression, anxiety, [30], premenstrual pain [31] and improving memory [32]. Clinical studies on rose have shown that it reduces 10.25 mm Hg in systolic blood pressure and 8.35 mm Hg in diastolic blood pressure, indicating a significant effect on systolic and diastolic blood pressure [33].

Pomegranate

Scientifically named *Punica granatum* belongs to the Punicaceae family of native trees of Iran. Pomegranate contains 85% water, 10% sugar, 1.5% pectin, ascorbic acid, phenolic compounds and other compounds [34]. In addition, pomegranate is a rich source of thiamine, riboflavin, jasmine, and vitamins A and B. Antioxidants such as tannins, anthocyanins, flavonoids and polyphenols have important medicinal properties [35]. Pomegranate has antioxidant, anti-cancer, anti-inflammatory and anti-cardiovascular properties [36]. The effects of lowering blood pressure on antioxidants such as vitamin C, flavonoids, vitamin E, and beta-carotene have been shown to lower blood pressure. Pomegranate-soluble polyphenols, including anthocyanin and tannins, also have antioxidant and anti-atherogenic properties that are effective in lowering blood pressure [37,38].

Olive

It is a plant belonging to the family Oleaea with the scientific name *Olea europaea*. The used sections are itsfruits, leaves and bark [39]. Olive skin has a blood pressure lowering property. The leaves of the olive tree lower blood pressure by opening up the superficial vascular ducts without having a detrimental effect on the heart [40]. Olives contain the oleuropein compound, which has pharmacological properties. The loosening effect of oleuropein on the walls of isolated animal arteries has been discovered [41].

Poleigamander

Scientifically known as *Teucrium polium*, is an herbaceous and perennial plant mint genus. In traditional medicine, this plant has anti-inflammatory, anti-diabetic and anti-ulcer effects [42,43]. This plant contains tannins, terpenoids, saponins, and flavonoids [44,45]. Poleigamander has relaxing effects on the smooth muscle of the vascular wall. Poleigamander extract also blocks calcium channels and lowers blood pressure. It is effective in curing cardiovascular diseases [46,47].

Lavender

Lavandula angustifolia belongs to the mint family, which is effective in traditional medicine in treating anxiety, fatigue, headaches, gastrointestinal and liver problems [48]. More than 40 effective substances are known in this plant. Its main ingredients include Linalool acetate, Cineol, Turpin, and Camphor [49]. It has various antioxidant and cardiovascular effects. Linalyl acetate in extracorporeal conditions causes the progression of endothelial artery-dependent carotid artery relaxation. It also reduces sympathetic activity and increases the activity of Wake Gastric nerve, reduces renal sympathetic activity and lowers blood pressure [50].
Angiotensin converting enzyme is a key component of the renin-angiotensin system and its inhibition with this plant lowers blood pressure. IHence, its inhibition is the main target of lowering blood pressure [51].

Alpha Lipoic Acid (ALA)

Significantly reduces systolic and diastolic blood pressure. Alpha lipoic acid as an antioxidant by removing superoxide ions increases NO accessibility and activates the secondary cGMP prophet, relaxing vascular smooth muscle cells and expanding them [52].

Nettle

Scientifically named *Urtica Dioica*, belongs to the Urticacease family. It is used to reduce inflammation and treat rheumatoid arthritis, bladder and urinary tract infections [53]. This plant also has a reducing effect on blood pressure [54]. Nettle leaves contain compounds such as histamine, flavonoids, peptides and amines [55]. Nettle dilates blood vessels and lowers blood pressure by increasing nitric oxide [56]. The flavonoid compounds in nettle are one of the possible mechanisms for lowering systolic blood pressure.

Cinnamon

Scientifically known as *Cinnamomum zeylanicum* (cinnamon) from the Loraceae family, is a plant with strong antioxidant, antiviral and antispasmodic properties [57]. Cinnamon has its effects on lowering blood pressure through increasingly active proximal receptor receptors and inhibiting the formation of the final product of glycosylation. There are also various phenolic agents such as catechins, epicatechins, proxyanidin B2 and phenolic polymers that play a role in lowering blood pressure [58].

Licorice

Licorice or *Glycyrrhiza glabra* is a genus of peas and has a strong therapeutic value in medical and traditional medicine. It has therapeutic effects in cancer, heart

disease, hepatitis and cough [59]. Nitric oxide is an important endogenous substance that, with its relaxing effects, plays an important role in regulating and maintaining vascular tone [60]. Nitric oxide is made by a variety of Isoforms that produce NO enzymes, which include the NO in the neurons of the nNOS endothelial enzyme or eNOS epithelial [61]. The flavonoids in licorice reduce cochlear contractions of acetylcholine by cholinergic pathway by antagonizing muscarinic receptors and lowering blood pressure. Glatachin flavonoids increase nitric oxide and vasodilation [62]. It also has the property of inhibiting the adrenergic system and the effects in line with the cholinergic system, causing a drop in blood pressure [63].

Garlic

Garlic with the scientific name of *Allium sativum* belongs to the bee family. The compounds in garlic are divided into two main groups: sulfur and non-sulfur compounds. The medicinal properties of garlic are mainly due to the sulfur compounds called allysine [64]. Garlic is one of the plants that has antimicrobial properties. When garlic is used, the enzyme alliinase is secreted, and alliin converts a type of amino acid to allysine. Lysine not only has antihypertensive properties but also has anti-platelet and antibiotic activity. Garlic lowers blood pressure through the action of methyl allyl trisulfide, a component of the allyl triol sulfide group. It imposes this effect by dilating the walls of the arteries [65]. Another study found that garlic effect is through prostaglandins, which reduce peripheral vascular resistance [66]. Garlic also lowers blood pressure by inhibiting angiotensin [67].

Walnut tree

Walnut tree (*Juglans regia*) belongs to the Juglandacea family and belongs to the genus Juglans. Walnut leaves contain compounds such as phenolic acids and flavonoids, and the most important flavonoids in the leaves are quarantine galactoside, quercetin pentoseid, quaracine arabinose, quercetin gylenoside mibentin, and quercetin. The leaves of this plant contain tannins, essential fatty acids, ascorbic acid, flavonoids, caffeic acid and paraacomaric acid. Blue leaf extract has been shown to reduce blood pressure by reducing the contraction of noradrenaline in the aortic isola, blocking calcium channels and interacting with the adrenergic system [68].

Discussion

So far, the positive effects of a large number of medicinal plants have been shown to moderate the effects of hypertension. In this study, medicinal plants and some of their effective compounds were presented, which through various mechanisms such as increasing nitric oxide production, vascular relaxation, and activating intracellular cGMP, expanding the vasodilator effect, and blocking calcium channels reduce blood pressure.

Phenolic and flavonoid compounds with antioxidant properties also have antithyrogenic effects in lowering blood pressure, activating the renin system of angiotensin and inhibiting it with plant compounds, inactivating the sympathetic system, increasing the receptor activating receptors and inhibiting it. The formation of the final product due to glycosylation, activation of the cholinergic pathway and the effects of prostaglandin suspicion cause a decrease in blood pressure.

Hypertension is one of the most common and important diseases of the present age, often imposed by modern lifestyles, especially reduced physical activity and a high-fat diet. Blood pressure often develops cardiovascular diseases or acute heart failure, so hypertension should be controlled and treated. At the same time, the use of herbal medicines has increased in the world [69]. High blood pressure is a common, asymptomatic, and easily treatable disease. If left untreated, it can be a risk factor for cardiovascular disease and subsequent death [2]. High systolic blood pressure alone increases the risk of myocardial infarction as well as cardiovascular deaths in both general population and seemingly low-risk groups. Interestingly, both traumatic pressure and high systolic pressure independently predispose to the risk of coronary artery disease [70]. The drugs of high blood pressure, such as beta-blockers, calcium blockers, angiotensin-converting enzyme inhibitors, or diuretics, in common doses have significant side effects. Therefore, it is appropriate to use alternative methods, including the use of medicinal plants that have a corrective effect on blood pressure [71]. The main physiological causes of high blood pressure can be one when the blood volume in the healthy arteries increases and the other when the normal blood volume passes through the narrow blood vessels [2,3]. Arterial hypertension, in which hypertension causes endothelial dysfunction and increases arterial stiffness, also causes high blood pressure. Oxidative stress is also known as increased oxidative material relative to endogenous antioxidant capacity. Arterial hypertension leads to increased production of free radicals in tissues and arteries and can lead to cardiac hypertrophy and increased arterial pressure. Nitric oxide deactivation also causes hypertension as an important factor in reducing vasodilation associated with endothelium [72]. Nitric oxide plays an important role in maintaining normal blood pressure and hemostasis of body fluids. Primary hypertension is associated with impaired nitric oxide production or function. So, oral administration of Nω-Nitro-L-arginine methyl ester hydrochloride (L-NAME) as an inhibitor of nitric oxide production has caused hypertension [73,74].

Table 1 Important medicinal plants and their compounds with potential mechanism actions on hypertension

English Name	Scientific Name	Family	Active Organ(s)	Active Compound (S)	Potential Action Mechanism of Atherosclerosis Amelioration
Green Tea	*Camellia sinensis*	Theaceae	Leaves	Phenolic acids such as gallic acid and amino acid thinine	Vascular relaxation
Rose	*Rosa × damascena*	Rosaceae	Petals	Terpene alcohols such as geraniol, L-citronellol	Vascular relaxation
Berberis	*Berberis vulgaris*	Breberidacea	Fruits and leaves	Flavonoids Berberine	The release of EDRF from the vascular endothelium, Enable intracellular cGMP and Expanding the vasodilator effect also causes blockage of calcium channels.
Pomagranate	*Punica granatum*	Punicaceae	Fruit, peel	Antioxidants such as tannins, anthocyanin, flavonoids and polyphenols	Anthocyanins and tannins also have antioxidant and anti-atherogenic properties that are effective in reducing blood flow
Olive	*Olea europaea*	Oleaceae	Leaves, peel and fruit	Oleuropein composition	Loosen the smooth muscles of the arteries
Poleigamander	*Teucrium polium*	Lamiaceae	Flowering branches	Tannins, terpenoids, saponins, flavonoids	Blocking calcium channels 2. Relaxing smooth muscle vessels
Lavender	*Lavandula angustifolia*	Lamiaceae	Leaves	Linalol, Acetate, Cineole, Turpinine and Camphor	Activation of its inhibitory renin-angiotensin system with the plant and Inactivation of the sympathetic system reduce blood pressure
Alpha lipoic acid (ALA)	ALA	ALA	Leaves	Alpha lipoic acid	Enhance NO access and activate cGMP secondary messenger
Nettle	*Urtica Dioica*	Urticacease	Leaves	Flavonoids, peptides and amines	Increased nitric oxide
Cinnamon	*Cinnamomum zeylanicum*	Loraceae	peel	Various phenolic agents such as catechin, epicatechin, proscyanidin B2	Increasing proxy zoom activating receptors and Inhibiting glycosylated end product formation
Licorice	*Glycyrrhiza glabra*	Fabaceae	Underground stems and roots of the plant	Galactin flavonoids and other flavonoids	Cholinergic pathway and Production of nitric oxide
Garlic	*Sativum Allium*	Iridaceae	Garlic cloves	Sulfur compounds called allysine	Methyl allyl trisulfide function, vasodilation Prostaglandin-like effect

Other factors that affect blood pressure include minerals such as potassium. Decreased extracellular potassium concentrations and increased sympathetic activity and sodium levels in vascular smooth muscle cause narrowing of blood vessels and increased blood pressure[75]. On the other hand, increasing the NO of the vascular endothelium and dilating the arteries reduce blood pressure. In addition to their antioxidant properties, phenolic compounds play a role in increasing the activity of potassium channels, thus helping to lower blood pressure [76]. In addition to medication, lifestyle adjustments such as low-sodium, low-fat, high-potassium diets, weight loss in obese people, daily exercise, reduction of anxiety, and exercise can help reduce blood pressure [77]. Studies have shown that medicinal plants have beneficial effects on human health due to their active ingredients and medicinal and antioxidant compounds, and have therapeutic effects on various organs of the body and various diseases [78-85].

Conclusion

Hypertension is known to be one of the most common and important diseases of today. The use of herbs can be an alternative to chemical drugs due to their ease of access, lower side effects and reasonable prices. Studies have shown that medicinal plants have a variety of mechanisms, including relaxation of blood vessels, production of nitric oxide (NO), blockage of calcium channels, increase in potassium, inhibition of renin-angiotensin pathway, and activation of intracellular cGMP and inactivation of the 7 ietic system. Expanding the vasodilator effect will help treat high blood pressure. Most studies have focused on the effect of herbs on the treatment of hypertension. However, fewer studies have been performed on the mechanism of action of these plants on disease. Familiarity with these mechanisms can be effective in synthesizing new drugs. Further studies are needed to evaluate the effect of medicinal plants and their chemical compounds on the treatment of hypertension.

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