Research Article

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American Journal of Ethnomedicine
ISSN 2348-9502

2017
Vol. 4 No. 1:2

DOI: 10.21767/2348-9502.100002

Medicinal Plants that can Cause Changes in Blood Pressure and Interactions with Antihypertensive Agents

Katrine Teixeira[1], Patrícia dos Santos[1,3], Vanilde Citadini-Zanette[2], Silvia DalBó[3,1] and Patrícia de Aguiar Amaral[3]*

1 Faculdade de Farmácia, Universidade do Extremo Sul Catarinenses, Santa Catarina, SC, Brasil
2 Herbário Padre Raulino Reitz, Brasil
3 Laboratório de Plantas Medicinais (LaPlaM), Programa de Pós-Graduação em Ciências Ambientais (PPGCA), Brasil

Corresponding author: Amaral PA

amaral@unesc.net

Universidade do Extremo Sul Catarinense. Avenida Universitária, CEP 88806-000, Criciúma, SC, Brasil.

Tel: 48 3431 2535

Citation: Teixeira K, dos Santos P, Citadini-Zanette V, DalBó S, Amaral PA (2017) Medicinal Plants that can Cause Changes in Blood Pressure and Interactions with Antihypertensive Agents. Am J Ethnomed. Vol. 4 No. 1:2

Abstract

Objectives: Systemic arterial hypertension is a multifactorial clinical condition, characterized by sustained high levels of blood pressure. The secondary metabolites of medicinal plants may work in part through modification of haemodynamics including blood pressure alteration. This study aimed to conducted a literature review of medicinal plants that can cause blood pressure changes and interactions with antihypertensive drugs.

Method: The literature search was made using terms as: hypertension, hypotensive, anti-hypertensive and blood pressure.

Results: We found 138 medicinal plants that cause changes in blood pressure; 84 were reports of popular use and 78 were scientific studies. 22 plants caused interference in the regulation of blood pressure due to interaction with antihypertensive drugs.

Conclusion: Most of the plants that cause changes in blood pressure have a documented hypotensive effect and such effects can be observed both in plants used popularly and also scientifically, notably in both cases, the potentiating of the medicine's effects.

Keywords: Medicinal plants; Hypertension; Interactions of medicinal plants

Received: October 28, 2016, **Accepted:** Febraury 22, 2017 **Published:** Febraury 27, 2017

Introduction

Systemic arterial hypertension is a multifactorial clinical condition characterized by sustained high levels of blood pressure, and is often associated with functional and/or structural changes in target organs, and metabolic changes with consequent increased risk of cardiovascular events [1].

The circulatory system is endowed with a complex mechanism for controlling the blood pressure, which is determined approximately by the ratio between the volume of total flow and systolic arterial distensibility tree. Any condition that affects the movement either of these two factors will also affect blood pressure [2,3].

Initially, systemic arterial hypertension is asymptomatic in almost all patients, yet its chronic and largely silent nature affects patient's quality of life, bringing consequences such as admissions for technical procedures of high complexity, deaths and early retirements [3].

According to the Ministério da Saúde (Brazil), hypertensive patients are defined by asystolic blood pressure equal or superior to 140 mmHg, and a diastolic blood pressure greater than or equal to 90 mmHg; these values being found in at least in two measurements taken within the same clinic visit and within close proximity of each other [4].

Treatment for hypertension includes, besides the use of drugs, modification of lifestyle [5] and the main objective is not to reduce symptoms, since almost all patients are asymptomatic, but to prevent cardiovascular complications [6]. The main classes of drugs available for treatment of hypertension are diuretics, sympatholytics, vasodilators, and calcium channel blockers, inhibitors of angiotensin converting enzyme, angiotensin receptor II blockers and direct renin inhibitors [7].

Despite the recognition of hypertension as a public health problem, its adequate control is far from being achieved. This is mainly due to failure of prescribed treatments, including non-compliance, and also associated with other factors such as side effects and cost, prompting the patient, in many cases, to make

use of complementary and alternative therapies. Among them, phytotherapy is considered a strategy of low cost and free of side effects. However, in many cases, it can further compromise blood pressure control [8].

Herbal medicine is characterized by the use of medicinal plants or plant parts containing substances or classes of substances responsible for their therapeutic action after collection processes, stabilization when applicable, and drying, and may exist in full form, grodd and chopped [4]. Co-administration of medicinal plants along with prescription medications can cause unexpected interactions [9] through carelessness in relation to their use, often driven by philosophies of life, personal and cultural customs. Some of these factors derive from patients, but may also arise through health professionals without expertise in this area [10].

Therefore, this study aimed to review the literature on medicinal plants that may cause changes in blood pressure and cross-reference established knowledge concerning interactions resulting from concomitant use of these plants with antihypertensive medications, trying to understand and classify these interactions and identify the compounds responsible for them.

Materials and Methods

This work included a literature search through articles, magazines, periodicals, monographs, dissertations and theses, published in the last 16 years (1998-2014). In some situations this time frame was expanded due to a lack of information.

For this work, the identification of medicinal plants that can cause changes in BP was achieved through literature listed in Instruction No. 5 of 2010 [4] and from other sources available in the Professor Eurico Back Library - UNESC, using the search terms 'hypertensive', 'hypotensive', 'anti-hypertensive' and 'blood pressure', and their appropriate translations. To survey plant/drug interactions, research was also carried out using Medline, PubMed, Science Direct, academic Google and Scielo, using the terms 'antihypertensive drugs' (antihypertensives), 'high blood pressure' (hypertension) and 'drug interactions', associated with the scientific name of plants identified as causing blood pressure alterations.

Results and Discussion

Fifty-six different literature sources were consulted and out of these, 31 (55.3%) contained information on medicinal plants affecting blood pressure, including 138 individual species. Among these, 84 (60.9%) were reports of popular use and 78 (56.5%) detailing scientific studies performed *in vitro*, *in vivo* or in humans **(Table 1)**. In the Tables, medicinal plants that have a documented effect on blood pressure as reported through popular use are indicated with an asterisk (*).

The literature review was conducted using the scientific name (Latin binomial) avoiding unreliable information, since the same plant can have many common names in different regions and the same popular name may be used for different species. For medicinal plants with more than one scientific name, a search was performed for all synonymies.

In this work, a plant's effect on blood pressure was classified as hypotensive when it causes a reduction in blood pressure and hypertensive when it causes a blood pressure increase. For plants identified through popular use, hypotensive actions have been reported in 82 (97.6%), and hypertensive actions in 2 (2.4%), whereas for those identified through scientific studies, hypotensive actions have been reported in 68 (87.2%) and hypertensive actions in 10 (12.8%).

The effects of medicinal plants on blood pressure are due to the presence of diverse secondary metabolites. Secondary metabolites are substances that the plant synthesizes and stores during its growth, and usually in any given plant comprise several active components, of which one or a group determines the main action or pharmacological activity [11].

We have focused our discussion of the mechanism(s) of action of identified plants on blood pressure on those cited in more than three references. Relevant species in popular use include: *Alpinia zerumbet, Cymbopogon citratus*, *Eugenia uniflora L.* (12.9%), *Cuphea carthagenensis* (16.1%) and *Allium sativum L.* (29%). Those identified in scientific studies include: *Pausinystalia johimbe* (12.9%), *Olea europaea L.* (16.1%), *Crataegus oxyacantha, Viscum album L.* (19.3%), *Rauvolfia serpentina* (22.5%) and *Allium sativum L.* (45.1%).

In pharmacological tests, it has been shown that the antihypertensive action of *Alpinia zerumbet* is related to the presence of flavonoids and a vasodilatory action through the release of nitric oxide stimulated by bradykinin via the beta 2 receptors [12,13]. This same vasodilator effect has been used to justify the hypotensive effect attributed to the plant *Cuphea carthagenensis* [14].

For *Eugenia uniflora L.*, one study suggests that its hypotensive effect is mediated by both a direct vasodilating action and a weak diuretic effect which could be related to an increase in renal blood flow [15]. Although these actions have been proven, the chemical compounds responsible have not yet been described [16].

Cymbopogon citratus has been reported to be responsible for changing blood pressure, and there are scientific studies on its hypotensive effects. This plant induces hypotension probably due to decreased vascular resistance which may be caused by inhibition of calcium influx. The compounds responsible for this have not been reported [17].

A vasodilatory effect through calcium channel blockade is also attributed to the hypotensive effect of *Panax* ginseng [18], whose vasodilation may also be mediated through nitric oxide release and a depressive action on the central nervous system due to its ginsenosides. This plant exhibits a peripheral vasoconstrictor effect at low doses and peripheral vasodilation at high doses. It seems that these effects are due to the presence of saponins [19].

The set of sulfur compounds, particularly allicin, which has vasodilatory effect, maybe responsible for the hypotensive effect of *Allium sativum*, the most cited plant in theliterature with activity on blood pressure. However, fructosans, through their diuretic effect, may act as adjuvants [20-24].

Table 1: Medicinal plants with documented ability to effect changes in blood pressure.

Scientific Name	Popular Name	Used Part	Action	Reference
Acacia adstringens Mart.	Barbatimão	Bark	Hypotensive	[50]
**Achillea millefolium* L.	Mil-folhas, Mil-em-rama	Flores	Hypotensive	[4,51]
Agrimonia eupatoria L. *Agrimonia pilosa* Ledeb.	Agrimonia	Whole plant	Hypertensive	[4,12]
**Allium cepa* L.	Cebola	Bulb	Hypotensive	[3,6,35]
**Allium sativum* L.	Alho	Bulb	Hypotensive	[3,4,6,12,20,23,30, 32,41, 35,48,50,58,61]
Alpinia nutans (L.) Roscoe	NC	Leaves	Hypotensive	[20]
**Alpinia speciosa* (Wendl.) K. Schum. *Alpinia zerumbet* (Pers.) B.L. Burtt. and R.M. Sm.	Colônia, cardamomo, jardineira, noz-moscada, vindicá, pacova	Leaves	Hypotensive	[32,34,19]
Angelica pubescens Maxim.	Angélica pubescente	Root	Hypotensive	[50]
**Apium graveolens* L.	Aipo	Fruit	Hypotensive	[4,41]
Arnica Montana L.	Arnica	Dried Flowers	Hypotensive	[63]
Artemisia scoparia Waldst. and Kit	NC	NC	Hypotensive	[50]
**Baccharis trimera* (Less.) DC.	Carqueja	NC	Hypotensive	[10,20]
**Boerhavia diffusa*L.	Erva-tostão, pega-pinto, solidônia, tangaracá	Root	Hypotensive	[32]
Cannabis sativa L.	Maconha	Seeds	Hypotensive	[23,26]
Capsella bursa-pastoris (L.) Medik	Bolsa-de-pastor	Whole Plant	Hypotensive	[4,23,41]
Carthamus tinctorius L.	Açafrão, açafrão-americano, açafrão bastardo	Dried Flowers	Hypotensive	[63]
Cassia occidentalis (L.) Link	NC	NC	Hypotensive	[7]
Catha edulis Forssk.	Flor-do-paraiso	NC	Hypertensive	[23]
Caulophyllum thalictroides (L.) Michx.	Caulophyllum	Root and rhizome	Hypertensive	[4,23]
**Cecropia glaziovi* Snethl.	Árvore-da-preguiça, embaúba, embaúba-branca, imbaúba, torém	leaves	Hypotensive	[10,32,34]
**Chelidonium majus* L.	Celidônia, erva-andorinha	Leaves and root	Hypotensive	[6]
Chlorella pyrenoidosa Starr and Zeikus	Chlorella	NC	Hypotensive	[30]
Cimicifuga racemosa (L.) Nutt.	Cimicífuga	Root and rhizome	Hypotensive	[4,23]
Cinnamomum camphora (L.) Presl.	Canfora	NC	Hypotensive	[35]
**Crataegus laevigata* (Poir.) DC. *Crataegus oxyacantha* L.	Cratego, espinheiro-alvar, espinho-branco, monógina, oxicanto	Flowers and fruit	Hypotensive	[3,4,7,23,30,62]
**Cuphea carthagenensis* (Jacq.) Macbr. *Cuphea gutinosa* Cham. et Schltdl.	Erva-de-sangue, pé-de-pinto, sete-sangrias,	Whole plant	Hypotensive	[32,38]
Cynara scolymus L.	Alcachofra	Leaves and root	Hypotensive	[6]
Daucus carota L.	Cenoura-silvestre	Whole plant	Hypotensive	[23]
**Echinodorus macrophyllus* (Kunth) Micheli	Chapéu-de-couro	Leaves	Hypotensive	[6]
Elettaria cardamomum (L.) Maton	Cardamomo	NC	Hypotensive	[30]
Ephedra nevadensis S. Watson	Ephedra	Whole plant	Hypertensive	[4,7,23,61]
**Equisetum arvense* L. *Equisetum hyemale* L.	Cavalinha	Green shoots	Hypotensive	[6,13]
**Eugenia uniflora* L.	Ginja, ibipitanga, pitanga, pitanga-branca, pitangueira	Leaves	Hypotensive	[50]
Foeniculum vulgare Mill.	Erva-doce, funcho	Ripe fruit	Hypotensive	[63]
Fumaria officinalis L.	Fumaria	Whole plant	Hypotensive	[4,23]
Gentiana lutea L.	NC	Root and Rhizome	Hypertensive	[4]
Geumur banum L.	NC	NC	Hypotensive	[4]
Ginkgo biloba L.	Ginkgo	Leaves	Hypotensive	[7,60]
Guaiacum officinale L.	Guaiaco	Stalk	Hypotensive	[6]
Guazuma ulmifolia Lam.	Embira, guamaca, ibixuna, mutambo, periquieira, pojó	Bark	Hypotensive	[32]
Harpagophytum procumbens DC. Ex Meisn.	Garra-do-diabo	Root	Hypotensive	[4,23]

Hydrastis canadenses L.	Hidraste	Root and rhizome	Hypotensive	[4,23]
Hyptis suaveolens (L.) Poit	Alfavacão, alfavaca-brava, batônica, cheirosa, celine, erva-cidreira, pataquera	Flowers and Leaves	Hypotensive	[32]
Imperata exaltata (Roxb.) Brongn	Sapé	NC	Hypotensive	[12]
Inula helenium L.	NC	Root and Rhizome	Hypotensive	[4]
Kalanchae brasiliensis Cambess.	Saião	Leaves	Hypotensive	[6]
Larix decídua Mill.	NC	NC	Hypotensive	[35]
**Lippia alba* (Mill.) N.E. Br. Ex Britton	Alecrim-do-campo, erva-cidreira, salsa, sálvia	NC	Hypotensive	[20]
Luffa operculata (L.) Cogn.	Buchinha-do-norte	Stalk and Leaves	Hypotensive	[6]
Myrica cerifera L.	NC	Bark of root	Hypertensive	[4]
Myrcia sphaerocarpa DC.	Pedra-ume-caá	Leaves and Root	Hypotensive	[6]
**Ocimum basilicum* L. *Ocimum selloi* Benth.	Alfavaca	Whole plant	Hypotensive	[6,56]
Ocimum tenuiflorum L.	Alfavaca-da-india, basilico-sagrado, manjericão-santo	Leaves	Hypotensive	[32]
**Olea europaea* L.	Oliveira	Leaves	Hypotensive	[3,7,12,30,58]
Panax ginseng C. A. Mey	Ginseng, ginseng coreano	Root	Hypertensive	[4,7,31]
*Parkinsoniaaculeata*L.	Chile, cina-cina, sensitivo, turco	NC	Hypotensive	[32]
Pausinystalia johimbe (K. Schum.) Pierre ex Beille	Casca de ioimba, ioimbé, yohimbe	NC	Hypertensive	[7,12,23,31]
**Petroselinum crispum* (Mill.) Fuss.	Salsa	Root, leaves and seeds	Hypotensive	[4,23]
Phytolacca americana L. *Phytolacca decandra* L.	NC	Root	Hypotensive	[4]
Piper marginatum Jacq.	Bitre, nhandi, pimenta-do-mato	NC	Hypotensive	[20]
Pimpinella anisum L.	Anis, pimpinelle	Dried fruit	Hypotensive	[63]
**Plantago major* L.	Plantagem, sete-nervos, tansagem, transagem	Leaves	Hypotensive	[4,23,32,42]
**Plectranthus barbatus* Andr.	Boldo-do-reino, falso-boldo, malva-santa	NC	Hypotensive	[38]
Portulaca pilosa L.	Amor crescido, alecrim-de-são-jose, beldroega, perrexi	NC	Hypotensive	[20]
Rauvolfia serpentina (L.) Benth. Ex Kurz	Raiz de rauwolfia, rauvolfia	Root	Hypotensive	[7,12,23,31,48,50,61]
**Rosmarinus officinalis* L.	Alecrim, erva-da-graça, rosmarinho	Leaves	Hypotensive	[32,35,23]
Ruscus aculeatus L.	Gilbarbeira	NC	Hypertensive	[23]
Ruta graveolens L.	Arruda	NC	Hypotensive	[23]
Sarothamnus scoparius (L.) Koch	NC	Flowers	Hypertensive	[4]
Stachys officinalis (L.) Trevis.	Betônica	NC	Hypotensive	[23]
**Stevia rebaudiana* (Bertoni) Bertoni	Capim-doce, erva-adocicada, erva-doce, estévia	Leaves	Hypotensive	[32]
Tribulus terrestres L.	NC	Dried fruit	Hypotensive	[64]
Uncaria rhynchophylla (Miq.) Miqex Havil. *Uncaria sinensis* (Oliv.) Havil. *Uncaria tomensosa* (Willd.) ex Roem and Schult.) DC.	Trepadeira de gambir, uncaria, unha de gato	Stalk and Branches with thorns	Hypotensive	[4,23,64]
Urtica dioica L.	Urtiga	Whole plant	Hypotensive	[4,23]
Waltheria douradinha A.St.-Hil.	Douradinha, malva-branca, valva-veludo	Shell of branches	Hypotensive	[32]
Valeriana officinalis L.	Valeriana	Root and Rhizome	Hypotensive	[6,12]
Veratrum álbum L. *Veratrum viride* Aiton	Heléboro-americano	Root	Hypotensive	[3,12,23]
**Viscum álbum* L.	Visco, visco europeu, visco da amoreira branca	Stalk and Branches of leaves	Hypotensive	[3,4,6,12,23,48]

NC: Not included.

Oligomeric flavonoids, as procyanidins, present in plants such as *Crataegus laevigata,* exert vasodilatory effect with consequent reduction in blood pressure [25,26]. *Crataegus laevigata* also has its hypotensive activity justified by the presence of amines in their fresh flowers, as tyramine [20] and by angiotensin converting enzyme inhibition [27].

Pausinystalia johimbe contains the alkaloid yohimbine, known as an antagonist of the alpha 2-adrenoceptor [11,28,29]. Hypertension induced by this plant may be the result of increased activity of the sympathetic nervous system, changes in renal blood flow and retention of salt and water [30].

The alkaloid reserpine, among others, is present in *Rauvolfia serpentina*, which causes a reduction in blood pressure by interfering with the action of central neurotransmitters [20,23]. Reserpine lowers blood pressure by decreasing cardiac output, peripheral vascular resistance, heart rate and rennin [31].

Viscum album L. has hypotensive effects due to the presence of some flavonoids with diuretic action and vasodilator amines that act in the vasomotor centre, such as histamine, tyramine and choline, also present in Phytolacca Americana L. and *Capsella bursa-pastori* [20,25]. The vasodilatory effect of Viscum album can also be related to inhibition of calcium channels [8].

The hypotensive effect of an aqueous extract of Olea europaea L. is demonstrated by inhibition of angiotensin converting enzyme, an effect attributed to the metabolite oleacina [24]. Its metabolite oleoeuropeoside has demonstrated vasodilatory action [20].

Regarding the hypotensive action of Melissa officinalis and Lippia alba, it was assumed that hypotension occurs through vasodilatation, since it is known that a stressed state, heart rate, blood flow and consequently raising blood pressure [32].

Certain medicinal plants have differential effects on blood pressure depending on the part used and the method of preparation. As an example, Foeniculum vulgare has a hypotensive effect only when its extracts are subjected to boiling, suggesting that the active ingredient may be a metabolite produced upon heat transformation. Another such example is Uncaria sinensis, as researchers have shown that excessively long cooking reduces its antihypertensive potential, and also that the thorns on the branches do not possess pharmacological activity. This demonstrates the importance of retention of knowledge related to medicinal plant use [33].

Based on the literature, we found 22 (15.9%) medicinal plants with demonstrated interactions with antihypertensive drugs, interfering with the therapeutic efficacy of these drugs and consequently, in regulating blood pressure **(Table 2)**. Among these, 1(4.6%) was reported through popular use only to have an effect on blood pressure, 5 (22.7%) were reported through both popular use and by scientific studies, while16 (72.7 %) were reported to have an effect on the blood pressure by scientific studies.

These highlighted interactions were based on results of research and studies conducted by experimental models and the potential interaction was classified as follows: enhanced when the plant: drug combination causes increased effect (↑), and antagonized when the plant: drug combination cause decreased effect of the drug (↓).

The interactions of medicinal plants with antihypertensive drugs identified to be most widely documented through this study were those involving Crataegus oxyacantha, Ginkgo biloba and Pausinystalia johimbe. However, other medicinal plants with effects on blood pressure, as evidenced by scientific studies, may also display the potential to interact with this drug class, and there is need for further studies related to this subject.

We can observe that an antihypertensive can have its effects antagonized (27.3%) when used with medicinal plants with hypertensive activity, thus leading to vasoconstriction and fluid retention, or, in some cases, potentiated, (72.7%) when used with plants with hypotensive activity, in turn leading to vasodilation and/or diuretic actions. For a more in depth understanding of these reports we cite as an example the interactions between antihypertensive medications and Allium sativum and Pausinystalia johimbe.

For Alexandre et al. [34] the possible interaction between Allium sativum and antihypertensive medication such as angiotensin converting enzyme inhibitors can be explained by the fact that the sulfur compounds in garlic may mediate nitric oxide release, enhancing the hypotensive effect of the drug when used concomitantly. This same mechanism of interaction maybe attributed to other medicinal plants with vasodilating action.

Pausinystalia johimbe has an alkaloid known as yohimbine that is antagonist alpha 2-adrenoceptor, so it causes interaction with antihypertensive drugs that actin the same place, antagonizing its effects and increasing blood pressure [28,29,35].

It can be seen that interactions between conventional drugs, in this case the antihypertensive, and the chemical components present in herbals, occur and can affect the absorption, distribution, metabolism and excretion of the drug, resulting in broadening or reducing the expected effects and the mechanisms [34].

The popular belief that herbal medicines do not cause negative health effects needs to be clarified with patients and a clear assessment of need on a cost versus benefit analysis of their use is always warranted, as with any other medication [36].

It is incumbent on a country's health authorities to provide for the means to ensure the correct use of safe and effective medicinal plants through supplementary measures to current pharmaceutical legislation, such as the regulation of registration, production and marketing of the herbal industry, from the application of standards at the plant selection level, through cultivation, correct use and development of quality control techniques [21].

Patients should be reminded to report all medications that they take, whether or not they are conventional or alternative, because the use of undeclared medication may result in public health problems such as leading to significant delays inappropriate care and selection of optimal therapy [28].

Table 2: Possible interactions between medicinal plants that may alter blood pressure and concomitant antihypertensive medication.

Scientific Name	Popular Name	Potential interaction	Drugs that Interact		Reference
Achillea millefolium L.	Mil-folhas	Potentiates	ACEI	↓	[23]
Allium sativum L.	Alho	Potentiates	ACEI	↓	[2b,55]
Capsella bursa-pastoris (L.) Medik	Bolsa-de-pastor	Potentiates	NC	↓	[23]
Catha edulis Forssk	Flor-do-paraiso	Antagonizes	Sympatholytic	↑	[23]
Caulophyllum thalictroides (L.) Michx.	Caulophyllum	Antagonizes	NC	↑	[23]
Cimicífuga racemosa (L.) Nutt.	Cimicifuga	Potentiates	NC	↓	[23,43]
Crataegus oxyacantha L. *Crataegus laevigata* (Poir.) DC.	Cratego oxicanto, espinheiro-alvar	Potentiates	VD and ACEI	↓	[23,43,46,52]
Cynara scolymus L.	Alcachofra	Potentiates	Diuretics	↓	[43]
Daucus carota L.	Cenoura-silvestre	Potentiates	NC	↓	[23]
Ephedra nadensis	Ephedra	Antagonizes	Sympatholytic	↑	[23,52]
Fumaria officinallis L.	Fumaria	Potentiates	NC	↓	[23]
Ginkgo biloba L.	Ginkgo	Antagonize	Diuretics		[21,25,29]
Hydrastis canadenses L.	Hidraste	Potentiates	NC	↓	[23]
Panax ginseng C. A. Mey.	Ginseng	Potentiates	Diuretics	↓	[2b]
Pausinystalia johimbe (K. Schum.) Pierre ex Beille	Casca de ioimba, ioimbé	Antagonize	IECA and Sympatholytic		[23,31,52,55,57]
Rauvolfia serpentina (L.) Benth. Ex Kurz	Raiz de rauwolfia, rauvolfia	Potentiates	Sympatholyticand Diuretics	↓	[23,61]
Ruscus aculeatus L.	Gilbarbeira	Antagonize	Sympatholytic	↑	[23]
Ruta graveolens L.	Arruda	Potentiates	VD	↓	[23]
Stachys officinalis (L.) Trevis.	Betônica	Potentiates	NC	↓	[23]
Taraxacum officinale L.	Dente-de-leão	Potentiates	Diuretic	↓	[23,59]
Uncaria tomentosa (Willd. ex Roem. and Schult.) DC.	Uncaria	Potentiates	NC	↓	[23]
Viscum album L.	Visco, visco europeu	Potentiates	CCB and diuretic	↓	[23]

CCB: calcium channel blockers; ACEI: Angiotensin converting enzyme inhibitors; NC: not included; PA: blood pressure; VD: direct vasodilator; ↑: blood pressure elevation; ↓: lowering blood pressure.

Given the prevalence of cardiovascular diseases, including hypertension, in the population, and the myriad of natural products that have pharmacological effects on cardiovascular parameters, this review highlights the need for caution in the combined and particularly undeclared use of such substances. Pharmacists are in an optimal position to advice on concomitant medications, and should always enquire as to all herbal and other supplements patients are taking as part of every consultation. As with any suspected case of drug interactions, those that occur between conventional drugs and herbs should be reported to the relevant authorities [28,37-64].

Conclusion

This study reviewed the risks of concomitant use of medicinal plants with anti-hypertensive drugs for patients with hypertension. Most plants that cause changes in blood pressure, both through reports of popular use and by scientific studies, have hypotensive action (97.6 and 87.2%) respectively, with the most reported species from both sources being Allium sativum (29 and 45.1%). Of those plants with the potential for interaction with antihypertensive drugs the most common effect of concomitant use was blood pressure elevation (72.7%). Among those medicinal plants that cause changes in blood pressure reported through the popular use, 24 (28.5%) has their hypotensive effects borne out by scientific studies, with 5 (20.8%) having demonstrable interaction with antihypertensive medication.

Based on these results, we suggest the need for further studies on popular medicinal plants that can cause blood pressure changes and their possible interactions with antihypertensive drugs, especially regarding the mechanistic aspects of such interactions. Another important recommendation is the development of further education resources for health professionals, so that they can guide the population of risk, since many patients ignore these issues when making concomitant use of drugs and medicinal plants.

A significant number of medicinal plants may cause changes in blood pressure, regardless of their therapeutic use, and although they may offer, depending on their chemical constituents, potential treatments for cardiovascular diseases including hypertension, they may also have unintended effects including serious consequences for users.

Acknowledgments

This work was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (Capes) and Conselho nacional de desenvolvimento científico e tecnológico (CNPq) and Fundação de Amparo à pesquisa de Santa Catarina (FAPESC).

References

1 Brandão AA (2010) VI Diretrizes brasileiras de hipertensão: Conceituação, epidemiologia e prevenção primária. Revista Bras Hipertens 1: 7-10.

2 Guyton AC, Hall JE (1998) Fisiologia humana e mecanismo das doenças. (6thedn) Rio de Janeiro Guanabara Koogan.

3 Toledo MM, Rodrigues SC, Chiesa AM (2007) Educação em saúde no enfrentamento da hipertensão arterial: uma nova ótica para um velho problema. Texto & Contexto Enferm 2: 233-238.

4 Governo do Brasil (2001) Agência Nacional de Vigilância Sanitária (ANVISA). Ministério da Saúde. Resolução no 14, de 31 de março de 2010. Dispões sobre o Registro de medicamentos fitoterápicos, Brasília, 2010.

5 Peres DS, Magna JM, Viana LA (2003) Portador da hipertensão arterial: atitudes, crenças, percepções, pensamentos e práticas. Rev Saude Pública 5: 635-642.

6 Barretto ACP, Santello JL (2002) Manual de hipertensão: entre a evidência e a prática clínica. São Paulo: Lemos Editorial.

7 Goodman LS, Gilman A, Brunton LL (2012) Goodman & Gilman: as bases farmacológicas da terapêutica. Rio de Janeiro: McGraw-Hill.

8 Mion Junior D, Pierin AMG, Guimarães A (2001) Tratamento da hipertensão arterial respostas de médicos brasileiros a um inquérito. Rev Assoc Med Bras 3: 249-254.

9 Colalto C (2010) Herbal interactions on absorption of drugs: Mechanisms of action and clinical risk assessment. Pharmacol Res 3: 207-227.

10 Dias MG, Salgueiro L (2009) Interações entre preparações à base de plantas medicinais e medicamentos. Revista de Fitoterapia 1: 5-22.

11 Teske M, Trentine AMM (1997) Herbarium: compêndido de fitoterapia. (3rdedn) Curitiba: Herbarium Laboratório Botânico.

12 Costa AMAC, Morais SM, Dantas MCBR, Lobo RACM, Fonteles MC (1998) Flavonóides com atividade hipotensora de Alpinia zerumet (Pers.) Burtt. et Smith (colônia). Rev Bras Farmacogn 79: 96-98.

13 Moura RS, Emiliano AF, Carvalho LC, Souza MA, Guedes DC, et al. (2005) Antihypertensive and endothelium-dependentvasodilator effects of Alpiniazerumbet, a medicinal plant. Cardiovasc Pharmacol 3: 288-294.

14 Schuldt EZ, Ckless K, Simas ME, Farias MR, Ribeiro DV-RM (2000) Butanolic fraction from Cuphea carthagenensis Jacq McBride relaxes rat thoracic aorta through endothelium-dependent and endothelium-independent mechanisms. J Cardiovasc Pharmacol 2: 234-239.

15 Consoline AE, Baldini OAN, Amat AG (1999) Pharmacological basis for the empirical use of Eugenia uniflora L. (Myrtaceae) as antihypertensive. J Ethnopharmacol 1: 33-39.

16 Cirqueira RT, Alves MJQF (2005) Efeitos hipotensivo e diurético dos extratos aquosos de pitanga (Eugenia uniflora L.) e jambolão (Eugenia jambolana Lam.) em ratos normotensos anestesiados. Rev Bras Pl Med 2: 86-91.

17 Moreira FV, Bastos JFA, Blank AF, Alves PB, Santos MRV (2010) Chemical composition and cardiovascular effects induced by thees sential oil of Cymbopogon citratus DC. Stapf, Poaceae, in rats. Braz J Pharmacog 6: 904-909.

18 Naseri MKG (2008) Arabian M, Badavi M, Ahangarpour A. Vasorelaxant and hypotensive effects of Allium cepa peel hydroalcoholic extract in rat. Pak J Biol Sci 12: 1569-1575.

19 Agrawal M, Nandini D, Sharma V, Chauhan, NS (2010) Herbal Remedies for treatment of hypertension. Int J Pharm Sci Res 1: 1-21.

20 Alonso JR (2008) Fitomedicina: curso para profissionais da área da saúde. São Paulo: Pharmabooks 197.20

21 Lorenzi H, Matos FJA (2008) Plantas medicinais no Brasil: nativas e exóticas. São Paulo: Instituto Plantarum.

22 Bruneton J, Del Fresmo AV (2001) Farmacognosia. Fitoquímica. Plantas medicinales. (2ndedn) Zaragoza: Acribia: 1099.

23 Simões CMO (2003) Farmacognosia: da planta ao medicamento. (5thedn) Rev Ampl Porto Alegre: UFRGS: 1102.

24 Vanaclocha BV, folcará SC (2003) Fitoterapia: vademécum de prescripción. (4thedn) Barcelona: Masson.

25 Barnes J, Anderson LA, Phillipson JD (2002) Herbal medicines: a guide for healthcare professionals. (2ndedn) London.

26 Magos GA, Mateos JC, Páez E, Fernández G, Lobato C, et al. (2008) Hypotensive and vasorelaxant effects of the procyanidin fraction from Guazuma ulmifolia bark in normotensive and hypertensive rats. J Ethnopharmacol 1: 58-68.

27 Sharifi N, Souri E, Ziai AS, Amin G, Amanlou M (2013) Discovery of new angiotensin converting enzyme (ACE) inhibitors from medicinal plants to treat hypertension using an in vitro assay. Daru 2013 1: 21-74.

28 Fetrow CW (2000) Manual de medicina alternativa: para o profissional. Rio de Janeiro: Guanabara Koogan.

29 Levin JS, Jonas WB (2008) Tratado de medicina complementar e alternativa. São Paulo: Manole.

30 Coleman JJ, Martin, U (2006) Drug-induced systemic hypertension. Adverse Drug React Bull 239: 915-918.

31 Frishman WH, Sinatra ST, Moizuddin M (2004) The use of herbs for treating cardiovascular disease. Semin Integr Med 1: 23-25.

32 Oliveira CJ, Araujo TL (2007) Plantas medicinais: usos e crenças de idosos portadores de hipertensão arterial. Rev Elet Enferm 1: 93-105.

33 Botsaris AS (1995) Fitoterapia chinesa e plantas brasileiras. São Paulo: Ícone Editora.

34 Alexandre RF, Bagatine F, Simões CMO (2008) Interações entre fármacos e medicamentos fitoterápicos à base de ginkgo ou ginseng. Rev Bras Farmacog 18: 117-26.

35 Tres JC (2006) Interacción entre fármacos y plantas medicinales. Centro de Farmacovigilância de Navarra 2: 233-252.

36 Nicoletti MA, Carvalho KC (2010) Oliveira Junior MA; Bertasso CC; CaporossI PY; Tavaves APL. Uso popular de medicamentos contendo drogas de origem vegetal e/ou plantas medicinais: principais interações decorrentes. Rev Saúde 1: 25-39.

37 Newall CA, Phillipson JD, Anderson LA (2002) Plantas medicinais: guia para profissional de Saúde. São Paulo: Premier: 308.

38 Batista RS, Corrêa AD, Quintas LEM (2003) Plantas medicinais: do cultivo à terapêutica. (6thedn) Rio de Janeiro: Vozes.

39 Blumenthal M, Busse WR (1998) The complete german commission e monographs: therapeutic guide to herbal medicines. Boston: American Botanical Council.

40 Governo do Brasil (2006) Ministério da saúde. Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Departamento de Assistência Farmacêutica e Insumos Estratégicos. A fitoterapia no SUS e o Programa de Pesquisas de Plantas Medicinais da Central de Medicamentos, Distrito Federal: 149.

41 Carneiro DM, Freire RC, Honório TCD, Zoghaib I , Cardoso FFSS, et al. (2014) Randomized, Double-Blind Clinical Trial to Assess the Acute Diuretic Effect of Equisetum arvense (Field Horsetail) in Healthy Volunteers. Evid Based Complement Alternat Med.

42 Costa GH, MO, Fechine FV, Frota Bezerra FA, Silveira ER, Canuto KM, et al. (2013) Vasorelaxant and antihypertensive effects of methanolic fraction of the essential oil of Alpinia zerumbet. Vasc Pharmacol 58: 201.

43 Di Stasi LC, Hiruma-lima CA (2002) Plantas medicinais na Amazônia e na Mata Atlântica. (2ndedn) rev e ampl São Paulo: UNESP: 604.

44 Fernandez LF, Palomino OM, Frutos G (2014) Effectiveness of Rosmarinus officinalis essential oil as antihypotensive agent in primary hypotensive patients and its influence on health-related quality of life. J Ethnopharmacol 1: 509-516.

45 Fugh-berman A (2000) Herb-drug interactions. Lancet: 134-138.

46 Girgih AT, Alashi A, He R, Malomo S, Aluko RE (2014) Preventive and treatment effects of a hemp seed (Cannabis sativa L.) meal protein hydrolysate against high blood pressure in spontaneously hypertensive rats. Eur J Nutr. 5: 1237-1246.

47 Izzo AA, Carlo GD, Borrelli F, Ernst E (2005) Cardiovascular pharmacotherapy and herbal medicines: the risk of drug interaction. Int J Cardio 1: 1-14.

48 Kalluf LJH (2008) Fitoterapia funcional, parte 1: dos princípios ativos à prescrição de fitoterápicos. São Paulo.

49 Matos FJA (2002) Farmácias vivas: sistema de utilização de plantas medicinais projetado para pequenas comunidades. (4thedn) Rev e Ampl Fortaleza: UFC.

50 Medical Economics Company (2000) PDR for herbal medicines. (2ndedn) Montvale: Medical Economics Company.

51 Mors WB, Rizzini CT, Pereira NA. Medicinal plants of Brazil. Reference Publications, 2000: 501.

52 Nhiem NX, Bui HT, Phan VK, Chau VM, Nguyen XC, et al. (2001) Inhibitory activity of Plantago major L. on angiotensin I-converting enzyme. Arch Pharm Res 3: 419-423.

53 Rigelsky JM, Doce BV (2002) Hawthorn: pharmacology and therapeutic uses. Am J Health-Syst Pharm 2002 5: 417- 422.

54 Schulz V, Hansel R, Tyler VE (2002) Fitoterapia racional: um guia de fitoterapia para as ciências da saúde. (4thedn) São Paulo: Manole: 386.

55 Souza P, Gasparotto A, Crestani S, stefanello MÉ, Marques MC, et al. (2007) Hypotensive mechanism of the extracts and artemetin isolated from Achille amillefolium L. (Asteraceae) in rats. Phytomedicine 18: 819-825.

56 Tachjian A, Viqar M, Jahangir A (2010) Use of herbal products and potentialinteractions in patients with cardiovascular diseases. J Am Coll Cardio 6: 515-525.

57 Umar A, Imam G, Yimin W, Kerim P, Tohti I, et al. (2010) Antihypertensive effects of Ocimum basilicum L. (OBL) on blood pressure in renovascular hypertensive rats. Hypertens Res 7: 727-730.

58 Valli G, Giardina EGV (2002) Benefits, adverse effects and drug interactions of herbal therapies with cardiovascular effects. J Am Coll Cardiol 7: 1083-1095.

59 Veiga, VF, Pinto AC, Maciel MAM (2005) Plantas medicinais: cura segura? Quim Nova 3: 519-528.

60 Xiong XJ, Liu W, Yang XC, Feng B, Zhang YQ, et al. (2014) Ginkgo biloba extract for essential hypertension: a systemic review. Phytomedicine 10: 1131-1136.

61 World Health Organization (1999) WHO monographs on selected medicinal plants. World Health Organization, Geneva, Switzerland 1: 1-295.

62 World Health Organization (2004) WHO monographs on selected medicinal plants. World Health Organization, Geneva, Switzerland 1: 1-358.

63 World Health Organization (2007) WHO monographs on selected medicinal plants. World Health Organization, Geneva, Switzerland 1: 1-390.

64 World Health Organization (2009) WHO monographs on selected medicinal plants. World Health Organization, Geneva, Switzerland 1: 1-456.