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*Review Article*

# Pharmaceutical Properties of *Hibiscus sabdariffa*, Toward an Ideal Treatment for Hypertension

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**Abstract**

High blood pressure is the main risk factor for cardiovascular disease and should be controlled primarily by changes in lifestyle, such as regular exercise, a low-salt diet, and weight loss in overweight or obesity. If lifestyle changes are not enough, many types of medications can be used to control high blood pressure; however, side effects constitute one of the most critical limitations of conventional medicines associated with high blood pressure. For this reason, the use of traditional and herbal medicines has been welcomed by the public for many years. *Hibiscus sabdariffa* is one of the most suitable herbal medicines for hypertension. According to research results, it has the same effect as conventional medicines without serious side effects. The present study introduces sour tea as a suitable herbal medicine for high blood pressure to provide readers of this article with a comprehensive understanding of the medicinal properties of *Hibiscus sabdariffa* for the treatment of hypertension and its effects on several other common diseases, including cancer.

## Introduction

Long-term use of herbs introduced in traditional medicines approves their value in drug discovery. Based on several historical studies, herbal therapies have been used for centuries to treat numerous diseases. Herbal medicine has always played an important role in Iranian civilization and culture. Hundreds of books and thousands of years of history have placed Iranian folk medicine among the ancient and most popular alternative medications.[1,2]

*Hibiscus sabdariffa L.* (HS) is an annual herb from the family Malvaceae. It is generally known as Roselle or Red Sorrel in English.[3-5] This plant is a tropical shrub frequently grown in various tropical areas worldwide, mainly in central and west Africa, India, South East Asia, and America.[3,4] Different parts of the HS, such as the calyx, leaves, and flowers, are used therapeutically for the treatment of numerous disorders; the aqueous extracts of dried calyces or fresh flowers are also widely used to produce sour tea.[4,6] Pharmacological and phytochemical analyses of HS have revealed its bioactive compounds, mainly polyphenols such as anthocyanidins, anthocyanins, phenolic, flavonoids, and organic acids.[7,8] Among them, anthocyanins have been recognized as the major compound of polyphenols in the HS plant, conferring the red pigment to the calyces of the HS flower.[9] It has been used conventionally as a kind of beverage in herbal drinks, food, fermented drinks, jellied confectioneries, as a flavoring agent in the food industry, and as an herbal medicine.[10,11] Based on evidence from clinical trials and several important studies, HS affects lipid metabolism and also has remarkable anti-oxidant, anti-inflammatory,[12] antibacterial, anti-diabetic, and anti-hypertensive properties,[13,14] which might be linked to antioxidant solid activities, inhibition of angiotensin-converting enzymes (ACE), inhibition of α-glucosidase and α-amylase, and calcium channel modulation or a direct vasorelaxant effect.[10,13] In general, HS is considered an important plant by scientists and researchers because of its varied richness. Owing to the limitations and side effects of conventional medicines, the use of HS extracts seems to be an ideal option for treating a wide range of diseases, high blood pressure being one of them for which sour tea has been shown to be accepted by the public and increasingly effective because of its special properties. Despite, HS consumption can modify the pharmacokinetics and efficiency of other prescribed medicines. These changes can lead to beneficial or harmful interactions in the body that should be considered.[15] The main aims of the present study are to introduce and discuss HS as a suitable and

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reliable herbal remedy for the treatment of high blood pressure.

## Search Strategy

Online databases (PubMed and Scopus) were searched for relevant papers published from 2000 to 19 Oct. 2021 using the keywords "*Hibiscus sabdariffa*" OR "Sour tea" AND "Hypertension". All search hits from both databases equaled 153 papers (83 from Scopus and 70 from PubMed). Duplicate articles were removed. Then, the title and abstract of all search results were reviewed for eligibility, and eventually, 82 articles were selected for the current review study.

## *Hibiscus sabdariffa* Properties

The HS plant has many characteristics, including different names, compounds, scattered geography, and other effects on various diseases and disorders.[16] In this section, the different characteristics of the HS plant will be discussed.

## Phytochemicals of *Hibiscus sabdariffa*

HS is mostly cultivated for its calyx which comes in red, dark, and green types. Red calyces are used extensively for their high concentration of anthocyanin.[16,17] Cyanidin 3-sambubioside and delphinidin 3-sambubioside are the main anthocyanins, and amino acids, organic acids, vitamin C, minerals and carotene comprise the other vital components of HS.[17,18] The concentration of sugar in different parts of *Hibiscus sabdariffa* varies depending on its diversity and geographical area.[18] The main components of the HS plant are presented in Figure 1.

## The Names and Terms of *Hibiscus sabdariffa*

*Hibiscus sabdariffa* is known by different names depending on the country and geographic area. For example, it is known as karkade in Egypt, Germany, Italy; Sudan tea in East Africa; and Susur in Indonesia.[19,20] Some primarily used names are presented in Figure 1.

## Pharmacological Properties of *Hibiscus sabdariffa*

The HS plant has a wide range of medicinal properties, some of the most important of which are listed in Figure 1. This plant has been shown to play a direct and influential role in many diseases.[21]

## The Structure of *Hibiscus sabdariffa*

*Hibiscus sabdariffa* has different parts, including stalks, roots, flowers, and seeds or fruits, and each part has different phytochemical elements and, thus, various medicinal properties.[20] The main parts of *Hibiscus sabdariffa* are presented in Figure 1.

The main phytochemicals found in HS flowers are organic acids, largely malic and acids citric, anthocyanins, numerous glycosides and flavonoids, and fiber.[22-24] The calyces have equal organic acid and anthocyanin ingredients, but the amounts of glycosides and flavonoids are negligible.[21] Anthocyanins, mainly cyanidin-3 sambubioside and delphinidin-3-sambubioside, are believed to be the active ingredients responsible for the hypocholesterolemia[19], anti-hypertensive, and antioxidant effects of HS, as they are found in high relative extents in aqueous extracts.[25,26] The nutritional value of HS is presented in Table 1.[3,11,27,28]

## *Hibiscus sabdariffa* in Traditional Medicine

HS has been found to have biochemical effects on reproductive hormones such as testosterone, luteinizing hormone, and prolactin.[29,30] Improved postprandial vascular function and CVD risk reduction and modified postprandial flow-mediated dilatation (FMD) of the brachial artery were demonstrated after consumption of HS calyces (HSC).[31] According to the World Health Organization (WHO), cancer is the second biggest cause of death after cardiovascular diseases and is responsible for an expected more than 9.5 million deaths in 2018.[32] It has been estimated that approximately 29.5 million people will be diagnosed with cancer by the year 2040.[33] Although the underlying mechanisms remain unclear, HS is a candidate for chemotherapeutic applications due to its phytochemicals, and it is known as an effective

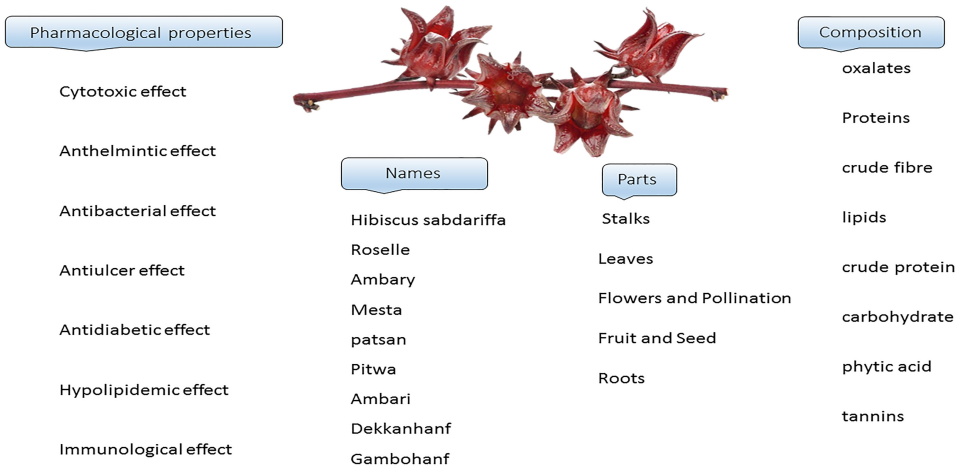


**Figure 1.** *Hibiscus sabdariffa* properties.

**Table 1.** Nutritional value of *Hibiscus sabdariffa*.

| Nutrient | Leaves | Seeds | Calyces | Ref. |
|---|---|---|---|---|
| Protein | 3.3 g/100 g | 27.78 | 1.9 g/100 g | Taken from: Naturlan[3,11,27,28] |
| Fat | 0.3 g/100 g | 21.85 | 0.1 g/100 g | |
| Carbohydrate | 9.2 g/100 g | 21.25 | 12.3 g/100 g | |
| Ascorbic Acid | 54 mg/100 g | - | - | |
| β-carotene | 4135 µg/100 g | - | 300 µg/100 g | |
| Vitamin A | 1000 g | - | - | |
| Vitamin C | 2.3 g | 9 | 17 | |
| Calcium | 240 g | 350 | 150 | |
| Iron | 5 g | 9 | 3 | |

anticancer agent.[34,35] Compounds like protocatechuic acid and delphinidin-3-sambubioside need an appropriate clinical trial to identify its chemotherapeutic potential and synergistic activity with chemotherapeutic drugs.[34,35] Inhibition of the B16-F1 cell migration and suppressed HUVECs tube formation were reported as an anticancer aspect of HS.[35] In recent years, researchers have been attracted by the antimicrobial activity of the HS plant. The ethanol extract of HS showed antimicrobial activities against *Salmonella enteritidis, Staphylococcus aureus*, *Cronobacter sakazakii, Listeria monocytogenes*, *Escherichia coli*, and *Bacillus cereus.*[36] Anthocyanins extracted from dried calyx displayed an anti-angiogenic effect in a time- and concentration-dependent manner when injected into chick embryos. HS inhibits angiogenesis and, therefore, can be helpful in treating angiogenesis-related diseases, including hypertension.[37] HS induces apoptosis in human gastric carcinoma cells through the p38 MAPK/FasL cascade pathway and p53 phosphorylation. In other words, HS extract acts as an apoptosis inducer in human gastric carcinoma (AGS) cells, and these discoveries are promising perspectives in human gastric cancer treatment.[38] *H. sabdariffa* L. leaf extract (HLE) acts as an apoptosis inducer in LNCaP cells, and showed interesting perspectives for human prostate cancer treatment strategies.[39] Protocatechuic acid (PCA) is one of the most important phenolic compounds isolated from HS dried flowers and has antitumor and antioxidant properties.[40] The results of one original research showed that HS has a significant effect on blood lipid profiles in patients with diabetes. In other words, HS can be considered as a suitable herbal medicine for diabetic patients.[41,42] Polyphenol extracts from HS reduced nephropathy in experimental type 1 diabetes by increasing catalase and glutathione activity and decreasing lipid peroxidation.[43] Similarly, the ethyl acetate fraction from HS (EFHS) reduced diabetes-associated cognitive deficiency in rats. Study results have also shown the EFHS significantly improved hyperphosphorylation tau signaling, cholinergic system, and anti-oxidant activity.[44] In general, HS has a variety of medicinal applications in connection with a wide range of diseases. The most significant functional mechanisms are apoptosis, oxidative stress response, antimicrobial activity, and hormonal changes. Figure 2 schematically shows these mechanisms. The relative mechanisms of HS plant activities in traditional medicine are presented in Table 2.

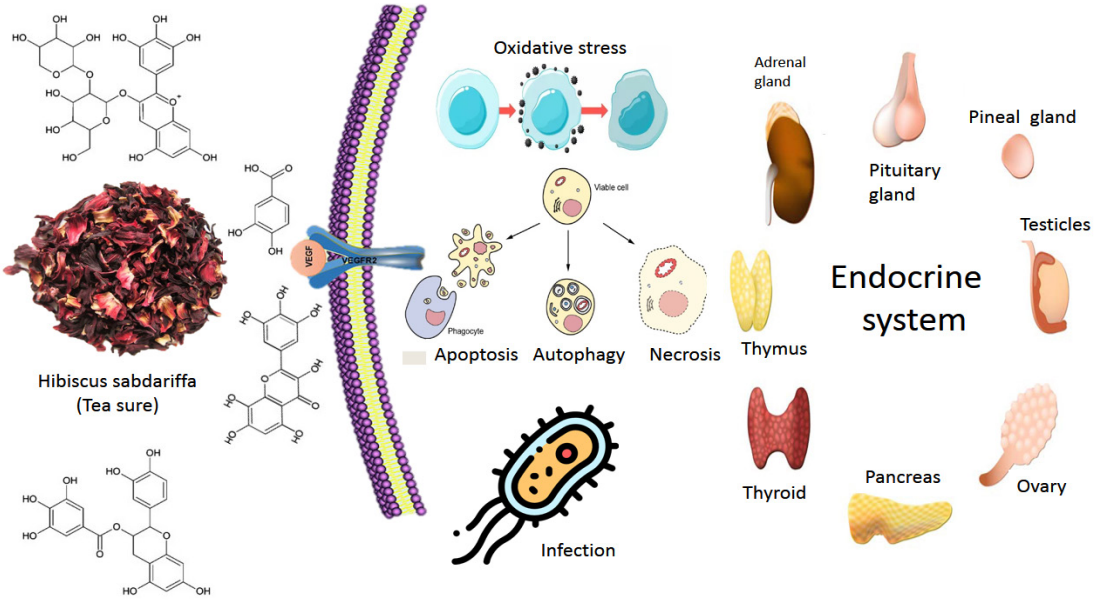


**Figure 2.** The main therapeutic mechanisms of *Hibiscus sabdariffa*.

**Table 2.** *Hibiscus sabdariffa* in traditional medicine and the relative mechanisms of actions.

| Used part | Disorders | Model | Mechanisms and potential of actions | Ref. |
|---|---|---|---|---|
| Whole part | Reproduction | Rat | Decrease in testicular protein concentration | 45 |
| HSC | Reproduction | Rat | Biochemical effects on reproductive hormones such as testosterone, luteinizing hormone, and prolactin | 29 |
| Aqueous extract | Reproduction | Rat | Effect on male reproductive system | 30 |
| HSC | Inflammation, CVD, Blood Lipids | Human | Improves postprandial vascular function and CVD risk reduction, improves postprandial FMD of the brachial artery | 31 |
| Aqueous extract | Cancer, Melanoma | Murine | Inhibition of melanoma cell growth, migration, and tube formation in vitro as well as inhibition of presence of lung metastasis and subcutaneous tumor growth | 35 |
| Aqueous extract | Antibacterial activity | Food | Inhibition of various food-borne pathogens as well as both gram-positive and gram-negative pathogens | 36 |
| Dried calyx | Anti-angiogenic | Chick embryo | Binds to (VEGFR2) and impedes its activity | 37 |
| Aqueous extract | Cancer of gastric cavity | Human | p38 MAPK/FasL cascade pathway and p53 phosphorylation | 38 |
| HLE | Prostate cancer | Human | (HLE) acts as an apoptosis inducer in LNCaP cells | 39 |
| Dried flower | Leukemia | Human | Apoptosis inducer, RB phosphorylation, and Bcl-2 protein | 40 |
| Sour Tea | Diabetes | Human | Lipid profiling | 41 |
| Polyphenol extract | Nephropathy | Human | Increased catalase glutathione activity and reduced lipid peroxidation | 43 |
| Ethyl acetate extract | Cognitive | Rat | EFHS significantly enhanced cholinergic system, hyperphosphorylation tau signaling, and antioxidant | 44 |

FMD: Flow-mediated dilatation, CVD: cardiovascular disease, HSC: *Hibiscus sabdariffa* calyces, VEGFR2: vascular endothelial growth factor receptor 2, HLE: *H. sabdariffa* L. leaf extract

## *Hibiscus sabdariffa* Pharmacokinetics

Several patients take herbs along with their medications. Such practice may result in either beneficial or harmful herb-drug interactions. Accordingly, some studies have reported that HS consumption can change the pharmacokinetics and potential efficacies of prescribed medicines.[46] Among the best-defined health benefits of *H. sabdariffa* L. is the control of high blood pressure. Some patients taking conventional antihypertensive drugs may also consume *H. sabdariffa* L. extracts.[46,47] It has been shown that co-administration of HS aqueous extract can change the pharmacokinetic profile of captopril; for that reason, its co-administration should be avoided.[48] Several studies have indicated that HS extracts can reduce the levels of TG, Tc, LDLc, and LDLc/HDLc in humans and animal models.[49] The aqueous extract of HS lowered $T_c$ better than simvastatin and improved antihyperlipidemic activity when co-administered at low doses in an animal model.[50] Research results have also revealed that patients should avoid the simultaneous usage of a HS herbal beverage and hydrochlorothiazide (HCT) diuretics to control hypertension.[51] An innovative study showed that co-administration of *Z. officinale* or *H. sabdariffa* with amlodipine increased its pharmacodynamic response.[52] An original study revealed that the herb-drug interaction between Z. *officinale*-losartan and H. *sabdariffa*-losartan could occur in rats.[53] In general, the simultaneous use of herbal and synthetic medicines can have either positive or toxic effects (Figure 3).

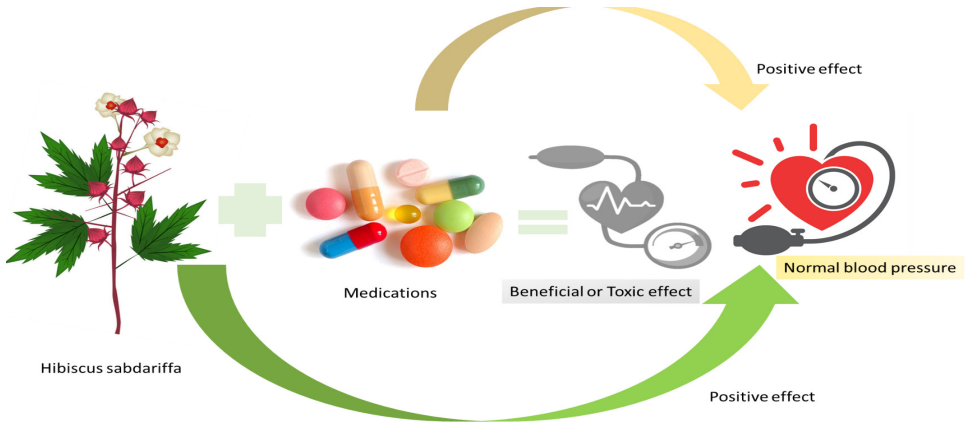


**Figure 3.** Positive or toxic effects because of simultaneous use of herbal and synthetic medicines.

**Table 3.** *Hibiscus sabdariffa* pharmacokinetic and drug interactions.

| Medication | Model | Pharmacokinetic and drug interactions | Ref. |
|---|---|---|---|
| Captopril | Animal | HS aqueous extract changed the pharmacokinetic profile | 48 |
| Simvastatin | Human/Rat | Reduced $T_c$ better than simvastatin and improved antihyperlipidemic activity | 50 |
| Hydrochlorothiazide | Animal | - | 51 |
| Amlodipine | Human | Co-administration of *Z. officinale* or *H. sabdariffa* with amlodipine increased its pharmacodynamic response | 52 |
| Losartan | Rat | Clinical trial required for further results | 53 |

The interactions between some antihypertensive medicines and herbal teas are summarized in Table 3. It shows that the simultaneous use of herbal and synthetic medications to control blood pressure should be adopted with caution. Moreover, based on research results and due to the lack of experimental work, further clinical trial studies are recommended.

## Hypertension Medications

Numerous blood pressure medications, known as anti-hypertensives, for reducing high blood pressure (HBP) are accessible by prescription. There are several classes of high blood pressure medications which contain many different drugs, the most important of which include diuretics, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), calcium channel blockers, alpha-blockers, alpha-beta-blockers, central agonists, vasodilators, aldosterone receptor antagonists, and direct renin inhibitors.

As shown in Table 4, a variety of drug groups are used for the treatment of HBP.[54-56] It is noteworthy that the side effects of the mentioned drugs are, in some cases, severe and problematic. Therefore, researchers and pharmacists are always seeking alternative remedies. Herbal preparations seem to be a good option, according to the results of various studies, and in most cases, they show no side effects; however, they may have low therapeutic properties.

## Herbal Preparations for Hypertension

Taking antihypertensive medications has inherent side effects and restrictions. Conversely, the consumption of herbal medicines can be a great choice with reduced adverse effects if used in proper amounts.[5,57] Uncontrolled hypertension can also lead to other conditions such as blindness, congestive heart failure, and kidney diseases. Conventional antihypertensive drugs are commonly associated with several side effects, some that can be serious. Thus, the use of herbal medicines has been popular since ancient times.[58] This section includes the introduction of some of the most important herbal remedies for high blood pressure. *Allium sativum* (Garlic) has multi-fold beneficial effects that have been known for thousands of years by different cultures worldwide and have attracted the interest of health practitioners and pharmacologists. Garlic is recognized not only for its antihypertensive capabilities, but also its anti-cancer, anti-inflammatory, antibacterial, antioxidant, and hypocholesterolemic properties.[59] Increased flow-mediated dilation (FMD) after consumption of *Camellia sinensis* was investigated.[60] *Coriandrum sativum* is one of the critical antihypertensive plants. Inactivated ROS produced by β-adrenoceptor stimulation was reported as the main mechanism.[61] Consumption of *Salvia miltiorrhiza* decreases ROS, increases antioxidants, serum glutathione (GSH), glutathione reductase (GSSG-R), superoxide dismutase (SOD), paraoxonase (PONase), and reduces blood pressure.[62] *Zingiber officinale* inhibits lipid peroxidation and scavenges ROS toward

**Table 4.** Antihypertensive drugs and their side effects.

| Group | Drugs | Side effects | Ref. |
|---|---|---|---|
| Diuretics | Chlorthalidone, Chlorothiazide Hydrochlorothiazide, Indapamide, Metolazone | Increase blood sugar levels; decrease body supply of potassium | 54-56 |
| ACE inhibitors | Enalapril maleate, Lisinopril, Moexipril, Ramipril, Trandolapril | Skin rash, ageusia, chronic dry, hacking cough, kidney damage (in rare cases) | |
| ARBs | Candesartan, Eprosartan mesylate, Irbesarten, Telmisartan | Occasional dizziness, fetus disorders | |
| Calcium channel blockers | Amlodipine besylate, Bepridil, Felodipine, Nicardipine | Heart palpitations, swollen ankles constipation, headache dizziness | |
| Alpha-blockers | Doxazosin mesylate, Prazosin hydrochloride, Terazosin hydrochloride | Tachycardia, dizziness | |
| Central agonists | Alpha methyldopa, Clonidine hydrochloride, Guanabenz acetate | Feeling weak or faint, drowsiness or sluggishness, dryness of mouth, fever, anemia | |
| Vasodilators | Hydralazine hydrochloride, Minoxidil | Headaches, excessive hair growth, swelling around the eyes, heart palpitations, aches and pains in joints | |

ACE: Angiotensin converting enzyme, ARBs: Angiotensin II receptor blockers.

lower blood pressure. This plant also inhibited angiotensin I-converting enzyme, iron (II), and sodium nitroprusside-induced lipid peroxidation in the heart of a rat model in an *in vitro* study.[63] *Annona muricata* is a member of the family of custard apple trees and grows natively in Central America and Caribbean. It has been revealed that the leaf extract of this plant reduces elevated blood pressure by decreasing peripheral vascular resistance.[64] *Desmodium styracifolium* showed antihypertensive properties in two ways: a: mediation through cholinergic receptor stimulation, and b: potentiation by barriers of the autonomic ganglion and alpha-adrenoreceptor.[65] It has been found that *Lepidium latifolium* has hypotensive effects in rats due to its diuretic action; therefore, it can be used as an antihypertensive plant.[66] *Viscum album* presents biologically active principles that may act as inducers of the nitric oxide/soluble guanylate cyclase pathway.[67] Studies in this field have shown that a wide range of herbal remedies can be used for the treatment of hypertension. The studies in this section are summarized in Table 5.

The main point of the studies discussed in this section and shown in Table 5 is that most research has been developed on animal models, and there are few clinical trial studies. The primary purpose of the current study is to introduce HS as an herbal remedy for high blood pressure, as discussed below.

### *Hibiscus sabdariffa* for Hypertension

Angiotensin-converting enzyme (ACE) is an essential part of the renin–angiotensin system (RAS) which controls blood pressure by regulating the volume of body fluids.[68,69] Leonard T. Skeggs, Jr. discovered this enzyme in 1956. This enzyme converts the hormone angiotensin I to the active vasoconstrictor (angiotensin II).[68] Ultimately, ACE raises blood pressure by constricting vessels. ACE inhibitors are widely used as pharmaceutical drugs in cardiovascular diseases.[69,70] The ability of HS aqueous extract to block the action of ACE is an additional hypotensive mechanism. Anthocyanins, as the main HS extract, compete with the ACE binding site, thereby inhibiting the formation of Ang II, which is an effective vasoconstrictor. The ability of HS extract to impede ACE activity was explored in a randomized clinical study.[71] Daily consumption of HS can effectively treat high blood pressure in stage one hypertension along with dietary and lifestyle modifications.[72,73] It has been revealed that daily consumption of hibiscus tea in a concentrated bio-energized form may prove to be an influential component in cardiovascular health management and lead to lower blood pressure levels.[74] Improving a patient's lipid profile is the main therapeutic effect of HS. The anthocyanins in this plant, inhibit low-density lipoprotein oxidation and consequently reduce the atherosclerotic process.[75] Moreover, *H. sabdariffa* extracts significantly inhibit adipogenesis by regulating adipogenic signaling pathways, modulating the gene expression of certain microRNAs, decreasing LDL oxidation, and through transcription factors.[75] It has been shown that HS contains a compound that causes the release of nitric oxide from the vascular endothelium and increases renal filtration, thereby lowering blood pressure.[76] It has also been exhibited that HS can decrease the systolic and diastolic blood pressure (BP).[77] Consumption of HS with adapted doses between 10-20 g daily for one month was associated with an improvement in both diastolic and systolic BP, even in patients simultaneously taking antihypertensive medications.[78] An interesting study showed that HS has cardioprotective and antihypertensive effects in vivo and agreed with the public belief that HS can be a valuable antihypertensive agent. Vitamin C and anthocyanin are the main antioxidant compounds in the HS plant. Accordingly, that these antioxidants act as free radical scavengers in 2K-1C hypertension remains hypothetical.[79] The antihypertensive effects of HS calyces was revealed in a report. This result possibly interfered with the endothelium-derived nitric oxide-cGMP-relaxant pathway and inhibition of calcium ($Ca^{2+}$)-influx into vascular smooth muscle.[80] Another research showed that continuous consumption of HS calyx extract improved myocardial capillarization in spontaneously hypertensive rats.[81] In an innovative study, the effects of

**Table 5.** Frequently used antihypertensive plants with their relative mechanism of action.

| Plants | Model | Mechanism of action | Ref. |
|---|---|---|---|
| *Allium sativum* | Human | Reduces NADPH activity, increases antioxidants, scavenges ROS | 59 |
| *Camellia sinensis* | Human | Increases flow-mediated dilation (FMD) | 60 |
| *Coriandrum sativum* | Rat | Deactivates ROS produced by β-adrenoceptor stimulation | 61 |
| *Salviae miltiorrhizae* | Rabbit | Reduces ROS, increases antioxidants, serum glutathione (GSH) levels, glutathione reductase (GSSG-R), superoxide dismutase (SOD), paraoxonase (PONase) | 62 |
| *Zingiber officinale* | Rat | Inhibits angiotensin I-converting enzyme, iron (II), and sodium nitroprusside-induced lipid peroxidation | 63 |
| *Annona muricata* | Rat | Decreases peripheral vascular resistance | 64 |
| *Desmodium styracifolium* | Rat | Mediated through cholinergic receptor stimulation, potentiated by barriers of autonomic ganglion and alpha-adreno receptor | 65 |
| *Lepidium latifolium* | Rat | Has hypotensive effects due to its diuretic action | 66 |
| *Viscum album* | Rat | Some biologically active principles that may act as inducers of the nitric oxide/soluble guanylate cyclase pathway | 67 |

co-administration of HS plus captopril (CAP) and CAP alone on renin-angiotensin-aldosterone system (RAAS) biomarkers and blood pressure were compared in a two-kidney-one-clip (2K1C) model of hypertensive rats. It was established that HS could be ingested as a supplement to captopril without any extraction but may not show further benefit.[82] The flower of HS presented a beneficial effect in controlling preclinical hypertension through the modulation of some molecular networks.[83] Another study reported that intravenous injection of adaptive HS showed hypotensive, anti-hypertensive, and adverse chronotropic effects. This study further reported the inhibition of nitric oxide synthase (NOS) as the primary associated mechanism in lowering blood pressure.[84] Whether low dose HS can successfully reduce blood pressure was explored, and the results confirmed various animal antihypertensive studies on HS. Additionally, the finding provides evidence that daily consumption of HS at the optimum dose has no side effects.[85] In sum, based on the results of several studies, no significant harmful alterations in triglyceride, serum creatinine, cholesterol, BUN, or Na and K levels were perceived within two weeks after the termination of the medication. In other words, the HS plant seems to be more effective than other herbal remedies. A pharmacological study found that HS and *C. Micranthum,* used as brews or tablets, were as effective as the standard treatment, captopril, in controlling hypertension over a 6-month follow-up.[86] Several studies on the antihypertensive properties of HS are summarized in Table 6.

Notes of this section and Table 6 include: A) Different parts of the HS plant have nutritional and medicinal value. B) The nutritional, medicinal, and chemical compositions of various parts of the HS plant are different, the details of which were introduced in sections 3-4. C) The results of several studies have shown that acidic compounds, antioxidants, and anthocyanins were the most important factors related to reducing blood pressure. D) The results of studies have shown that daily consumption of low dose of HS showed no side effects. E) Despite the progress made in identifying the exact mechanism of the HS plant in lowering blood pressure, more details, especially in human studies, have not been fully elucidated until now.[87] HS carried out different pathways in lowering blood pressure.[88,89]

## Conclusion

The consumption of current antihypertensive medications has inherent limitations and side effects. Herbal preparations could be a great choice with fewer side effects if used in the proper dose. Nevertheless, for a comprehensive understanding, such usages must be linked to modern medicine, and more systematic studies are needed to validate the efficiency and clarify the safety of such herbal remedies for their antihypertensive potential. The current study provides a basic understanding of medicinal plants used to treat high blood pressure to support future phytochemical and pharmacological investigations. The main limitation of suggesting the HS plant as a blood pressure-lowering agent or an anti-lipidemic medication is the heterogeneity of clinical trial protocols. We recommend the widespread cultivation of this plant across the globe for not only nutritional but also pharmacological industries. The studies on antihypertensive effects suggest that HS is comparatively effective compared with other pharmaceutical antihypertensive drugs and is probably a safe and well-accepted treatment option for mild to moderate essential hypertension. In confirmation of previous studies, the present work emphasizes that sour tea could be considered as the first line of defense against rising blood pressure in healthy individuals.

**Table 6.** *Hibiscus sabdariffa* for hypertension and the relative mechanisms of action.

| Model | Mechanisms and potential of actions | Ref. |
|---|---|---|
| Human | - | 72 |
| Human | Effective component in cardiovascular health management and leads to lower blood pressure | 74 |
| Human | Inhibits adipogenesis by regulating adipogenic signaling pathways, modulates gene expression of certain microRNAs, decreases LDL oxidation, and transcription factors | 75 |
| Human | Inhibits ACE activity | 71 |
| | Releases nitric oxide from vascular endothelium and increases renal filtration | 76 |
| Human | Decreases the systolic and diastolic blood pressure (BP) | 77 |
| Human | Improves both diastolic and systolic BP, even in patients simultaneously taking antihypertensive medications | 78 |
| Rat | Antioxidants act as free radical scavengers in 2K-1C hypertension | 79 |
| Rat | Inhibits calcium ($Ca^{2+}$)-influx into vascular smooth muscle cells | 80 |
| SHR | Extracted calyces improve myocardial capillarization in the SHRs | 81 |
| Rat | - | 82 |
| Pig | Beneficial effects can result from the modulation of some molecular networks inducing each other | 83 |
| Rat | Inhibits nitric oxide synthase (NOS) | 84 |
| Human | - | 85 |

ACE: Angiotensin-converting enzyme, SHR: Spontaneously hypertensive rat

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## Author Contributions

RK: Conception or design of the work, MT and MG: the acquisition, analysis, HN and SMBF: interpretation of data for the work, MA: drafting the work or revising it critically for important intellectual content. All authors read and approved the final manuscript.

## Conflict of Interest

The authors report no conflicts of interest.

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