



Medicinal Herbs with Potential Anti-Hypertensive Properties: a Systematic Review of Human and Animal Studies

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Abstract

Blood pressure is one of the vital signs, and is the pressure of circulating blood on the walls of blood vessels. When the large arteries lose their natural elasticity and strength, and the smaller ones are narrowed, blood pressure rises and the pressure is exerted by blood on the walls of blood vessels. High blood pressure is dangerous and very harmful for the heart and blood vessels, and is a major cause of mortality in all nations. Many patients tend to use herbal products for controlling their blood pressure, as they are concerned of the side effects of the chemical drugs. There are huge amount of research work exploring the safety and efficacy of a single herb, or combined herbal products on lowering blood pressure, among which some have shown certain effects, and some are negative in results. Grape seed, Garlic, Saffron, Green and White Mulberry, Quince, and some other herbs have more scientific evidence in lowering blood pressure. In this study, we systematically reviewed the scientific literature of clinical trials and animal studies, in which the safety and effectiveness of herbs on lowering blood pressure were evaluated.

Keywords: Blood pressure; Plant; Herb; Extract

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Introduction

Hypertension (HTN) is a global health concern in which BP in the arteries is considerably elevated [1]. The World Health Organization has reported that high BP is the major cause of death among cardiovascular diseases. World HTN League (WHL) also recognized that more than 50% of people with HTN are unaware of their ailment [2]. Long term HTN can enhance the risk for coronary artery disease, stroke, heart failure and chronic kidney disease [1].

Diet, obesity, smoking, alcohol consumption, low physical activity level, stress, and genetic factors are predisposing causes for high BP [3]. Apart from weight management and life style changes, taking biochemical and herbal medicine can be helpful to control HTN and prevent chronic diseases [4]. For available pharmaceutical interventions such as atenolol, amlodipine, diltiazem, losartan, etc., several adverse effects such as tiredness, hypotension, bradycardia, cold extremities, postural hypotension, depression, nausea have been reported [5]. Due to high tendency of people to medicinal herb consumption, studies focus on the efficacy and side effects of herbs with potential anti-hypertensive properties in animal and human studies [6]. There was some systematic review available regarding medicinal herbs with antihypertensive effects. However, they investigated only a number of medicinal herbs and there was no particular investigation about all of the medicinal herbs with antihypertensive properties [7]. In the present study, we aimed to summarize the

effect of medicinal herbs on BP considering several factors such as their active agents, therapeutic dosage, side effects, and possible mechanisms in animal and human studies. To best of our knowledge, this is the first systematic review taking into account all of the studies on medicinal herbs with antihypertensive and hypertensive properties.

Methods

PubMed, Scopus, Science Direct, and google scholar electronic data bases were searched for publications about the medicinal plants used for controlling HTN. The articles published till December 2016 with English language were included. Key terms used for systematic search were as follows: “BP” “plants”, “extract”, “extracts”, “herb”, “herbal”, and “herbs”.

Both animal and human studies were included. Non-English papers, case reports, review articles, theses, abstract in symposium and congress, and In vitro studies were excluded. The articles were evaluated based on the eligibility appraise. The name of medicinal herbs used for lowering BP, their active agents, the part of the plant, form (extract, powder, etc), dosages and the mechanism of action were extracted.

Results and Discussion

Among 1084 publications, 524 papers were duplicated and excluded. After evaluating titles and abstracts, 456 papers were excluded due to the following reasons: irrelevant (n = 167), review articles (n = 12) and articles for being thesis, conference abstracts (n = 216),

non-English language (n = 17), underlying disease (n = 44). Finally, 104 papers (84 animal studies and 20 human studies) were included

(Figure 1). After the full texts had been checked, 100 articles were chosen for the review.

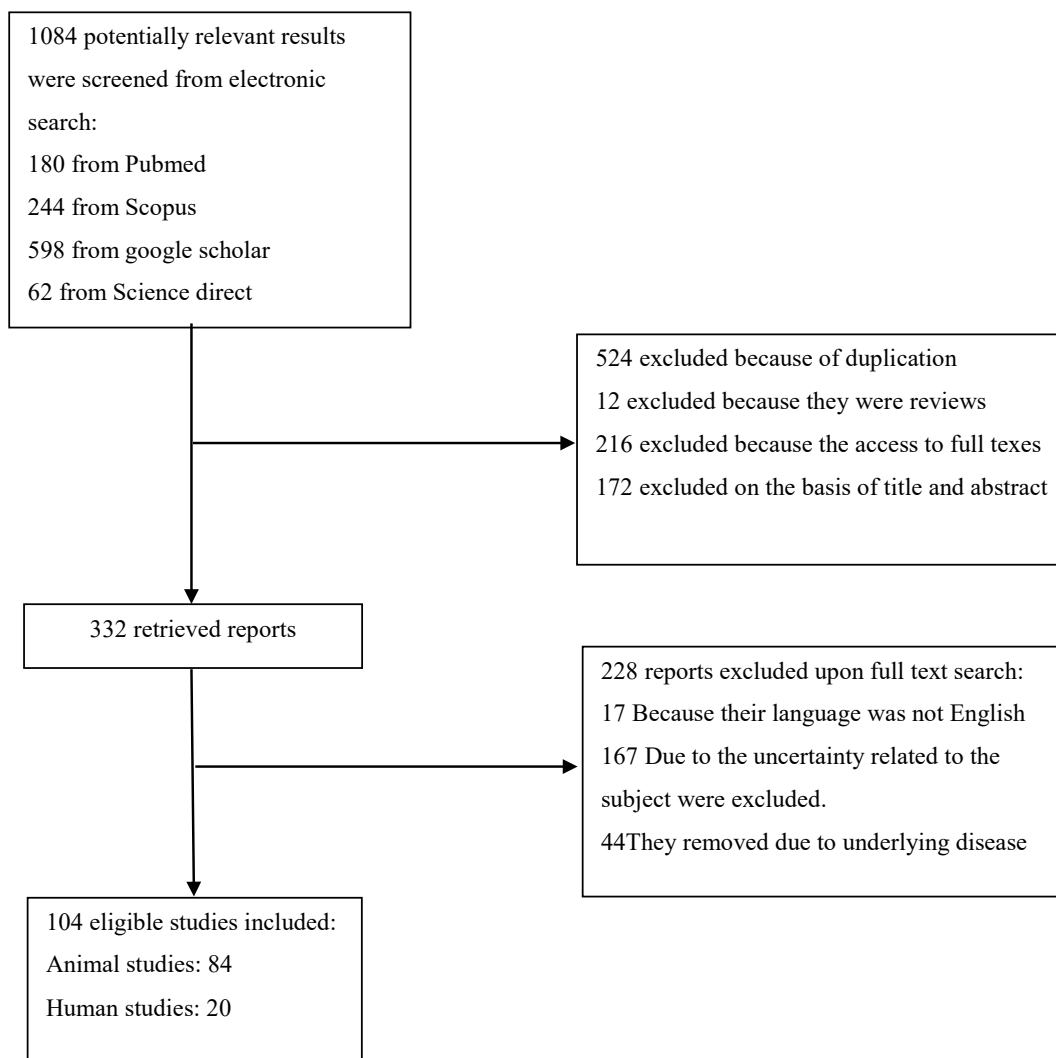


Figure 1. Schematic library diagram of project

Angiotensin converting-enzyme (ACE) inhibitor

Animal studies: *Juglans regia* L. decreased systolic (SYS) and diastolic (DIA) blood pressure (BP) [69]. After using *Rehmannia glutinosa/Aconitum variegatum* L., systolic blood pressure (SBP) decreased through a reduction in atrial natriuretic peptide depressor response [73]. *Olea europaea* L. had a dose dependent prophylactic effect

against the rise in BP. Its mechanism of action includes the content of oleuropein acting synergistically with other active principles to exert antioxidant, ACE inhibitor, and possibly calcium channel blocking activities [76]. In another study, *Boletus aestivalis* lowered SBP, DBP and heart rate [91]. *Asystasia gangetica* (L.) lowered SYS, DIA, and mean arterial BP dose-dependently.

However, reduction in heart rate was not dose-dependently (10-400mg/kg from leaf extract) [128].

Human studies: *Hibiscus sabdariffa* L. had also a significant lowering effect on arterial BP (dose: 15mg/kg) [149]. In a human study, a mixture of onion and pumpkin seed oil reduced the SYS pressure by 9.09 mmHg and the DBP by 4.06 mmHg. Its extract seems to aid individuals who would like to monitor their BP by applying lifestyle changes and diet [163].
Ca channel blocker

Animal studies: *Portulaca oleracea* L. increased mean arterial BP while in 40 % of rats BP was reduced. It is suggested to act through the postsynaptic α -adrenoceptors and transmembrane calcium influx interference [98]. *Acorus calamus* L. exhibited a vasoconstrictor effect on the baseline by Ca^{2+} antagonism in addition to a nitric oxide pathway [100]. *Sclerocarya birrea* A. (Rich. Hochst.) caused a dose-dependent fall in mean arterial BP by nitric oxide release or intracellular calcium decrease [108]. Moreover, *Solenostemon monostachyus* (P Beauv.) Briq., containing ESOMO, induced a significant decrease in arterial BP by cardio depression and vasodilation, dose dependently [124].

Human studies: *Olea europaea* L., had a dose-dependent BP lowering effect. However, in order to determine the exact mechanism of action, further studies are required [162]. *Zingiber officinale* lowers SYS and DIA BP and heart rate, although their effects were not statistically significant [150].

Vasodilators

Animal studies: There was a significant reduction in mean arterial BP in response to 50 mg/100gr of aqueous extract of *Crocus sativus* L. (dose-dependent), which was through the reduction of contractile response of vas deferens to epinephrine without any changes in contraction [70]. *Crocus sativus* L. reduced the BP in a dose-dependent manner through relaxation and vasodilatory effect [111]. In another study, *Crocus sativus* L. reduced SYS BP dose dependently (10/20/40 mg/kg for 5 week) with the agents called crocin/safranal. The mechanism of action is through the hypolipidemic effect of crocin in rats, in which crocin inhibits pancreatic lipase [130].

The extract of *Teucrium polium* L., had a positive inotropic effect on heart, reduced the BP, and neutralized by inotropic effects [117]. *Cinnamomum zeylanicum* with its phenolic constituents decreased SYS BP after an hour [121]. *Erythrophleum suaveolens* (Guill and Perr.) Brenan induced relaxation of aortic ring segments through its vasodilating activities [122]. *Crataegus Tourn. ex L.* possessed hypotensive action and it had a greater effect on DIA BP rather than SYS BP. It acted through relaxing isolated aorta and mesenteric arteries. It reduced peripheral vascular resistance (by causing vasodilatation) to lower BP [129].

Human studies: For *Ginkgo biloba* (GBE) L., stiffness index was slightly higher in GBE group compared to placebo group and other outcome variables were unaffected [161]. According to a study, *Ginkgo biloba* L. had a significant BP lowering effect during low

dose experiment (120 mg/day) [165].

Diuretics

Animal studies: *Bredemeyera floribunda* Wild. I. acts as a diuretic; therefore it decreased renal BP and it showed dose-dependent and reversible hypotensive responses with dosage of 76 mg/kg and in high doses, the extract led to bradycardia and death. At dosages of 36 to 70 mg/kg, reversible reduction in BP was observed. At higher doses, irreversible hypotensive responses were also reported [77].

Human studies: *Hibiscus sabdariffa* L. had a significant lowering effect on arterial BP. Its hypotensive effect may occur through the reduction of vascular reactivity during sympathetic nervous system activation [153].

The nitric oxide (NO) secretion

Animal studies: *Cudrania tricuspidata* (Carrière.) Bur. ex Lav. had restored SYS BP to its normal level by decreasing urinary sodium and stimulating nitric oxide release from vascular tissues [78]. *Coffea arabica* L. decreased SYS and DIA BP during ingestion by this mechanism [82]. *Panax ginseng* L. with the active component of Ginsenoside/ Nitric oxide (NO), lowered SYS BP which improved vessel wall thickening and alleviated HTN in SHR. A maximum decrease of SBP 4-6 h postadministration in SHR. [84]. *Terminalia superba* Engl. and Diels decreased BP and muscle sensitivity and improved endothelial function through decreased TMSE with a special emphasis on NO pathway and oxidative stress [86]. *Vitis*

vinifera L. had a lowering and stabilizing effect on BP because of the concentration of nitric oxide in grape seed [139]. SYS BP was on average 11.5 ± 2.2 mmHg lower, using *Passiflora edulis* Sims. [136].

Human studies: In the case of *Vitis vinifera* L., BP was modestly affected by GSE, (3.0 mmHg for SBP; 1.4 mmHg for DBP). Therefore, consumption of GSE did not decrease the arterial BP. It showed a relaxing effect on the smooth muscle in the vessel [157]. *Vitis vinifera* L. or grape juice had no effect while the grape wine indicated a significant lowering effect on BP via decreasing the plasma endothelin 1 concentrations [159]. According to a study on *Vitis vinifera* L., it reduced both SBP and DBP significantly compared to the placebo group. The endothelium dependent relaxation evoked by the extract that is mediated by the activation of the PI3K/Akt signaling pathway. Moreover, it led to the phosphorylation of eNOS through a redox-sensitive mechanism [166]. Based on studies, green coffee had positive effects on BP, which seems to be useful in patients with mild HTN [155].

Baroreceptor reflex

Animal studies: In animal studies, *Glycyrrhiza glabra* L. decreased DIA and SYS BP. It acted as Chronotropic (+) and Inotropic (-). It can act through lowering tension in the isolated aorta and increasing heart rate, causing baroreceptor reflex [68]. With *Glycyrrhiza glabra* L., a significant decrease in SYS, DIA and mean BP was shown by the modulatory mechanism of adrenergic system

and synergistic effect with the cholinergic system [93].

Quercetin

Animal studies: *Chromolaena odorata* L. King and H.E. Robins contains kaempferol, quercetin, and sitosterol. It lowered the SYS, DIA, pulse, mean arterial pressures of treated rats, dose dependently [112].

Flavonoids

Human studies: The consumption of these plants may reduce the risk of heart disease and obesity. Anthocyanin in purple corn seems to be useful as an anti-hypertensive agent; however, more long-term studies are needed to making decision about its effect [164].

Cholinomimetics

Animal studies: *Commiphora opobalsamum* (L.) Engl. reduced systemic arterial BP by 20% and decreased heart rate by 14% [80]. *Eucommia ulmoides* Oliv showed an antihypertensive effect right after drug administration. Doses over 3 mg/kg exhibited tendencies with a plateau effect and decreased SYS BP. Its extract showed an agonistic effect on the nervous system and influenced upon muscarinic acetylcholine receptors [94]. The different fractions of *Ficus exasperate* Vahl decreased BP by aforesaid mechanism [118]. *Tridax procumbens* Linn decreased BP by 72 hours after consuming extract and it increased pulse pressure by altering the SYS and pulse pressures [75]. *Tridax procumbens* L. caused a reduction in mean arterial BP in a dose-

related manner. Furthermore, the dosages of 6 and 9 mg/kg caused a reduction in heart rate [127]. With *Parinari curatellifolia* Planch. ex Benth, a great decrease in q D amplitude in cat BP was shown, which was facilitated by the release of vasoactive amines blockade of neurotransmitters such as acetylcholine [142]. *Gongronema latifolium* Benth resulted in BP reduction in the same way as the parasympathomimetic drugs by affecting muscarinic receptors and N-hexane and ethyl acetate fractions [143].

A-blockers

Animal studies: *Cleistanthus collinus* (Roxb.) Benth induced HTN; however, did not influence the effects of adrenergic or dopaminergic agents on BP [135]. With *Camellia sinensis* (L.) Kuntze, contractile responses were greatly inhibited in the presence of GTE in a dose-dependent manner by blocking adrenergic α 1-receptors [137]. *Brillantaisia nitens* resulted in a biphasic dose-related hypotensive effect via α 1-adrenoceptors blockade and β -adrenergic vasodilation [144].

Beta-blockers

Animal studies: The decrease in BP inhibited by propranolol, phentolamine, atenolol or b2-antagonist was shown with *Tinospora crispa* L. and its extract possesses at least three cardiovascular active components to cause an increase in BP and heart rate [103]. *Persea americana* Mill decreased mean arterial pressure and reduced heart rate and BP [133].

Other mechanisms

The animal studies for medicinal herbs with antihypertensive properties:

Morus alba L. with an active agent of flavenoids (routin and quercetin) lowered the SYS BP [71]. *Dombeya buettneri* K.Schum decreased the BP by muscarinic cholinergic pathway, relaxation of the blood vessels and the mean arterial BP, induced by sodium [72]. Lycoris Radiat (L'Hér.) Herb with an active agent of lycoretine decreased BP in rats and anesthetized dogs and increased BP in conscious dogs through α -adrenergic blocking activities and vasopressin activity [74]. *Bulbus fritillariae* prevented the increase of SBP by stimulation of nitric oxide release from vascular tissues that causes vasodilation [79]. *Cinnamomum camphora* L. decreased DIA BP by an unknown mechanism [81]. *Moringa peregrina* (Forssk) Fiori has active components including lupeol, α - and β -amyrin, β -sitosterol, apigenin, rhamnetin, neochlorogenic acid, and quercetin. It reduced SBP but it was partially hypertensive and had an antioxidant effect [83]. *Cydonia oblonga* Mill. Had a hypotensive effect on rats through an unknown mechanism [85]. With *Schinus molle* L., the mean arterial BP was reduced by inhibiting the effects of noradrenaline on arterial BP. Methanol/dichloromethane is an active component of this herb [87]. *Ageratum conyzoides* L. lowered SYS BP and caused greater fall in DIA pressure compared to that of SYS pressure in anaesthetized rats but the mechanism was not mentioned in this study [88]. *Allium sativum* L. lowered SYS BP by an unknown mechanism. Garlic and Aged

Garlic have different mechanisms for their lowering effect on SYS BP [89]. *Ipomoea batatas* (L.) Lam. lowered BP by ± 4.38 mmHg by increasing the expression of eNOS, increasing the SOD level as an endogenous antioxidant, thus decreasing MDA level in the blood [90].

Ginkgo biloba L. had a strong antithrombotic effect and lowered BP, having an antioxidant activity [92]. *Vernonia polyanthes* less decreased arterial BP dependently. The mechanism has not been elucidated yet [95]. *Azadirachta indica* A. Juss induced bradycardia initially followed by cardiac arrhythmia and dose related fall in BP. It also caused absence of p-wave, bradycardia, and ventricular arrhythmia [96]. *Echium orientale* L. and *Citrus \times aurantiifolia* increased and decreased BP, respectively. Both of them decreased heart rate, but the mechanism of action was not mentioned in this study [97]. *Clerodendrum trichotomum* Thunb increased urinary flow and Na excretion but had no significant effect on BP after intravenous injection of CTT extract, mechanism of which was not mentioned [99].

Antihypertensive and antioxidant effect of *Ferula foetida* L. was evident and significant reduction in SBP was shown in index-induced rats. It contains ferulic acid. It increased total peripheral resistance and hemodynamic changes, increased vascular pressure responsiveness and increased sympathetic, renin-angiotensin system activities [101]. *Withania somnifera* L. lowered Arterial and DIA BP and it prevented the hypotensive effect of acetylcholine and increased

the hypotensive effect of adrenaline by stimulation of cholinergic receptors and blockage of hypotension actions, having cholinergic agonist effect [102]. Tian Ma Gou Yen (TGY) significantly altered the development and prevented HTN by acting on sympathetic vasomotor activity [105]. *Vitis vinifera* L. (GSPE) increased eNOS expression and NO production in an AMPK/SIRT1 dependent manner and it-attenuated ouabain induced HTN. The mechanism was through endothelial nitric oxide synthase expression in vessel cells and KLF2 induction [106]. *Farayola* (avocado+garlic) caused no significant change in hematological parameters but had a significant reduction in cholesterol and triglyceride values. It lowered SYS and DIA BP [107]. *Vitex doniana* produced a hypotensive dose-dependent effect and the BP was reduced markedly. It affects the smooth muscle of the vascular system but the exact mechanism is not mentioned [109]. *Salvia miltiorrhiza* Bunge. contains Magnesium Tanshinoate B-enriched (MTB), which caused greater fall in BP compared to SME. It relaxed isolated rat and rabbit coronary arteries and this effect was mimicked by its hydrophilic components, tanshinones [110]. *Pleurotus tuber-regium* (Rumph. ex Fr.) Singer, with its flavonoids content, could moderate all the BP indices and manage HTN [113]. For *Artemisia persia*, the most effective dose was 400 mg/kg and none of the doses affected the DIA BP or heart rate and the oral consumption of AP reduced SYS BP after 20 minutes [114]. *Juniperus oxycedrus* L.

induced a significant decrease in SYS basal pressure, at adose of 18 mg/kg and a reduction in DIA basal pressure at 6 and 18 mg/kg, with its methanol dichloromethane content, because of the Presence of sesquiterpenoids [115].

With *Vaccinium corymbosum* L., SBP was reduced by 19% at week 4 and 30% lower, through its antioxidant mechanism [116]. In the case of *Adenantha pavonina* L. bilirubin, the protein and globulin fraction was significantly high in AP treated group and the study showed that AP seed has BP lowering potential because of the presence of cardiac glycosides in this plant, which has an antihypertensive effect [119].

The administration of Alibernet Red Wine (AWE) failed to reduce BP and improve endothelial function in the femoral arteries [120]. *Sansevieria liberica* Thunb immediately and dose-dependently lowered SYS BP by altering the SYS and pulse pressure. 250mg/kg dose lowered both SYS and DIA BP and Maintained 192 hr after exertion [123].

The study suggests that using *Persea americana* Mill the extract may produce a lipid profile at 500 mg/kg dose level and reduce the SYS and DIA BP by 45.2% it contains high potassium levels [125]. *Chlorella* sp. showed a full of an average of 63mmHg, 1hour after injection [126]. *Prunus domestica* L. might prevent cardiovascular diseases but It was not mentioned wether the BP decreased or not [131]. When used *Ajuga remota* SYS BP dropped 38mmHg. Treatment with *A. remoata* extract can arrest

and reverse cardiovascular diseases [132]. Dose dependent depression of BP and heart rate was seen with *Viscum album* L. through non-adrenergic and non-cholinergic system [134]. *Elaeis guineensis* Jacq attenuated BP increases in nitric oxide deficient rats significantly [138].

Mean arterial BP was reduced by 32%-55% using *Ferula persica* L., mechanism of which was not mentioned [140]. At 100 and 200 mg doses of *Berberis integerrima* extract significant decrease in JT and TpTe intervals was shown through Blocking fast sodium channels [141].

Oral consumption of *Rhodiola rosea* L. extract decreased SYS BP in a dose dependent manner by β -endorphin secretion [145]

The animal studies for medicinal herbs with hypertensive properties

Catha edulis (Vahl) Endl with the active component of cathinone increased both SYS and DIA BP, time-dependently by QT prolongation [146].

Neurada procumbens L. increased SYS and DIA BP, heart rate, and BP of conscious SHR. It had a significant vasoconstrictive effect on aortic strips and the vasoconstrictive effect caused by *Neurada procumbens* is mediated through α -adrenergic receptors [147]. *Echium orientale* L and *Citrus × aurantiifolia* had increased and decreased the BP, respectively. The heart rate for both cases increased [97]. After a 30-day diet with *Ginkgo biloba* L., the SYS BP increased, according to one study [148].

Human studies for medicinal herbs with antihypertensive effect through other mechanisms

Adenia cissampeloides (Planch. ex Hook.) decreased the BP significantly by reducing the muscular contraction. It had a very little effect on DIA BP [151]. *Ginkgo biloba* L. had a significant antihypertensive effect (both SYS and DIA BP) but the heart rate statistics were similar in placebo and EGB groups. This medicinal plant had an inhibitory effect on cardiovascular neuroendocrine responses during stress [152]. *Allium sativum* L. lowered DIA BP and inhibited the rate of progression of coronary artery calcification [154].

Ephedra sp. had no significant effect on BP, according to the studies [156]. In case of watermelon (*Citrullus lanatus* var. *lanatus*, family Cucurbitaceae), its extract lowered ankle BP, brachial BP and carotid wave reflection by lowering the wave reflection amplitude, independent of aortic stiffness and brachial BP [158]. *Citrus × aurantium* L. had no significant effect on BP [160].

Conclusion

In this review, *Hibiscus sabdariffa*, *Crocus sativus*, *Ginkgo Biloba*, *Vitis vinifera*, *Glycyrrhiza glabra* and *Tridax procumbens* showed anti-hypertensive properties. However, *Ephedra* sp. and *Citrus × aurantium* L. had no significant effect on HTN. It seems like even though pharmacological approach may come with adverse effects for some patients, the medicinal herbs presented in this review article cannot replace them. The fact that they contain antihypertensive

Table 1. animal studies for the efficacy and mechanism of action of different medicinal plants for HTN

Scientific name	Part and extract/ active constituent	Animal model	Dose	Duration	Result	Mechanism of action	Ref.
<i>Glycyrrhiza glabra</i> L.	Hydroalcoholic extract of root	Acetylcholine-induced HTN in rat	90 mg/kg	1 w	↓SBP & DBP Chronotropic+ Inotropic –	↓Tension in isolated aortic ↑HR Baroreceptor reflex	68
<i>Juglans regia</i> L.	Hydroalcoholic extract of blade	NaCl-induced HTN in dog	5,15,45 mg/kg	20 min	↓SBP & DBP of 15 minutes of administration Short time impression	Artery muscle relaxant Renin- angiotensin system	69
<i>Crocus sativus</i> L.	Petals	KCl-induced HTN in rat, Guinea pig	50 mg/100 g	3-4 w	↓MAP	Reduced the contractile responses of vas deferens to epinephrine without any changes in contraction	70
<i>Morus alba</i> L.	Leaf/ rutin & quercetin	Rat	1 mg/ml	1 w	↓SBP	ND	71
<i>Dombeya buettneri</i> K.Schum.	Aqueous extract of leaf	NaCl (8%)-induced HTN in rat	6 mg/kg	6 w	↓BP	relaxation of the blood vessels, muscarinic cholinergic receptor pathway	72
<i>Rehmannia glutinosa</i> (Gaertn.) DC./ <i>Aconitum variegatum</i> L.	Aqueous extract	SHR	600gr/1500ml water & 75 g/1500 ml water	120 min	↓SBP	↓Atrial natrioretic peptide depressor response Renin-angiotensin-aldosterone	73
<i>Lycoris radiate</i> (L'Hér.) Herb.	Bulb/ lycorenine	Surgical femoral HTN in rat & dog	10-40 mg/kg	4 h	↓BP in rats ↑BP in conscious dogs ↓BP in anesthetized dogs	α-adrenergic blocking activities Vasodepressor action of lycorenine	74
<i>Tridax procumbens</i> (L.) L.	Leaf	Salt-loaded diet in rat	150-200 mg/kg	192 h	↓BP by 72 h after extract ↑pulse pressure	Alteration of SBP & pulse pressure	75
<i>Olea europaea</i> L.	Leaf	L-NAME-induced HTN in rat	50 mg/kg	4 w	Dose-dependent prophylactic effect against the rise in BP	Oleuropein acting synergistically with other active principles to exert antioxidant, ACE inhibitory and possibly Ca ²⁺ channel blocking activities	76
<i>Bredemeyera floribunda</i> Willd.	Crude extract of roots	NaCl-induced HTN in rat	20-80 mg/kg	50 min	↓renal BP with doses 76 & higher the effect was irreversible/ bradycardia & death in high doses At dose of 36-70 mg/kg reversible decrease in BP	Diuretic effects	77

<i>Cudrania tricuspidata</i> (Carrière.)Bur. ex Lav.	Aqueous extract	L-NAME-induced HTN in rat	60 mg/kg	4-6 w	Restored SBP to normal level	Urinary blood Na ⁺ stimulation of NO release from vascular tissues	78
<i>Fritillaria ussuriensis</i> MAXIM.	Bulb/water extract	L-NAME-induced HTN in rat	60 mg/kg	4 w	Prevents the increase of SBP	stimulation of nitric oxide release from vascular tissues that causes vasodilation	79
<i>Commiphora opobalsamum</i> (L.) Engl.	Branch extract/fresh leaf & flowers	NaCl-induced HTN in rat	4 mg/kg	ND	Systemic ABP by 20%, ↓HR by 14%	Activation of muscarinic cholinergic receptors	80
<i>Cinnamomum camphora</i> L.	Aqueous extract	Orthostatic hypotension in rat	20 mg/kg	1-3 w	↓DBP	ND	81
<i>Coffea arabica</i> L.	Bean extract	Spontaneous hypertensive rats	140 mg/kg	4 w	↓SBP & DBP	NO-mediated vasodilation	82
<i>Moringa peregrina</i> (Forssk.) Fiori.	Hydroalcoholic leaf extract/ lupeol, α- and β-amyryrin, β-sitosterol, apigenin, rhamnetin, neochlorogenic acid, quercetin	Dexamethasone (30 μg/kg) & saline (1ml/kg)- induced HTN in rat	100, 200, 400 mg	14 d	↓SBP	Antioxidant effect	83
<i>Panax ginseng</i> L.	Root/ ginsenoside, NO	NaCl-induced HTN in rat	500 mg/kg	4 w	↓SBP improved vessel wall thickening, A maximum decrease of SBP 4-6 h post-administration	Affecting the Akt-dependent phosphorylation of eNOS/ Increased NO	84
<i>Cydonia oblonga</i> Mill.	Leaf extract	NaCl 0.9%-induced HTN in rat	25 mg/kg	2 w	↓HTN	ND	85
<i>Terminalia superba</i> Engl.& Diels	Extract	SHR	150 mg/kg	5 w	↓BP & sensitivity of muscles, improves endothelial function	TMSE decrease special emphasis to NO pathway and oxidative stress	86
<i>Schinus molle</i> L.	Methanolic extract of leaf	Saline-induced HTN in rat	32-38 mg/kg	30 min	↓MAP & SBP	Inhibition of the effects of noradrenaline on ABP	87
<i>Ageratum conyzoides</i> L.	ND	Nerve-diaphragm hypertensive rat & rabbit	2-6 mg/kg	2 min	↓SBP & DBP Better effect on DBP than SBP in anaesthetized rats	ND	88
<i>Allium sativum</i> L.	Bulb	SHR	ND	10 w	↓SBP Garlic & aged garlic have different mechanisms for their lowering effect on SBP	ND	89
<i>Ipomoea batatas</i> (L.) Lam.	Aqueous extract of tubers	NaCl-induced HTN in rat	ND	4 w	↓±4.38 mmHg BP	Increased expression of eNOS & SOD, decreasing MDA level	90

<i>Boletus aestivalis</i> (Paulet) Fr.	Hot water extract of mushrooms	SHR	77 mg/kg	2-18 w	↓SBP & DBP ↓HR	Converts inactive angiotensin I to vasopressor angiotensin II	91
<i>Ginkgo biloba</i> L.	Extract	Stroke prone/ electric field stimulation in rat	60, 120 mg/kg	3 w	↓BP, antioxidant activity	Strong antithrombotic effect	92
<i>Glycyrrhiza glabra</i> L.	Hydroalcoholic extract	Normotensive rat	0.01 mg/kg	45 min	↓SBP, DBP, mean BP	Modulation of adrenergic system and synergistic effect with cholinergic system	93
<i>Eucommia ulmoides</i> Oliv.	Leaf extract	Pre-hypertensive & SHR	3, 10, 30 mg/kg	3 w	↓SBP -Doses over 3mg/kg exhibited tendencies with a plateau effect	Agonistic effect on nervous system & acted on muscarinic acetylcholine receptors	94
<i>Vernonia polyanthes</i> Less.	Leaf extract	LiCl (60 mmol/100 g body weight)-induced HTN in rat	0.5, 1 mg/kg	7 d	↓ABP, ↑Creatinine clearance ↑Glomerular filtration rate	The precise mechanism underlying the arterial pressure falls induced by CHE-treatment has not yet been identified	95
<i>Azadirachta indica</i> A.Juss.	Leaf extract	Rat	100, 300, 1000 mg/kg	ND	Initial bradycardia Cardiac arrhythmia ↓BP dose-dependently	Caused absence of p-wave, bradycardia & ventricular arrhythmia	96
<i>Echium orientale</i> L.	Petals, fruit / Aqueous extract	Phenylephrine-induced HTN in rat	30, 180, 250 mg/kg	6 d	↓BP & HR	ND	97
<i>Portulaca oleracea</i> L.	Aqueous extract of leaf	Rat	1.4, 56 mg/kg	1-2 min	↑MAP In 40 % of rats BP was decreased	Acted on postsynaptic α -adrenoceptors and by interference with trans-membrane Ca^{2+} influx	98
<i>Clerodendrum trichotomum</i> Thunb.	Leaf	Saline-induced HTN in rat & dog	0.24 gcTT equivalent per kg	1 w	↑Urine flow & Na excretion No significant change in BP	ND	99
<i>Acorus calamus</i> L.	Extract of rhizome	Saline-induced HTN in rat & rabbit	10, 50 mg/kg	1 h	Exhibited a vasoconstrictor effect on baseline	Ca^{2+} antagonism in addition to NO pathway	100
<i>Ferula foetida</i> (Bunge) Regel.	Stem extract/ ferulic acid	Dexamethasone-induced HTN in rat	200/400/800 mg/kg	18 d	↓SBP, Antioxidant activity	Increased total peripheral resistance & hemodynamic changes ↑Vascular pressure responsiveness ↑Sympathetic, renin-angiotensin system activities	101
<i>Withania somnifera</i> L.	Roots	Adrenaline/ saline-induced HTN in dog	120, 240 mg/kg	32 min	↓DBP & ABP Prevention of the hypotensive effect of acetylcholine & increased the hypotensive effect of adrenaline	Stimulation of cholinergic receptors	102
<i>Tinospora crispa</i> L.	Stem	Saline-induced HTN in rat	1-100 mg/kg	40 min	↓BP inhibited by propranolol,	β_2 -antagonists	103

					phenolamine, & atenolol		
<i>Hibiscus sabdariffa</i> L.	Calices	Saline-induced HTN in rat	60, 125 mg/kg/d	1 w	↓BP ↑Metabolism Anti-inflammatory & antioxidant activities	Diuresis & inhibition of the angiotensin 1 converting enzyme	104
Tian Ma Gou Yen containing <i>Rhizoma Gastrodiae</i> and <i>Fructus Gardeniae</i> as chief ingredients	-	SHR	5 mg/kg	15 w	Significantly altered the development & prevented HTN	Action on sympathetic vasomotor activity	105
<i>Vitis vinifera</i> L. (GSPE)	Seed	Saline-induced HTN in rat	250 mg/kg/d	5 w	↑eNOS expression and NO production in an AMPK/SIRT1 dependent manner ↓BP	Increase in eNOS expression in vessel cells KLF2 induction	106
Farayola (<i>Persea americana</i> + <i>Allium sativum</i>)	ND	Adrenaline-induced HTN in rat	1000, 2500, 5000 mg/kg	14 d	↓Cholesterol & triglyceride, ↓SBP & DBP	ND	107
<i>Sclerocarya birrea</i> A. Rich. Hochst.	Leaf extract	Saline-induced HTN in rat	10 ⁻⁷ to 10 ⁻⁵ mg/ml	ND	↓MAP dose-dependently	NO release or intracellular Ca ²⁺ decrease	108
<i>Vitex doniana</i> Sweet	Stem bark	Saline-induced HTN in rat	200-800 mg/kg	5	↓BP dose-dependently	Affects the smooth muscle of the vascular system	109
<i>Salvia multiorrhiza</i> Bunge.	Root/ Magnesium Tanshinolate B-enriched	Saline-induced HTN in rat	0.7-175 mg/kg	3 min	The enriched extract caused greater fall in BP compared to the whole plant extract	Relaxed isolated rat and rabbit coronary arteries by tanshinones	110
<i>Crocus sativus</i> L.	Petals	Electrical field stimulation in rat, Guinea pig	50 mg/100 g b.w.	3-4 w	↓BP dose-dependently, Reduced contractile responses of vas deferens to epinephrine	Relaxatory and vasodilation	111
<i>Chromolaena odorata</i> (L.) King & H.E. Robins.	Leaf/ kaempferol, quercetin, β-sitosterol	Salt loaded diet in rat	100, 200 mg/kg	8 d	↓SBP, DBP, MAP dose-dependently	Antihypertensive effect and improvement of functional vascular changes	112
<i>Pleurotus tuber-regium</i> (Rumph. ex Fr.) Singer	Sclerotia/ flavonoids	Salt loaded diet in rat	100-200 mg/kg	10 d	Can moderate all the BP indices & manage HTN	Presence of flavonoid & phytosterol (β-sitosterol)	113
<i>Artemisia persia</i>	Leaf	Ephedrine-induced HTN in rat	300, 400, 500 mg/kg	40 min	Most effective dose was 400mg/kg None of the doses affected BP or HR ↓SBP after 20 min	ND	114
<i>Juniperus oxycedrus</i> L.	Leaf & stem	Saline-induced HTN in rat	2-48 mg/kg	ND	↓Systolic basal pressure at dose of 18 mg/kg & diastolic basal	Presence of sesquiterpenoids	115

					pressure at 6 & 18 mg/kg		
<i>Vaccinium corymbosum</i> L.	Fruit	NaCl 1% in stroke-prone rat	3% freeze-dried BB extract	8 w	↓SBP	Antioxidant effects	116
<i>Teucrium polium</i> L.	Stem bark & leaf extract	Normal saline in rabbit	20, 40, 80 mg/kg	ND	Positive inotropic effect on heart ↓BP	Relaxant and vasodilator on smooth muscles	117
<i>Ficus exasperata</i> Vahl.	Leaf extract	Rabbit	0.25-40 mg/kg	ND	↓BP with different fractions	Cholinomimetic effect	118
<i>Adenantha pavonina</i> L.	Seed	Saline-induced HTN in rat	200 mg/kg	4 w	↓BP, Bilirubin, protein & globulin fraction were significantly high in extract treated group	The presence of cardiac glycosides in this plant has antihypertensive effect	119
<i>Vitis</i> sp. (as Alibernet Red Wine, AWE)	Fruit/ wine	Normotensive & hypertensive rat	24.2 mg/kg/day	3 w	No significant change in BP & endothelial function	ND	120
<i>Cinnamomum zeylanicum</i> Blume	Stem bark/ phenolic compounds	NaCl 9%-induced HTN in rat	5, 10, 20 mg/kg	60 min	↓SBP	Vasorelaxant & vasodilatory activity Reducing cardiac activity	121
<i>Erythrophleum suaveolens</i> (Guill. & Perr.) Brenan	Stem bark	Rat/ guinea pig	0.1-100 µg/ml	ND	Induced relaxation of aortic ring segments	Vasodilatory activity	122
<i>Sansevieria liberica</i> Thunb.	Leaf	Salt loaded diet in rat	200, 250 mg/kg	7 w	↓SBP dose-dependently ↓SBP & DBP 250 mg/kg	Alteration of the systolic & pulse pressure	123
<i>Solenostemon monostachyus</i> (P Beauv.) Briq.	Leaf	Rat/ guinea pig	0.6-17.6 mg/kg	ND	↓ABP dose-dependently	Ca ²⁺ channel blocking Cardiodepression & vasodilation	124
<i>Persea Americana</i> Mill.	Seed extract	Pre-hypertensive rat	200, 500, 700 mg/kg	4 w	↓SBP & DBP by 45.2% Improvement of lipid profile parameters	High content of potassium	125
<i>Chlorella</i> sp.	Algae leaf	Rat	15-30 mg/rat	5 h	↓BP of an average of 63 mmHg	ND	126
<i>Tridax procumbens</i> L.	Leaf extract	Saline-induced HTN in rat	3-6-9 mg/kg	ND	↓ABP dose-dependently ↓HR with 6 & 9 mg/kg doses	Activation of muscarinic cholinergic receptors	127
<i>Asystasia gangetica</i> (L.) T. Anderson	Leaf extract	SHR	10-400 mg/kg	3 h	↓SBP, DBP, MAP dose, ↓HR dose-independently	Modulation of ACE, ANG 2 receptor, & HR	128

<i>Crataegus</i> sp.	Leaf & flower	Saline-induced HTN in rat	3.125,6.25,12.5,25 mg/kg	50 min	↓Both SBP & DBP with a better effect on DBP	Relaxing isolated aorta and mesenteric arteries/ reduces peripheral vascular resistance	129
<i>Crocus sativus</i> L.	Stigma/ crocin, safranal	DOCA salt-induced HTN in rat	10/20/40 mg/kg	5 w	↓SBP dose-dependently	ND	130
<i>Prunus domestica</i> L.	Fruit	SHR	ND	5 w	↓BP	Antioxidant properties	131
<i>Ajuga remota</i> Benth.	Leaf	Saline-induced HTN in rat	5-60 mg/lit	16 w	↓SBP 38 mmHg	ND	132
<i>Persea americana</i> Mill.	Seed extract	Rat	260 mg/kg	10 d	↓BP, MAP, HR	β-adrenoceptor blocker	133
<i>Viscum album</i> L.	Leaf extract	Pre-hypertensive rat	5-160 mg/kg	6 w	↓BP dose-dependently	Non-adrenergic, Non-cholinergic	134
<i>Cleistanthus collinus</i> (Roxb.) Benth.	Leaf extract	Saline-induced HTN in rat			↓BP	Exerts α-receptor blocking activity	135
<i>Passiflora edulis</i> Sims	Peel	SHR	10-50 mg/kg	4 w	↓SBP 11.5± 2.2 mmHg	NO modulation	136
<i>Camellia sinensis</i> (L.) Kuntze	Leaf	Phenylephrine-induced HTN in rat	0.3-1.2 mg/ml	4 w	Inhibition of contractile responses dose-dependently	Blockage of α ₁ -adrenergic receptors	137
<i>Elaeis guineensis</i> Jacq.	Frond	L-NAME-induced HTN in rat	ND	ND	↓BP	ND	138
<i>Vitis vinifera</i> L.	Seed	Pre-hypertensive rat	4 mg/kg/day	6 month	↓BP	NO-dependent vasodilation	139
<i>Ferula persica</i> L.	Stem, leaf, petal	Rat	30 mg/kg/d	1 month	↓MAP by 32%-55%	ND	140
<i>Berberis integerrima</i> Bunge	Fruit extract	Rat	50, 100, 200 mg/kg	2 w	↓JT&TpTe intervals with 100 & 200 mg/kg	Blocking fast Na ⁺ channels	141
<i>Parinari curatellifolia</i> Planch. ex Benth.	Bark, leaf, root	Snake venom-induced HTN in cat & rabbit	1 mg/ml	ND	↓q.Dcm amplitude in cat ↓BP	Release of vasoactive amines/ blockade of neurotransmitters such as acetylcholine	142
<i>Gongronema latifolium</i> Benth.	Leaf	Atropine & adrenaline-induced HTN in cat	1-5 mg of crude	ND	↓BP	Affecting muscarinic receptors	143
<i>Brillantaisia nitens</i> Lindau	Leaf	L-NAME-induced HTN in rat	10-40 mg/kg	4 w	Biphasic dose-related hypotensive effect	α ₁ -adrenoceptors blockade/ β-adrenergic vasodilation	144
<i>Rhodiola rosea</i> L.	Whole plant	Pre-hypertensive rat	30-35-75 mg/kg	2 w	↓SBP dose-dependently	β-endorphin secretion	145

MAP=mean arterial pressure, SBP=systolic blood pressure, DBP=diastolic blood pressure, L-NAME= nitro-l-arginine methylester, eNOS= endothelial nitric oxide synthase, ABP=arterial blood pressure, HTN= hypertension, HR= heart rate, NO= nitric oxide, DOCA= desoxycorticosterone acetate, KLF2= Krüpple like factor 2, AMPK= 5'-AMP activated protein kinase, MTB=magnesium tanshinoate B, SHR= spontaneously hypertensive rat, D= day, W= week, ND= not determined

Table 2. animal studies for the efficacy and mechanism of action of different medicinal plants which increases the blood pressure.

Scientific name	Part	Model	Does	Duration	Result	Mechanism of action	Ref.
<i>Catha edulis</i> (Vahl) Endl.	Shrub/cathinone	NaCl 9%-induced HTN in rat	3 g/kg	60 min	↑SBP & DBP time-dependently	↑QT interval	146
<i>Neurada procumbens</i> L.	Aqueous extract	SHR & saline injection in rat	1-2 g/kg	60-180 min	↑SBP, DBP, HR	Vasoconstrictive effect on aortic strips via α-adrenergic receptors	147
<i>Citrus × aurantiifolia</i>	Petals & fruit aqueous extract	Phenylephrine (1.672 mg)-induced HTN in rat	30, 180, 250 mg/kg	6 d	↑BP	ND	97
<i>Ginkgo biloba</i> L.	Leaf	Pre-hypertensive rat	0.05% -0.5%	30 d	↑SBP	ND	148

HTN= hypertension, MAP= mean arterial pressure, HR= heart rate, SBP= systolic blood pressure, DBP= diastolic blood pressure

Table 3. The list of medicinal plants used for treatment of HTN in human subjects.

Scientific name	Part	Study design	Does	Jadad score	Groups	Duration	Result	Mechanism of action	Ref.
<i>Hibiscus sabdariffa</i> L.	Aqueous calyx extract	Uncontrolled trial using cold pressor test	15 mg/kg	0	20 healthy subjects	ND	Elevation of MAP & HR were significantly lower with the extract	Reduction of vascular reactivity during sympathetic nervous system activation	149
<i>Zingiber officinale</i> Roscoe	Rhizome	Double-blind randomized trial	50, 100 mg/kg	2	Group A: distilled water Group B: 100 mg/kg of plant Group C: 50 mg/kg of plant	2-4 h	↓SBP, DBP, HR	Blockade of voltage dependent Ca ²⁺ channels	150
<i>Adenia cissampeloides</i> (Planch. ex Hook.) Harms	Extract	Single-blind trial	150 mg/kg	0	14 patients Group A: Test group Group B: Control group	1 year	↓BP with little effect on SBP	Reduction in muscular contraction	151
<i>Ginkgo biloba</i> L.	Leaf	Double-blind, placebo-controlled trial	120 mg	1	70 patients	Single-dose administration	↓SBP & DBP No significant effect on HR	Inhibition of cardiovascular neuroendocrine responses during stress	152
<i>Hibiscus sabdariffa</i> L.	Calyx	Randomized uncontrolled trial	15 mg/kg	1	20 healthy subjects	ND	↓MAP	Reduction of vascular reactivity during sympathetic nervous system activation	153

<i>Allium sativum</i> L.	Bulb	Placebo-controlled, double-blind, randomized trial	1000 mg	2	210 patients: 106 test 106 placebo	1 year	↓DBP	Inhibition of artery calcification rate	154
<i>Coffea arabica</i> L.	Been	Placebo-controlled, randomized, double-blind trial	140 mg/kg	2	28 patients: 14 placebo 14 test	14 w	↑BP Useful for mild hypertensive patients	NO-mediated vasodilation	155
<i>Ephedra</i> sp.	Sprout	Double-blind, randomized, placebo-controlled	15 mg extract 60 mg caffeine	2	13 healthy subjects	7 d	No significant change in any cardiovascular parameter	ND	156
<i>Vitis vinifera</i> L.	Seed	Double blind placebo-controlled randomized	300 mg/d	2	70 patients: 35 placebo 35 test	8 w	↓3.0 mmHg for SBP & 1.4 mmHg for DBP No significant change in ABP	NO synthesis dependent pathway Relaxes the smooth muscles on vessels	157
<i>Citrullus lanatus</i> var. <i>lanatus</i>	Whole fruit	Randomized, placebo-controlled trial	6 g/d	2	14 patients	6 w	↓Ankle BP, brachial BP, & carotid wave reflection	Reduction of wave reflection amplitude independent of aortic stiffness & brachial blood pressure	158
<i>Vitis vinifera</i> L.	Juice/ wine	Double-blind, placebo-controlled trial	800 mg	1	60 patients: 30 test 30 placebo	4 w	Wine: ↓BP, Juice: No significant change in BP	↓Plasma endothelin-1 concentrations	159
<i>Citrus × aurantium</i> L.	Fruit	Uncontrolled trial	80 mg/d	-	30 healthy adults	6 w	No significant change in BP & HR	ND	160
<i>Ginkgo biloba</i> L.	Leaf	Single-blind, randomized, placebo-controlled trial	6 capsules of 360 mg of the extract	1	14 young healthy male	6 h	↑Stiffness index (slightly higher)	ND	161
<i>Olea europaea</i> L.	Leaf	Randomized, open, controlled-parallel-group co-twin trial	500, 1000 mg/d	2	40 borderline monozygotic twins divided into treatment & placebo groups	8 w	↓Mean BP in high dose group	Cholesterol lowering action in humans	162
<i>Allium cepa</i> L. + <i>Cucurbita</i> sp.	<i>A. cepa</i> bulb, <i>Cucurbita</i> seed oil	Open-label, placebo-controlled pilot-study	ND	5	12 subjects	12 w	↓SBP 9.09 mmHg & DBP 4.06 mmHg	Antioxidant effects, Inhibition of angiotensin-converting enzyme activity	163
<i>Zea mays</i> L.	Grain	Double-blinded, placebo-controlled,	300 mg/d	3	30 healthy subjects	3 w	↓SBP & DBP	Anthocyanin seems to be useful in anti-	164

		randomized, crossover trial						hypertensive effect of purple corn	
<i>Ginkgo biloba</i> L.	Leaf & fruit	Double-blind, placebo-controlled, randomized trial	120 mg/d	3	54 patients	3 month	↓DBP	Vasodilatory properties in selected cerebral regions	165
<i>Vitis vinifera</i> L.	Seed	Single center, double-blind, placebo-controlled, randomized trial	300 mg/d	2	66 subjects	2 w	↓SBP & DBP	Endothelium dependent relaxation through activation of PI3K/Akt signaling	166

LDH=Lactate dehydrogenase, CK=creatine kinase, DBP=diastolic blood pressure, SBP=systolic blood pressure, ABP=arterial blood pressure, eNOS= endothelial nitric oxide synthase, MAP= mean arterial pressure, D= day

compounds does not indicate that patients can use it instead of drugs. So with these raw data available, patients should be advised against medicinal herb consumption, since they may cause several complications. Even though the desired effect for the medicinal herbs mentioned here has been proved by several human and animal studies, the safety of these compounds are not elucidated nor could it be a therapeutic course for patients with HTN.

Conflicts of Interest

None.

Acknowledgment

None.

List of abbreviations

Systolic= SYS

Diastolic= DIA

LDH=Lactate dehydrogenase

CK=creatine kinase

EGB=extract of ginkgo biloba

DBP=diastolic blood pressure

SBP=systolic blood pressure

BP=blood pressure

ABP=arterial blood pressure

eNOS= endothelial nitric oxide synthase

MAP= mean arterial pressure

SBP=systolic blood pressure

L-NAME= nitro-l-arginine methylester

Enos= endothelial nitric oxide synthase

ABP=arterial blood pressure

EL=eucommia leaf

GSPE= Grape seed proanthocyanidin extracts

KLF2= Krüpple like factor 2

AMPK= 5'-AMP activated protein kinase

MTB=magnesium tanshinoate B

AP=Artemisia Persia

SHR= spontaneously hypertensive rats

GTE= green tea extract

References

- [1] Walther D, Curjuric I, Dratva J, Schaffner E, Quinto C, Rochat T, Gaspoz JM, Burdet L, Bridevaux PO, Pons M, Gerbase MW, Schindler C, Probst-Hensch N. High BP: prevalence and adherence to guidelines in a population-based cohort. *Swiss Med Wkly* 2016;146:143-153
- [2] Bonde LO. Health musicing - music therapy or music and health? A model, empirical examples and personal reflections. *Music Arts Action* 2011;3:20.
- [3] Levy D, Larson MG, Vasan RS, Kannel WB, Ho KK. The progression from HTN to congestive heart failure. *JAMA*. 1996;275:1557.
- [4] Dahlöf B, Sever PS, Poulter NR, Wedel H, Beevers DG, Caulfield M, Collins R, Kjeldsen SE, Kristinsson A, McInnes GT, Mehlsen J, Nieminen M, O'Brien E, Ostergren J. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-BP Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. *Lancet* 2005;10-16:895-906.
- [5] <http://reference.medscape.com/drug/tenormin-atenolol-342356#4>
- [6] Astin, JA. Why patients use alternative medicine: results of a national study. *JAMA* 1998;279:1548-1553.
- [7] Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, Chalmers J, Rodgers A, Rahimi K. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet* 2016;387:957-967.
- [8] Rivlin RS. Historical perspective on the use of garlic. *J Nutr* 2001;131:951-954.
- [9] Jung F, pindur G. Effects of garlic thrombocyte aggregation, microcirculation and other risk factors. *Int Clin Pharmacol Ther Toxicol* 1991;29:151-155.
- [10] Pedraza J, Tapia E, Medina ON. Garlic prevents HTN induced by chronic inhibition of nitric oxide synthesis. *Life Sci*. 1998;62:71-77.
- [11] Ali M, Thomson M. Consumption of a garlic clove a day could be beneficial in preventing thrombosis. *Prostaglandins Leukot Essent Fatty Acids* 2001;53:211-212.
- [12] Mahan LK, Scott-Stump S. *Krause's Food Nutrition and Diet Therapy*. 10th ed. WB Saunders. Philadelphia 2000; pp 742-777 and 558-593.
- [13] Mirzaei M, Moayedallaie S, Jabbari L, Mohammadi M. Prevalence of HTN in iran 1980–2012: a systematic review. *J Tehran Heart Cent* 2016;11:159.
- [14] Ford ES, Li C. Metabolic syndrome and health-related quality of life among U.S. adults. *Ann Epidemiol* 2008;18:165-171.
- [15] Rastegar M, Tavana Z, Khademi R, Nabipour I. Ethnopharmacology of the native herbs of helleh River (Bushehr Province/Iran). *ISMJ* 2012;15:303-316.
- [16] Noguchi N, Niki E. Phenolic antioxidants: a rationale for design and evaluation of novel antioxidant drug for atherosclerosis. *Free Radical Bio Med* 2000;28:1538-1546.
- [17] Kessler RC, Davis RB, Foster DF. Longterm trends in the use of complementary and alternative medical therapies in the United States. *Ann Intern Med* 2001;135:262-268.
- [18] Eisenberg DM, Davis RB, Ettner SL. Trends in alternative medicine use in the United States, 1990-1997. Results of a follow-up national survey. *JAMA* 1998;280:1569-1575.
- [19] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high BP: the JNC 7 report. *JAMA* 2003;289:2560–2572..
- [20] Edzard E. The efficacy of herbal medicine—an overview. *Fund Clin Pharmacol* 2005;19:405-409.
- [21] Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of HTN: analysis of worldwide data. *Lancet* 2005;365:217-223.
- [22] Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, Galderisi M, Grobbee DE, Jaarsma T, Kirchhof P, Kjeldsen SE, Laurent S, Manolis AJ, Nilsson PM, Ruilope LM, Schmieder RE, Sirnes PA, Sleight P, Viigimaa M, Waeber B, Zannad F, Redon J, Dominiczak A, Narkiewicz K, Nilsson PM, Burnier M, Viigimaa M, Ambrosioni E, Caulfield M, Coca A, Olsen MH, Schmieder RE, Tsioufis C, van de Borne P, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Clement DL, Coca A, Gillebert TC, Tendera M, Rosei EA, Ambrosioni E, Anker SD, Bauersachs J, Hitij JB, Caulfield M, De Buyzere M, De Geest S, Derumeaux GA, Erdine S, Farsang C, Funck-Brentano C, Gerc V, Germano G, Gielen S, Haller H, Hoes AW, Jordan J, Kahan T, Komajda M, Lovic D, Mahrholdt H, Olsen MH, Ostergren J, Parati G, Perk J, Polonia J, Popescu BA, Reiner Z, Rydén L, Sirenko Y, Stanton A, Struijker-Boudier H, Tsioufis C, van de Borne P, Vlachopoulos C, Volpe M, Wood DA. 2013 ESH/ESC guidelines for the management of arterial HTN: the task force for the management of arterial HTN of the european society of HTN (ESH) and of the european society of cardiology (ESC). *Eur Heart J* 2013;34:2159-219.
- [23] Davids D, Gibson D, Johnson Q. Ethnobotanical survey

- of medicinal plants used to manage high BP and type 2 diabetes mellitus in Bitterfontein, Western Cape Province, South Africa. *J Ethnopharmacol* 2016;194:755-766.
- [24] Han L, Li JP, Sit JW, Chung L, Jiao ZY, Ma WG. Effects of music intervention on physiological stress response and anxiety level of mechanically ventilated patients in China: a randomised controlled trial. *J Clin Nurs* 2010;19:978-987.
- [25] Kamioka H, Tsutani K, Yamada M, Park H, Okuizumi H, Tsuruoka K, Honda T, Okada S, Park SJ, Kitayuguchi J, Abe T, Handa S, Oshio T, Mutoh Y. Effectiveness of music therapy: a summary of systematic reviews based on randomized controlled trials of music interventions. *Patient Prefer Adherence* 2014;8:727-754.
- [26] Maratos AS, Gold C, Wang X, Crawford MJ. Music therapy for depression. *Cochrane Database Syst Rev* 2008;1:CD004517.
- [27] Loomba RS, Arora R, Shah PH, Chandrasekar S, Molnar J. Effects of music on SYS BP, DIA BP, and heart rate: a meta-analysis. *Indian Heart J.* 2012;64:309-313.
- [28] Bradt J, Dileo C, Potvin N. Music for stress and anxiety reduction in coronary heart disease patients. *Cochrane Database Syst Rev* 2013;12:CD006577.
- [29] American Music Therapy Association. <http://www.musictherapy.org/about/quotes/>.
- [30] Grocke DE, Wigram T. Receptive methods in music therapy techniques and clinical applications for music therapy clinicians, educators, and students. Jessica Kingsley Publishers. London 2007.
- [31] Bonde LO. Health musicing - music therapy or music and health? A model, empirical examples and personal reflections. *Music Arts Action.* 2011;3:20.
- [32] Bradt J, Dileo C, Shim M. Music interventions for preoperative anxiety. *Cochrane Database Syst Rev* 2013;6:CD006908.
- [33] Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* 2009;62:1006-1012.
- [34] Borenstein M, Hedges LV, Higgins JP, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods* 2010;1:97-111.
- [35] Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD. The cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
- [36] Bekiroglu T, Ovayolu N, Ergun Y, Ekerbicer HC. Effect of Turkish classical music on BP: a randomized controlled trial in hypertensive elderly patients. *Complement Ther Med* 2013; 21:147-54.
- [37] Zanini CR, Jardim PC, Salgado CM, Nunes MC, Urzedo FL, Carvalho MV, Pereira DA, Jardim TS, de Souza WK. Music therapy effects on the quality of life and the BP of hypertensive patients. *Arq Bras Cardiol.* 2009;93:534-540.
- [38] Chan MF, Chan EA, Mok E, Kwan Tse FY. Effect of music on depression levels and physiological responses in community-based older adults. *Int J Ment Health Nurs* 2009;18: 285-294.
- [39] Schein MH, Gavish B, Herz M, Rosner-Kahana D, Naveh P, Knishkowsky B, Zlotnikov E, Ben-Zvi N, Melmed RN. Treating HTN with a device that slows and regularises breathing: a randomised, double-blind controlled study. *J Hum Hypertens* 2001;15:271-278.
- [40] Pandic S, Ekman I, Nord L, Kjellgren KI. Device-guided breathing exercises in the treatment of HTN - perceptions and effects. *CVD Prev Control* 2008;3:163-169.
- [41] Logtenberg SJ, Kleefstra N, Houweling ST, Groenier KH, Bilo HJ. Effect of device-guided breathing exercises on BP in hypertensive patients with type 2 diabetes mellitus: a randomized controlled trial. *J Hypertens* 2007;25:241-246.
- [42] Altena MR, Kleefstra N, Logtenberg SJ, Groenier KH, Houweling ST, Bilo HJ. Effect of device-guided breathing exercises on BP in patients with HTN: a randomized controlled trial. *Blood Press* 2009;18:273-279.
- [43] Tang HY, Harms V, Speck SM, Vezeau T, Jesurum JT. Effects of audio relaxation programs for BP reduction in older adults. *Eur J Cardiovasc Nurs* 2009;8:329-336.
- [44] Grossman E, Grossman A, Schein MH, Zimlichman R, Gavish B. Breathing-control lowers BP. *J Hum Hypertens* 2001;15:263-269.
- [45] Whelton PK, He J, Appel LJ, Cutler JA, Havas S, Kotchen TA, Roccella EJ, Stout R, Vallbona C, Winston MC, Karimbakas J. Primary prevention of HTN: clinical and public health advisory from The National High BP Education Program. *JAMA.* 2002;288:1882-1888.
- [46] Sutoo D, Akiyama K. Music improves dopaminergic neurotransmission: demonstration based on the effect of music on BP regulation. *Brain Res* 2004;1016:255-262.
- [47] Koch ME, Kain ZN, Ayoub C, Rosenbaum SH. The sedative and analgesic sparing effect of music. *Anesthesiology* 1998;89:300-306.
- [48] Menon V, Levitin DJ. The rewards of music listening: response and physiological connectivity of the mesolimbic system. *Neuroimage* 2005;28:175-184.
- [49] Patel HC, Hayward C, Ozdemir BA, Rosen SD, Krum H, Lyon AR, Francis DP, di Mario C. Magnitude of BP reduction in the placebo arms of modern HTN trials: implications for trials of renal denervation. *Hypertension* 2015;65:401-406.
- [50] Aubiniere-Robb L, Jeemon P, Hastie CE, Patel RK, McCallum L, Morrison D, Walters M, Dawson J, Sloan W, Muir S, Dominiczak AF, McInnes GT, Padmanabhan S. BP response to patterns of weather fluctuations and ef-

- fect on mortality. *Hypertension* 2013;62: 190-196.
- [51] Klassen JA, Liang Y, Tjosvold L, Klassen TP, Hartling L. Music for pain and anxiety in children undergoing medical procedures: a systematic review of randomized controlled trials. *Ambul Pediatr* 2008;8:117-128.
- [52] Ovayolu N, Ucan O, Pehlivan S, Pehlivan Y, Buyukhatipoglu H, Savas MC, Gulsen MT. Listening to Turkish classical music decreases patients' anxiety, pain, dissatisfaction and the dose of sedative and analgesic drugs during colonoscopy: a prospective randomized controlled trial. *World J Gastroenterol* 2006;12:7532-7536.
- [53] Hole J, Hirsch M, Ball E, Meads C. Music as an aid for postoperative recovery in adults: a systematic review and meta-analysis. *Lancet* 2015;386:1659-1671.
- [54] Akiyama K, Sutoo D. Effect of different frequencies of music on BP regulation in spontaneously hypertensive rats. *Neurosci Lett* 2011;487:58-60.
- [55] Jafari H, Emami Zeydi A, Khani S, Esmaeili R, Soleimani A. The effects of listening to preferred music on pain intensity after open heart surgery. *Iran J Nurs Midwifery Res* 2012;17:1-6.
- [56] Ioannidis JP, Lau J. Pooling research results: benefits and limitations of meta-analysis. *Jt Comm J Qual Improv* 1999;25:462-469.
- [57] Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P, Group C. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Ann Intern Med* 2008;148:295-309.
- [58] Gu Q, Yang X, Lin L, Li S, Li Q, Zhong S, Peng J, Cui Z. Genetic ablation of solute carrier family 7a3a leads to hepatic steatosis in zebrafish during fasting. *Hepatolgy* 2014;60: 1929-1941.
- [59] Ignarro LJ, Buga GM, Wood KS, Byrns RE, Chaudhuri G. Endothelium derived relaxing factor produced and released from artery and vein is nitric oxide. *Proc Natl Acad Sci USA* 1987;84:9265.
- [60] Palmer RMJ, Ferrige AG, Moncada S. Nitric oxide release account for the biological activity of endothelium-derived relaxing factor, *Nature* 1987;327:524.
- [61] di Rienzo M, Parati G, Radaelli A, Castiglioni P. Baroreflex contribution to BP and heart rate oscillations: time scales, time-variant characteristics and nonlinearities. *Philos Trans Royal Soc A* 2009;367:1301-1318.
- [62] Kotchen TA, Luepker RV, Nichaman MZ. Proceedng of the workshop on obesity and BP. *Ann Epidemiol* 1991;1:285-383.
- [63] National Research Council. Committee on Diet and Health, Food and Nutrition Board, Commission on Life Sciences, Diet and Health: Implication for reducing chronic disease. Washington DC, National Academy press 1989.
- [64] The trial of HTN prevention collaboborative research group. The effects of nonpharmacologic interventions on BP of person with high-normal levels, results of the trials of HTN prevention phase 1. *JAMA* 1992;267:1213-1220
- [65] Zhou D, Liang Z, Qin Q, Zhang M, Li S. Therapeutic efficacy and mechanisms of quercetin in a rat model of nonalcoholic fatty liver disease. *Chin J Hepatol* 2013;21:134-137.
- [66] García-Mediavilla V, Crespo I, Collado PS, Esteller A, Sánchez-Campos S, Tuñón MJ. The anti-inflammatory flavones quercetin and kaempferol cause inhibition of inducible nitric oxide synthase, cyclooxygenase-2 and reactive C-protein, and down-regulation of the nuclear factor kappaB pathway in Chang Liver cells. *Eur J Pharmacol* 2007;557:221-229.
- [67] Muller MD, Drew RC, Blaha CA, Mast JL, Cui J, Reed AB, Sinoway LI. Oxidative stress contributes to the augmented exercise pressor reflex in peripheral arterial disease patients. *J Physiol* 2012;590:6237-6246.
- [68] Khoshnam SI, Bahadolid A, Patriots J, Gholampour F, Khosravi AR. Effect of aqueous-alcoholic extract of *glycyrrhiza glabra* Expression on electrocardiogram and its interaction with cholinergic system in wistar male rats. *Armaghan Danesh, Journal of Yasuj University of Medical Sciences* 1394;20:9-11
- [69] Javadi S, Maham M, Rezapour V. The effect of intravenous administration of walnut extract on BP changes and renin and aldosterone levels. *Urmia Medical Journal.* 2013;24:11-16.
- [70] Fatehi M, Rashidabady T, Fatehi-Hassanabad Z. Effects of *Crocus sativus* petals' extract on rat BP and on responses induced by electrical field stimulation in the rat isolated vas deferens and guinea-pig ileum. *J Ethnopharmacol* 2003;84:199-203.
- [71] Siti A, Suwaldi, Fudholi A, Wahyono. The effect of encapsulated mulberry (*morus alba* l.) leaves extract on arterial bp in rats pengaruh enkapsulasi ekstrak daun murbei (*morus alba* l.) terhadap tekanan darah arteri pada tikus. *Trad Med J* 2014;19:149-155.
- [72] Okwari O, Ofem OE, Bisong SA, Ettarh RR. The aqueous leaf extract of *dombeya buttneri* produces bp lowering in albino wistar rats. *Int J Curr Res* 2011;2:92-96.
- [73] Do-Gon R, Yong-Gab Y, Jin-Goo N, Ho-sub L. Effect of *rehmanniae radix* and *radix aconiti* water extracts on bp in hypertensive rats. *medicinal resources research center.* 2001;18:171-175.
- [74] Miyasaka K, Hiramatsu Y. Pharmacological studies of lycorenine, an alkaloid of *lycoris radiate* herb.effects of BP in rats and dogs and the mechanism of tachyphylaxis to the vasodepressor action of lycorenine in rats. *Japan J pharmacol* 1980;30:655-664.
- [75] Ikewuchi JC, Ikewuchi CC. Hypocholesterolaemic effect of aqueous extract of *acalypha wilkesiana* 'godsefiana' muell arg on rats fed egg yolk supplemented diet:

- implications for cardiovascular risk management. *Res J Sci Tech* 2010;2:78-81.
- [76] Khayyala MT, El-Ghazalyb MA, Abdallaha DM, Nassara NN, Okpanyic SN, Kreuterd MH. BP lowering effect of an olive leaf extract (*olea europaea*) in l-name induced HTN in rats. *Arzneimittelforsch* 2002;52:797-802.
- [77] Bevevino LH, Vieira FSA, Cassolab AC, Sanioto SML. Effect of crude extract of roots of *brede-meyera floribunda* willd. i. effect on arterial BP and renal excretion in the rat. *J Ethnopharmacol* 1994;43:197-201.
- [78] Kang DG, Hur TY, Lee GM, Oh H, Won TO, Sohn EJ, Lee HS. Effects of *cudrania tricuspidata* water extract on BP and renal functions in NO-dependent HTN. *Life Sci* 2002; 70:2599-2609.
- [79] Kang DG, Sohn EJ, Lee YM, Lee AS, Han JH, Kim TY, Lee HS. Effects of *bulbus Fritillaria* water extract on BP and renal functions in the L-NAME-induced hypertensive rats. *J Ethnopharmacol* 2004;91:51-56.
- [80] Abdul-Ghani AS, Amin R. Effect of aqueous extract of *Commiphora opobalsamum* on BP and heart rate in rats. *J Ethnopharmacol* 1997;57:219-222.
- [81] Phytomedicine. Available from: <http://www.urbanfischer.de/journals/phytomed/Phytomedicine>.
- [82] Watanabe T. The BP-lowering effect and safety of chromogenic acid from green coffee bean extract in essential HTN effects of CGA in patients with essential HTN. *Clin Exp Hypertens* 2006;28:439-449.
- [83] Safaeian L, Asghari G, Haghjoo Javanmard S, Heidarnejad A. The effect of hydroalcoholic extract from the leaves of *Moringa eregrine* (Forssk.) Fiori. On BP and oxidative status in dexamethasone-induced hypertensive rats. *Adv Biomed Res* 2015;4:101.
- [84] Hong SY, Kim JY, Ahn HY, Shin JH, Kwon O. Panax ginseng extract rich in ginsenoside protopanaxatriol attenuates BP elevation in spontaneously hypertensive rats by affecting the akt-dependent phosphorylation of endothelial nitric oxide synthase. *J Agric Food Chem* 2012;28:3086-3091.
- [85] Zhoua WT, Abdurahman A, Abdusalam E, Yiming W, Abliz P, Aji Q. Effect of *Cydonia oblonga* Mill. Leaf extracts or captopril on BP and related biomarkers in renal hypertensive rats. *J Ethnopharmacol* 2014;153:635-640.
- [86] Tom EN, Girard-Thernier C, Martin H, Dimo T, Alvergnas M, Nappey M, Berthelot A, Demougeot C. Treatment with an extract of *terminalia superba* engler and diels decreases BP and improves endothelial function in spontaneously hypertensive rats. *J Ethnopharmacol* 2014;151:372-379.
- [87] Belle R, Barrachina L, Moreno E, Primo-Yufer, Espluques J. Effects on Arterial BP of the Methanol and Dichloromethanol Extracts from *Schinus molle* L. in Rats. *Phytother Res.* 1996;10: 634-635.
- [88] Achola KJ, Munenge RW. Activity of *ageratum conyzoides* on isolated rat phrenic nerve-diaphragm and BP on anaesthetised rats. *Int J Pharmacogn* 1997;35:31-37.
- [89] Harauma A, Moriguchi T. Aged garlic extract improves BP in spontaneously hypertensive Rats. *J Nutr* 2006;136:769S-773S.
- [90] Jawi M, Ayu Artini G, Nova Mahendra A, Suprpta DN. Purple sweet potato aqueous extract lowers BP and prevents oxidative stress in hypertensive elderly patients at nyuhkuning village, mas, ubud, bali. *J Biol Agriculture Healthcare* 2014;4:60-64.
- [91] Midoh N, Miyazawa N, Eguchi F. Effects of a Hot-Water Extract of porcini (*Boletus festivals*) Mushrooms on the BP and Heart Rate of Spontaneously Hypertensive Rats. *Biosci Biotechnol Biochem* 2013;77:1769-1772.
- [92] Sasaki Y, Noguchi T, Yamamoto E, Giddings JC, Ikeda K. Effects of ginkgo biloba extract (egb 761) on cerebral thrombosis and bp in stroke-prone spontaneously hypertensive rats. *Clin Exp Pharmacol Physiol* 2002;29:963-967.
- [93] Khoshnam SE, Bahaoddini A. The effect of hydro-alcoholic extract of *glycyrrhiza glabra* on the cardiovascular system of male rats with normal BP and its interaction with cholinergic and adrenergic systems. *Physiol Pharmacol* 2013;17:349-358.
- [94] Yamaguchi Y, Kawamura N, Tsuboi T, Yamaguchi Y, Hirata T, ueda T, Tagawa C. Effect of the *eucommia ulmoides* leaf extract on BP. *Int Symp Eucommia Ulmoides* 2007;1:55-62.
- [95] Romanezi da Silveira R, Foglio MA, Gontijo JA. Effect of the crude extract of *vernonia polyanthes* Less. on BP and renal sodium excretion in unanesthetized rats. *Phytomedicine.* 2003;10:127-131.
- [96] Koley KM, Lal J. Pharmacological effects of *azadirachta indica* (neem) leaf extract on the ECG and bp of rat. *Indian J Physiol Pharmacol* 1994;38:223-225.
- [97] Hamidi M, Khaksari M. Effects of the consumption of aqueous extract of ovine and omelette lemon on BP and heart rate before and after injection of phenylephrine in male rats. *Journal of Kerman University of Medical Sciences* 2011;18: 349-357.
- [98] Parry O, Okwuasaba F, Ejike C. Effect of an aqueous extract of *portulaca oleracea* leaves on smooth muscle and rat bp. *J Ethnopharmacol* 1988;22:33-34.
- [99] Lut G-W, Miura K, Yukimura T, Yamamoto K. Effects of extract from *Clerodendron trichotomum* on BP and renal function in rats and dogs. *J Ethnopharmacol* 1994;42:77-82.
- [100] Jabbar-Shah A, Gilani A. BP-lowering and vascular modulator effects of *acorus calamus* extract are mediated through multiple pathways. *J Cardiovasc Pharmacol* 2009;54:38-46.
- [101] Safaeian L, Ghannadi A, Haghjoo Javanmard S, Va-

- hidian MH. The effect of hydroalcoholic extract of *Ferula foetida* stems on BP and oxidative stress in dexamethasone-induced hypertensive rats. *Res Pharm Sci* 2015;10:326-334.
- [102] Ahumada F, Aspee F. *Withania somnifera* extract, its effect on arterial BP in anaesthetized dogs. *Phytother Res* 1991;5:111-114.
- [103] Pramana S, Mulvanyc MJ, Allenbachd Y, Marstond A, Hostettmannd K, Sirirugsab P, Jansakula C. Effects of an n-butanol extract from the stem of *Tinospora crispa* on BP and heart rate in anesthetized rats. *J Ethnopharmacol* 2011;133:675-686.
- [104] Joven J, March I, Espinel E, Fernández-Arroyo S, Rodríguez-Gallego E, Aragonès G, Beltrán-Debón R, Alonso-Villaverde C, Rios L, Martín-Paredero V, Menendez JA, Micol V, Segura-Carretero A, Camps J. *Hibiscus sabdariffa* extract lowers BP and improves endothelial function. *Mol Nutr Food Res* 2014;58:1374-1378.
- [105] Zhang TX, Wang YF, Ciriello J. The herbal medicine Tian Ma Gou Teng Yen alters the development of High BP in the Spontaneously Hypertensive Rat. *Am J Chin Med* 1989;3: 211-219.
- [106] Xiaopei C, Xiangju L, Hua F, Shaohua Z, Haiqing G. Grape seed proanthocyanidin extracts enhance endothelial nitric oxide synthase expression through 5'-amp activated protein kinase/surtuin 1-krüppel like factor 2 pathway and modulate bpin ouabain induced hypertensive rats. *Biol Pharm Bull* 2012;35:2192-2197.
- [107] Akande IS, Omenkuku U. Farayola anti-hypertensive herbal mixture improves bp and lipid profile of adrenaline-induced htn in rats. *J Basic Med Sci* 2009;1:16-21.
- [108] Belemtougri RG, Dzamitika SA, Ouedraogo Y, Sawadogo L. Effect of water crude leaf extract of *sclerocarya birrea* (a.rich) hochts (anacardiaceae) on normotensive rat bp. *J Biol Sci* 2007;7:570-574.
- [109] Ladeji O, Okoye ZSC, Uddoh F. Effects of *vitex doniana* Stem bark extract on BP. *Phytother Res* 1996;10:245-247.
- [110] Leung SWS, China PR. Effects of the aqueous extract of *salvia miltiorrhiza* (danshen) and its magnesium tanshinolate B-enriched Form on BP. *Phytother Res* 2010;24:769-774.
- [111] Fatehi M, Rashidabady T, Hassanabad Z. Effects of petals extracts of saffron on rat bp and on responses induced by electrical field stimulation in the rat isolated vas deferens and guinea-pig ileum. *J Ethnopharmacol* 2003;84:199-203.
- [112] Catherine CI, Edward OA, Eugene NO, Jude CI. Effect of aqueous extract of the leaves of *Sansevieria liberica* Gérôme and Labroy on BP indices and pulse rates of sub-chronic salt-loaded rats. *J Nat Rem* 2012;12:30-38.
- [113] Ikewuchia JC, Ikewuchia CC, Ifeanachoa MO, Igbohb NM. BP lowering activity of a flavonoid and phytosterol rich extract of the sclerotia of *Pleurotus tuberregium* (Fr) Sing in salt-loaded rats. *Biomed Prev Nutr* 2014;4:257-263.
- [114] Esmacili F, Sepehri G, Moshtaghi-kashanian G, khaksari M, Salari N, Sepehri E. The effect of acute administration of *Artemisia Persia* extracts on arterial BP and heart rate in rats. *Am J Appl Sci* 2009;6:843-847.
- [115] Bello R, Moreno L. Effects on Arterial BP of methanol and dichloromethanol extracts from *juniperus*. *Phytother Res* 1997;11:161-162.
- [116] Shaughnessya KS, Boswall IA, Scanlana AP, Gottschall-Passb KT, Sweeney MI. Diets containing blueberry extract lower BP in spontaneously hypertensive stroke-prone rats. *Nutr Res* 2009;29:130-138.
- [117] Romanezi da Silveira R, Foglio MA, Gontijo JA. Effect of the crude extract of *vernonia polyanthes* Less.on BP and renal sodium excretion in unanesthetized rats. *Phytomedicine*. 2003;10:127-131.
- [118] Amonkan AK, Konan AB, Kouakou L, Bleyere MN, Bouafou MGK, Kati-Coulibaly S. Comparative effects of different fractions of crude aqueous extract of *Ficus exasperata* leaves on BP. *Int Curr Pharm J* 2013;2:193-195.
- [119] Adedapo AD, Osude YO, Adedapo AA, Moody JO, Adeagbo AS, Olajide OA, Makinde JM. BP lowering effect of *adenanthera pavonina* seed extract on normotensive rats. *Rec Nat Prod* 2009;3:82-89.
- [120] Bališ P, Púzserová A, Slezák P, Šestáková N, Pecháňová O. Short-term administration of alibernet red wine extract failed to affect bp and to improve endothelial function in young normotensive and spontaneously hypertensive rats. *Physiol Res* 2013;62:631-641.
- [121] Wansi SL, Nyadjeu P, Ngamga D, Pami E. BP lowering effect of the ethanol extract from the stem bark of *cinnamomum zeylanicum* (lauraceae) in rats. *Pharmacologyonline* 2007;3:166-176.
- [122] Kamanyi A, Dongmo AB, Salah MA, Jatsa H, Wagner H. Endothelium mediated aortic relaxation and BP lowering effect of a procyanidin rich fraction of the stem bark extracts of *erythrophleum suaveolens*. *Pharm Biol* 2003;41:62-67.
- [123] Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* 2009;62:1006-1012.
- [124] Fidele KZ, Andre KB, Yao DJ, Michel OA. Action of hydroethanolic leaves extract of *solenostemon monostachyus* (lamiaceae) on cardiovascular system of mammals: BP lowering effects. *IJPBS* 2012;2:310-320.
- [125] Imafidon KE, Amaechina FC. Effects of aqueous seed extract of *persea americana* mill. (avocado) on bp and lipid profile in hypertensive rats. *Adv Biol Res*

- 2010;4:116-121.
- [126] Okamoto K, Lizuka Y, Murakami T, Miyake H, Susuki T. Effects of chlorella alkali extract on BP in SHR. *Jpn Heart J* 1978;19:622-623.
- [127] Salahdeen HM, Yemitan OK, Alada ARA. Effect of aqueous leaf extract of *tridax procumbens* on BP and heart rate in rats. *African Journal of Biomedical Research* 2004;7: 27-29.
- [128] Mugabo P, Raji IA. Effects of aqueous leaf extract of *asystasia gangetica* on the BP and heart rate in male spontaneously hypertensive Wistar rats. *BMC Complement Altern Med* 2013; 13:283.
- [129] Susan WS, Miranda MW, Ricky YK. Effects of an extract of hawthorn on arterial BP in anaesthetized rats. *Cardiovasc Pharmacol* 2013;2:6-8.
- [130] Imenshahidi M, Razavi BM, Hosseinzadeh H. The effect of chronic administration of saffron (*crocus sativus*) stigma aqueous extract on sys BP in rats. *Jundishapur J Nat Pharm Prod* 2013;8:175-179.
- [131] Negishi H. Effects of prune extract on bp elevation in stroke-prone spontaneously hypertensive rats. *Clin Exp Pharmacol Physiol* 2007;34:S47-S48.
- [132] Odek-Ogunde M, Rajab MS, Migwi GJ, Ndegwa JM. BP Responses to an Extract of *Ajuga remota* in Experimentally Hypertensive Rats. *Planta Med.* 1993;59:573-574.
- [133] Anaka ON, Ozolua RI, Stephen O. Effect of the aqueous seed extract of *persea americana* mill (Lauraceae) on the BP of sprague-dawley rats. *African Journal of Pharmacy and Pharmacology* 2009;3:485-490.
- [134] Eno AE, Ibokette UE, Ofem OE, Unoh FB, Nkanu E, Azah N. The effects of a nigerian specie of *viscum album* (mistletoe) leaf extract on the bp of normotensive and doca-induced hypertensive rats. *Nigerian Journal of Physiological Sciences* 2004;19(1-2):33-38.
- [135] Parasuraman S, Raveendran R. The effects of aqueous extract of *cleistanthus collinus* (Roxb.) (Euphorbiaceae) leaves on rat BP. *Pharmacognosy Res* 2012;4:178-180.
- [136] Zibadi S, Faridc R, Moriguchi S, Lue Y, Yeap Fooe L, Moslemzadeh Tehrani P, Ulreich JB, Ronald R, Watsona RR. Oral administration of purple passion fruit peel extract attenuates BP in female spontaneously hypertensive rats and humans. *Nutr Res* 2007;27:408-416.
- [137] Lim DY, Lee ES, Park HG, Kim BC, Soon-Pyo H, Lee EB. Comparison of green tea extract and epigallocatechin gallate on bp and contractile responses of vascular smooth muscle of rats. *Arch Pharm Res* 2003;26:214-223.
- [138] Jaffri J. Effects of oil palm frond methanolic extract on bp, antioxidant status and selected organs of nitric oxide-deficient rats [PhD thesis]. *Universiti Putra Malaysia, Malaysia*; 2009.
- [139] Allersa NJ, Haya L, Schuttea PJ, Steinmannb CML, du Plooyb SH, Böhmerb LH. Long-term effects of a low dosage of grape seed proanthocyanidin extract on BP in spontaneously hypertensive rats. *South African Journal of Science.* 2008;104:308-310.
- [140] Ghanbari M, Zahedi Khorasani M, Vakili A, Taherian A, Samani HR. On normal BP in rats (*Ferula persica*), the acute and chronic effects of aqueous plant extract. *Koomesh* 14.
- [141] Joukar S, Mahdavi N. Alterations of BP and ECG following two-week consumption of *berberis integerrima* fruit extract. *Int Sch Res Notices* 2014;2014:6.
- [142] Omale S, Auta A, Banwat SB, Amagon KI, Thomas YP. Effects of the ethanolic extract of *parinari curatellifolia* on cat BP and rabbit jejunum preparations. *IJPF* 2011;1:39-44.
- [143] Ezekwe CI, Okorie A, Ugwu Okechukwu PC, Nwodo OFC, Ezea SC. BP Lowering effect of extract of *gongronema latifolium*. *RJPBCS* 2015;2:6-9.
- [144] Bopda M. Effects of *brillantaisia nitens* lindau (acanthaceae) methylene chloride/methanol leaf extract on rat arterial BP and heart rate. *Pharmacologyonline* 2007;1:495-510.
- [145] Lee WL, Chung HH, Cheng YZ, Lin HJ, Cheng JT. *Rhodiola*-water extract induces b-endorphin secretion to lower bp in spontaneously hypertensive rats. *Phytother Res* 2013; 27:1543-1547.
- [146] Costa EC, Gonçalves AA, Areas MA, Morgabel RG. Effects of metformin on QT and QTc interval dispersion of diabetic rats. *Arq Bras Cardiol* 2008;9D:232:238.
- [147] Chen HB, Islam MW, Radhakrishnan R, Wahab SA, Naji MA. Influence of aqueous extract from *Neurada procumbens* L. on BP of rats. *J Ethnopharmacol* 2004;90:191-194.
- [148] Kubota Y, Tanaka N, Kagota S, Nakamura K. Effects of *Ginkgo biloba* extract on BP and vascular endothelial response by acetylcholine in spontaneously hypertensive rats. *JPP* 2006;58: 243-249.
- [149] Aliyu B., Oyeniyi YJ, Mojiminiyi FBO, Isezuo SA, Alada ARA. The aqueous calyx extract of *hibiscus sabbdariffa* lowers BP and heart rate via sympathetic nervous system dependent mechanisms. *Niger J Physiol Sci* 2014;29:131-136.
- [150] Ojulari LS, Olatubosun OT, Okesina KB, Owoyele BV. The effect of *zingiber officinale* (ginger) extract on BP and heart rate in healthy humans. *IOSR-JDMS* 2014;13:76-78.
- [151] Nyarko AA, Addy ME. Effect of aqueous extract of *adenia cissampeloides* on BP and serum analytes of hypertensive patients. *Phytother Res* 1990;4:25-28.
- [152] Jezova D, Duncko R, Lassanova M, Kriska M, Moncek F. Reduction of rise in BP and cortisol release during stress by *ginkgo biloba* extract (EGB761) in healthy volunteers. *J physiol Pharmacol* 2002;53:337-348.
- [153] Leung SWS, China PR. Effects of the aqueous extract of *salvia miltiorrhiza* (danshen) and its magnesium

- tanshinone B-enriched Form on BP. *Phytother Res* 2010;24:769-774.
- [154] Hom C, Budoff M, Luo Y. The effects of aged garlic extract on coronary artery calcification progression and blood pressure. *J Am Coll Cardiol* 2015;17:A1472.
- [155] Watanabe T. The BP-lowering effect and safety of chlorogenic acid from green coffee bean extract in essential HTN. *Clin Exp Hypertens* 2006;28:439-449.
- [156] Caron MF, Dore DD, Min B, Kluger J, Boguk I, White CM. Electrocardiographic and BP effects of the ephedra-containing trimspa thermogenic herbal compound in healthy volunteers. *Pharmacotherapy* 2006;26:1241-1246.
- [157] Ras RT, Zock PL, Zebregs YE, Johnston NR, Webb DJ, Draijer R. Effect of polyphenol-rich grape seed extract on ambulatory BP in subjects with pre- and stage I HTN. *Br J Nutr* 2013; 110:2234-2241.
- [158] Figueroa A, Sanchez-Gonzalez MA, Wong A, Arjmandi BH. Watermelon extract supplementation reduces ankle BP and carotid augmentation index in obese adults with prehypertension or HTN. *Am J Hypertens* 2012;25:640-643.
- [159] Draijer R, de Graaf Y, Slettenaar M, de Groot E, Wright CI. Consumption of a polyphenol-rich grape-wine extract lowers ambulatory BP in mildly hypertensive subjects. *Nutrients* 2015;7:3138-3153.
- [160] Talbott SM, Christopoulos AM, Richards E. Citrus aurantium extract has no effect on BP or heart rate in healthy adults. *FASEB* 2007(Abtract).
- [161] Keheyan G, Dunn LA, Hall WL. Acute effects of ginkgo biloba extract on vascular function and BP. *Plant Foods Hum Nutr* 2011;66:209-211.
- [162] Twins M, Perrinjaquet-Mocchetti T, Bradl B, Aydogan C. Food supplementation with an olive (*olea europaea* L.) leaf extract reduces BP in borderline hypertensive. *Phytother Res* 2008; 22:1239-1242.
- [163] Udani J, Yoshinari O, Moriyama H, Shiojima Y, Chien X. The efficacy and safety of a proprietary onion-pumpkin extract (OPTain120) on BP: an open-label study. *FFHD* 2015;5: 224-242.
- [164] Finkel ML, Sanchez S, Mak T, Granstein J, Lefkowitz A. Anthocyanin-rich purple corn extract and its effects on the BP of adults. *J Evidence-Based Complement Altern Med* 2013; 18:237-242.
- [165] Winther K, Randlov C, Rein E, Mehlsen J. Effects of ginkgo biloba extract on cognitive function and BP in elderly subjects. *Curr Ther Res* 1998;59:63-66.
- [166] Robinson M, Lu B, Edirisinghe I, Kappagoda CT. Effect of grape seed extract on BP in subjects with pre-HTN. *J Pharm Nutr Sci* 2012;2:155-159.