# EVIDENCE OF THE USE OF MEDICINAL PLANTS IN THE TREATMENT OF SYSTEMIC ARTERIAL HYPERTENSION

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## ABSTRACT

Introduction: Systemic Arterial Hypertension is one of the major health problems in the world and a crucial factor for the aggravation of cardiovascular diseases in the population, so its existence encourages the development of a range of treatments both to control symptoms and to improve the patient's quality of life. Thus, phytotherapy enters as one of the other types of therapeutic approach, since many herbal medicines have unique molecules in their composition, some of which whose potential beneficial to health is much studied, such as flavonoids and polyphenols, so that this article seeks to recognize plants that have useful properties in combating hypertension that are common in Brazil. Methodology: In this context, through a retrospective, cross-sectional study using the platforms PubMed, webofscience, Lilacs, Pubmed and Google Scholar, based on the keywords antihypertensive, arterial hypertension, high blood pressure, phytochemical, phytotherapy. Results and Discussion: 7 plants were found, whose antihypertensive properties were reported with evidence through clinical trials in animals or people, being Cymbopogon citratus (Capim santo); Bidens pilosa (Picão preto); Allium sativum (Garlic); Oryza sativa (Rice); Hibiscus sabdariffa (Sour pigweed); Cuphea igneous (St. Anthony's Flower); Ocimum basilicum (Basil) and Melicoccus bijugatus (Mamoncillo). Conclusions: Some mechanisms of action of these herbal medicines can be suggested through the studies carried out, but in order to categorically understand the efficacy and pharmacology of any of these active ingredients, a more in-depth specific study is necessary.

**Keywords:** Antihypertensive. Hypertension. Medicinal Plants. Phytotherapy.

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## INTRODUCTION

The World Health Organization (WHO) considers Systemic Arterial Hypertension (SAH) as a chronic disease characterized by systolic pressure above 140mmHg and diastolic pressure of 90mmHg, being an aggravating factor for a series of serious cardiovascular diseases, responsible for almost 18 million deaths worldwide per year (BHANDARI, 2024). Hypertension is multifaceted in its aggravations, as the disease evolves, so that there may be symptoms in cases whose systolic pressure is higher than 180mmHg, ranging from headaches, dizziness, and even more dangerous conditions, such as cardiac arrhythmias (DAVID, 2021).

According to data from the report presented by the World Health Organization (WHO), about one in three adults in the world has high blood pressure. It is observed that in the period from 1990 to 2019, the number of people with hypertension doubled, from 650 million to 1.3 billion, and also, about half of people with hypertension do not know they have the disease and do not receive adequate treatment (WHO, 2019).

Hypertension can cause strokes, heart attacks, heart failure, kidney damage, and other health problems. In Brazil, it is estimated that 45% of adults between 30 and 79 years old have hypertension, which is equivalent to 50.7 million people. Of this total, 62% have the diagnosis, but only 33% have their blood pressure controlled (SILVEIRA, 2023).

Brazil is not exempt from the world scenario, since according to the Ministry of Health, cardiovascular diseases, despite the reduction in incidence in the country, are among the biggest causes of death in the Brazilian population, diagnosed with hypertension, in 2019, about 5.3% of people over 18 years of age have already been diagnosed with some disease of this type (WHO, 2023). Thus, Brazil is in an unfavorable position, as the large number of existing hypertensive patients who are diagnosed every year have a direct impact on public health.

The treatment of systemic arterial hypertension has been one of the most researched, so much so that every year, new drugs are introduced on the market for this control, among them, diuretics, antihypertensives, such as methyldopa, beta-blockers (metoprolol), angiotensin-converting enzyme II inhibitors and, perhaps, one of the most used in Brazil, angiotensin II receptor antagonists (losartan). Even with all the pharmacological advances and due to systemic arterial hypertension being a practically asymptomatic disease, many patients abandon the use of these medications, which ends up corroborating aggravations over time, followed by unhealthy lifestyle habits.

The use of medicinal plants for the treatment of systemic arterial hypertension has been used since ancient times all over the world. In Brazil it is no different, it is even

assumed that more plant species with medicinal properties should be used for the treatment of SAH, because, because it has continental dimensions, 5 defined biomes, it has the greatest biodiversity on the planet, however, there is a lack of many studies that can clinically evidence the use of medicinal plants for the treatment of SAH (CAMARGO, 2023).

Extracts of bioactive compounds such as polyphenols, present in most medicinal species, emerge as an alternative to the treatment of cardiovascular conditions, since many of these are frequently studied for their various properties, including antihypertensive action. (MARHUENDA *et al*., 2021). Despite the knowledge obtained with the isolation and identification of organic compounds, quality control of medicinal plants in Brazil is still very precarious (CAMARGO, 2010).

Most cases of hypertension are classified as primary, that is, without apparent cause, but a portion of the cases seem to have their pathophysiology to the renin-angiotensin-aldosterone system, whose etiology is related to a malfunction of the kidneys (Maideen; Balasubramanian; Ramanathan, 2021; It has changed; Odeyemi; Dewar, 2020). Studies also report in several plants the presence of a range of alkaloids, flavonoids and polyphenols whose effects are hypotensive and cardioprotective, with the potential to promote a reduction in blood pressure in the short and long term. (Islam *et al*. 2023; Reddy *et al*., 2022; Zeeshan *et al*., 2023).

Phytotherapy, through the use of medicinal plants or even herbal medicines, has emerged every day as an alternative solution to allopathic medicines, becoming popular for its accessibility and low side effects, when compared to chemically defined drugs (Pakkir maiden; Balasubramanian; Ramanathan, 2020). Thus, this study proposes a bibliographic review to highlight the medicinal plants, most used, according to popular use, in the northern region of the country, which through studies developed present clinical evidence, corroborating to be used in the treatment of SAH.

## METHODOLOGY

This was a retrospective, cross-sectional study with a search using the following databases: PubMed, webofscience, Lilacs, Pubmed and Google Scholar, based on the keywords *antihypertensive, arterial hypertension, high blood pressure, phytochemical, phytotherapy.* The search period took place between the years 2018 and 2022, based on the title and abstract, all articles that corresponded to the use of plant species for the treatment of SAH in the northern region of Brazil were evaluated and selected.

The articles that presented studies containing evidence for the use of medicinal plants and herbal medicines in the control of SAH, which is cited, even though it is popular

in the northern region, were cataloged and recorded in an Excel spreadsheet. Selection criteria included studies: published within the last 5 years; adult population; evaluation of medicinal plants and herbal medicines with antihypertensive activities; species found in the Brazil region; Case studies, reports, conference abstracts, commentary articles, letters to editors, and policy briefs were excluded.

## RESULTS AND DISCUSSION

More than 120 articles were selected, which presented citations of medicinal plants used in the control of SAH, of these, more than half referred to species not found in the northern region, precisely in the Amazon, so they were disregarded. Among the medicinal plants selected in the articles, the following plant species were listed, widely used in the Amazon region, they are: *Cymbopogon citratus* (Capim santo)*; Bidens pilosa* (Black picão)*; Allium sativum* (Garlic)*; Oryza sativa* (Rice)*; Hibiscus sabdariffa* (Caruru azedo)*; Cuphea igneous* (Flor de Santo Antônio)*; Ocimum basilicum* (Handling) and *Melicoccus bijugatus* (Mamoncillo).

Considering the species described for the control of SAH, we sought information about the tests performed on the respective medicinal plants, which in a certain way clinically evidence the hypotensive action directly or indirectly, as in the case of antioxidant metabolites. In the vast majority of articles, in vitro tests are mentioned, some have evolved to pre-clinical and clinical tests.

The fact that there are not many publications of clinical trials involving medicinal plants, through their extracts, does not exclude the importance of therapeutic characterization of the respective species. Thus, new studies will be proposed to clinically evidence the plants mentioned in their uses for the treatment of SAH.

Among the selected articles, it was observed that lemongrass (*Cymbopogon citratus*) is an Indian herbaceous plant adapted to the tropical climate that grows on long, slender shrubs in warmer regions of several countries, such as Brazil (Figure 1) (SABOIA *et al*., 2022). This plant has evidence of health benefits, such as antioxidant, anti-inflammatory, and antibacterial effects (MUKARRAM *et al*., 2021; JOHNSON *et al*., 2021). In addition, the suggestion of antihypertensive action C. citratus is also noteworthy through a preclinical trial where a significant reduction in blood pressure was observed in male Wistar rats laboratory-induced to SAH by means of an alcohol saline solution (SILVA; BÁRBARA, 2022).

Figura 1- Cymbopogon citratus (Capim Santo)

Fonte: https://www.ncbi.nlm.nih.gov/datasets/taxonomy/66014/

The main biochemical mechanism by which the species, *Cymbopogon citratus* has pharmacological properties that acts in the reduction of SAH, is possibly characterized by its metabolites, citral, a predominant poly aldehyde of the essential oil extracted from the plant itself, being a molecule that acts directly on cell receptors of transient potential inducing, by some still unknown reactional chain, the vascular endothelium relaxation vessel (SILVA; BÁRBARA, 2022).

The species**,** *Bidens pilosa*, popularly known as Picão-preto, is a weed native to South America that, however, is present in most tropical regions of the world due to its great adaptability and accelerated reproduction capacity (Figure 2) (MTENGA; RIPANDA, 2022; KATO-NOGUCHI; KURNIADIE, 2024). This plant has great therapeutic potential, being used as an alternative herbal medicine for various diseases, since there is evidence of its various properties, such as anti-inflammatory, anti-allergic, and antioxidant (RODRÍGUEZ-MESA *et al*., 2023).

Figure 2- Bidens pilosa (Picão Preto)

Fonte: https://www.ncbi.nlm.nih.gov/datasets/taxonomy/42337/

Among the studies carried out with the species, mainly for the control of SAH, there is evidence in preclinical tests in rats that *Bidens pilosa* can reduce blood pressure, through vessel relaxation and diuresis, although more studies are needed to determine the mechanism by which this occurs (TCHEUTCHOUA *et al*., 2022). Although the secondary metabolites present are known, such as: simple aromatic hydrocarbons, which derive in acids such as vanille, salicylic and protocatechuic, phenylpropanoids and their phenolic acids derived, such as coumaric, ferulic, chlorogenic, tannic and gallic, flavonoids, which are divided into aurones, chalcones, flavanones, flavones and flavonols, terpenoids, which are divided into linear, sesquiterpenoids and triterpenoids and sterols, such as campesterol, phytosterin-B, β-sitosterol, β-sitosterol glucoside and stigmasterol, it was not evident in the tests carried out which of the compounds would act in the control of SAH (GILBERT, 2013).

A species, widely used, mainly for culinary purposes is *Allium sativum*, or simply garlic, it is an old acquaintance in popular herbal medicine of Asian origin, whose bulbous flowers grow in temperate and tropical climate regions, being commonly used as a culinary spice or in homemade healing recipes (SASI *et al*., 2021). The pharmacotherapeutic potential of *Allium sativum* is widely studied, so that there is a correlation between the use of extracts of this plant and anti-inflammatory, cardioprotective, antioxidant, antidiabetic, anticancer, and antibacterial effects (RECINELLA *et al*. 2021; TUDU *et al*. 2022).

In Brazil it is quite common to observe the use of garlic, not only to enhance the flavor of food, but also in primary health care. This use has been passed down from generations and remains strong today, however, few or almost no studies on popular use to ensure greater safety in homemade garlic preparations. Through preclinical studies, it was also possible to verify a strong influence of *Allium sativum extracts* on antihypertensive activity through the direct reduction of systolic and diastolic pressure in guinea pig rats, in addition to the influence on the increase of nitric oxide levels in the body, a molecule that preceptors the mechanisms of vessel relaxation (EL-SABER BATIHA *et al*., 2020).

According to El-Saber Batiha, 2020, in vivo experiments demonstrated the antihypertensive effect of aqueous garlic extract in the 2-kidney 1-clip hypertension model provoked in rats, reducing the level of thromboxane B2 and prostaglandin E2 and thus reducing hypertension in rats tested. The dosage of garlic at a dose of 100 mg/kg for 5 days resulted in the complete prevention of acute hypoxic pulmonary vasoconstriction caused by endothelin-1, a peptide responsible for vasoconstriction in pulmonary arteries isolated from rats, and it was demonstrated in this study that garlic reduces the production of endothelin 1 and angiotensin II (EL-SABER BATIHA *et al*., 2020).

Another mechanism of the antihypertensive action of the eye, with the use of extracts, was attributed to sulfur molecules present in its metabolites, which stimulate endothelial constriction and relaxation factors, leading to a reduction in blood pressure. It has also been shown in tests carried out on rats, that garlic stimulates the production of nitric oxide (NO) and hydrogen sulfide (H2S), which ultimately leads to vasodilation (EL-SABER BATIHA *et al*., 2020).

Rice (*Oryza sativa*) is an ancient plant widely spread in Brazil for its culinary properties, but outside kitchens, it has potential in phytotherapy, since a high content of flavonoids has been detected in some species of *Oryza sativa*. This property can be evidenced in rice bran, in which a range of bioactives for the health of the most diverse populations are found (Beaulieu *et al*., 2020; Suantai *et al*., 2022).

A study carried out in a group of 100 people, who were diagnosed with SAH, were submitted to a clinical study, and the participants ingested rice bran, and it was observed that the group that ingested rice bran over 12 weeks, had a significant decrease in systolic blood pressure, corroborating the clinical proof of its efficacy (OGAWA *et al*., 2019). Despite being a vegetable that is part of the food base of Brazilians, the study demystifies the belief that rice causes edema in the body and can compress vessels, leading to SAH.

In the use of rice bran, no other studies were found that could evidence its use. However, the metabolites found in the species must be considered, such as: starch,

proteins, lipids, iron, vitamins B1, PP and folic acid, potassium, magnesium, zinc, fiber and vitamin E, which are of great importance for the homeostatic balance of the human being. Other compounds identified in rice include vanillic, syringic, caffeic, gallic, prototechic, hydroxybenzoic, synapic and chlorogenic acids, and the esters 6'-O-(E)-feruloylsaccharose, 6'-O-(E)-synapylsaccharse and g-oryzanol (TIAN, 2004).

Another widely used plant species, popularly used for the treatment of SAH, is *Hibiscus sabdariffa*, it is a shrubby, Indian plant with calyx-shaped leaves, which has adapted to several tropical and subtropical regions around the world and which in Brazil is popularly known as Caruru-azedo (Figure 3) (MONTALVO-GONZÁLEZ *et al*. 2022). This species is widely used in cooking, however, its therapeutic properties have been evidenced in several studies, as it presents secondary metabolites in polar extracts, such as flavonoids and phenolic compounds, which confer antioxidant, potentially hypoglycemic, antilipemic and anti-inflammatory properties (JAMROZIK; BORYMSKA; KACZMARCZYK-ŚEBROWSKA, 2022; CHO URIELLE M'BE *et al*., 2023).

Figure 3- Hibiscus sabdariffa (Hibiscus)

Fonte: https://www.ncbi.nlm.nih.gov/datasets/taxonomy/183260/

Salem, et.al, 2022, conducted preclinical studies, which also suggested that hibiscus (*H. sabdariffa*) has antihypertensive properties. Tests on rats with hypertension, induced by L-NAME (N(G)-Nitro-L-arginine methyl ester), acting directly on renin inhibition during the process of pressure increase by the Renin-Angiotensin-Angiotensinogen system, results comparable to the action of captopril on the cardiovascular system (SALEM *et al*., 2022).

Secondary metabolites of hibiscus (*Hibiscus sabdariffa*) include: Alkaloids, Flavonoids, Phenols, Tannins. Hibiscus is a plant rich in phenolic compounds, such as organic acids and flavonoids, which have antioxidant and anti-inflammatory properties

(SOUSA, et.al, 2021). One of its active ingredients is hybiscic acid, which is responsible for some of its therapeutic properties.

Another species used, in the northern region as an antihypertensive, which was found in the research, was the Santo Antônio flower or cigar flower, popular denominations of *Cuphea ignea*, classified as a subshrub species of tropical and subtropical regions, whose tubular flowers give the plant its name (ISMAIL *et al*., 2020). In addition to unusual aesthetics, *in vivo studies* suggest a relationship between plant phytoconstituents and broadly beneficial health effects, with antitumor, antiviral, and antioxidant potential (Figure 4) (HASSAN *et al*., 2019; MAHMOUD *et al*., 2021).

Figure 4- Cuphea igneous (Flor de Sonto Antônio)

Autor: Kurt Stüber - https://commons.wikimedia.org/wiki/File:Cuphea_ignea3.jpg

There is also an association via preclinical study of *Cuphea ignea*, described by Hassan et.al., 2019, demonstrating hypotensive activity in L-NAME-induced hypertensive rats. The result of the test demonstrated that the extract of *the igneous Cuphe* species generated a relaxing action and decreased serum ACE levels by increasing the synthesis of nitric oxide in the body (HASSAN *et al*., 2019).

Another species used to control SAH and that was found in the research was *Ocimum basilicum*, a popular spice, well known as basil, is a shrubby herb that belongs to the *Lamiaceae family,* found in tropical and subtropical regions of the planet (SHAHRAJABIAN; SUN; CHENG, 2020), has several medicinal properties. According to an article published by Nabilah Sekar Azizah *et al*., 2023, it has potent antidiabetic, antibacterial, antiviral, and antioxidant activities.

It was also observed in another study that polar extracts of the plant also have applicability in reducing blood pressure, a fact corroborated by *in vivo* studies - where rats induced hypertension by L-NAME over 1 month showed significant improvement in their systolic BP (QAMAR *et al*., 2023). I believe that there is a lack of information, who knows how to discuss more.

*Melicoccus bijugatus*, popularly known as Spanish lime, is a small greenish fruit with sweet, slightly citrus pulp originating from a tree that grows in tropical regions, characteristic of South America (Figure 5) (WILSON; GOLDSON-BARNABY; BAILEY, 2019). This is a plant that is not very popular, but it has preclinical evidence of its efficacy in the treatment of SAH, and in two *in vivo studies (present the studies),* plant extracts decreased the HR, SBP, and DBP of rats with L-Name-induced hypertension (NWOKOCHA *et al*., 2020).

Figure 5- *Melicoccus bijugatus* (Spanish Lima)

Autor: Filo gèn' - https://commons.wikimedia.org/wiki/File:Melicoccus_bijugatus_%28Sapindaceae%29.jpg

In another experiment, Nwokocha *et al*., 2019, had observed an effect in rats with myocardial damage caused by ischemia and reperfusion through the left coronary artery, suggesting a cardioprotective effect possibly through the reduction of peripheral vascular resistance.

## CONCLUSIONS

Despite the vast medicinal flora that integrates the northern region, considering the largest equatorial forest on the planet, which integrates a number of species with medicinal properties for various pathologies. This has aroused the interest of researchers from all over the world in studying species, mainly native to Brazil.

Thus, it is concluded that the vast majority mentioned in the research are not native to the northern region, however, they are easily found and used by the local population. The popular use of these species has shown significant growth in recent years, which certainly points to a scientific technical development for more in-depth studies with these medicinal plants.

Clinical studies with some species were observed, however, in an observational way, because there is no statistics that can measure the effects of these species on the control of SAH in humans. Thus, it can be concluded that many studies should be carried out in order to highlight the therapeutic properties of the species mentioned to ensure access to the population in the control of systemic arterial hypertension.

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