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Review article

Pharmaceutical properties of sour tea (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. Sour tea (Hibiscus sabdariffa) is one of the most suitable herbal medicines for hypertension. According to research results, sour tea 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 sour tea for the treatment of hypertension and its effects on several other common diseases, including cancer.

Keywords: Hibiscus sabdariffa, hypertension, herbal medicine, traditional medicine

1. 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.\textsuperscript{1,2} 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.\textsuperscript{1,2}

\textit{Hibiscus sabdariffa}. \textit{L} (HS) is an annual herb from the family Malvaceae. It is generally known as Roselle or Red Sorrel in English.\textsuperscript{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.\textsuperscript{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.\textsuperscript{4,6} Pharmacological and phytochemical analyses of HS have revealed its bioactive compounds, mainly polyphenols such as anthocyanidins, anthocyanins, phenolic, flavonoids, and organic acids.\textsuperscript{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.\textsuperscript{9} \textit{Hibiscus sabdariffa} 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.\textsuperscript{10,11} Based on evidence from clinical trials and several important studies, HS affects lipid metabolism and also has remarkable anti-oxidant, anti-inflammatory,\textsuperscript{12} antibacterial, anti-diabetic, and anti-hypertensive properties,\textsuperscript{13,14} which might be linked to antioxidant solid activities, inhibition of angiotensin-converting enzymes (ACE), inhibition of $\alpha$-glucosidase and $\alpha$-amylase, and calcium channel modulation or a direct vasorelaxant effect.\textsuperscript{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.\textsuperscript{15} The main aims of the present study are to introduce and discuss sour tea as a suitable and reliable herbal remedy for the treatment of high blood pressure.
2. 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.

3. Hibiscus sabdariffa properties

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

3.1. Phytochemicals of Hibiscus sabdariffa

*Hibiscus sabdariffa* 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. 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. The concentration of sugar in different parts of *Hibiscus sabdariffa* varies depending on its diversity and geographical area. The main components of the HS plant are presented in Fig. 1.

3.2. 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. Some primarily used names are presented in Fig. 1.
3.3. 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 Fig. 1. This plant has been shown to play a direct and influential role in many diseases.

3.4. 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. The main parts of *Hibiscus sabdariffa* are presented in Fig. 1.

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

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

| Nutrient    | Leaves     | Seeds      | Calyces    | Ref          |
|-------------|------------|------------|------------|--------------|
| Protein     | 3.3 g/100 g| 27.78 g    | 1.9 g/100 g| Taken from:  |
| Fat         | 0.3 g/100 g| 21.85 g    | 0.1 g/100 g| Naturlan3,11,27,28 |
| Carbohydrate| 9.2 g/100 g| 21.25 g    | 12.3 g/100 g|              |
| Ascorbic Acid| 54 mg/100 g| -          | -          |              |
| Ascorbic Acid| 4135 µg/100 g| -          | 300 µg/100 g|              |
| β-carotene  | 1000 g     |            |            |              |
| Vitamin C   | 2.3 g      | 9          | 17         |              |
| Calcium     | 240 g      | 350        | 150        |              |
4. Sour tea in traditional medicine

Sour tea has been found to have biochemical effects on reproductive hormones such as testosterone, luteinizing hormone, and prolactin. Improved postprandial vascular function and CVD risk reduction and modified postprandial flow-mediated dilatation (FMD) of the brachial artery were demonstrated after consumption of *Hibiscus sabdariffa* calyces (HSC). 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. It has been estimated that approximately 29.5 million people will be diagnosed with cancer by the year 2040. Although the underlying mechanisms remain unclear, HS is a candidate for chemotherapeutic applications due to its phytochemicals, and it is known as an effective anticancer agent. Compounds like protocatechuic acid and delphinidin-3-sambubioside need an appropriate clinical trial to identify its chemotherapeutic potential and synergistic activity with chemotherapeutic drugs. Inhibition of the B16-F1 cell migration and suppressed HUVECs tube formation were reported as an anticancer aspect of sour tea. 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*. 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.
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.\textsuperscript{38} \textit{H. sabdariffa} L. leaf extract (HLE) acts as an apoptosis inducer in LNCaP cells, and showed interesting perspectives for human prostate cancer treatment strategies.\textsuperscript{39} Protocatechuic acid (PCA) is one of the most important phenolic compounds isolated from HS dried flowers and has antitumor and antioxidant properties.\textsuperscript{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.\textsuperscript{41,42} Polyphenol extracts from HS reduced nephropathy in experimental type 1 diabetes by increasing catalase and glutathione activity and decreasing lipid peroxidation.\textsuperscript{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.\textsuperscript{44} In general, sour tea 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.
Table 2. HS plant 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 extracts | Nephropathy      | Human  | Increased catalase glutathione activity and reduced lipid peroxidation        | 43  |
| Ethyl acetate | 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

5. Hibiscus sabdariffa pharmacokinetic

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. 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. 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.\textsuperscript{48} Several studies have indicated that HS extracts can reduce the levels of TG, Tc, LDLc, and LDLc/HDLc in humans and animal models.\textsuperscript{49} The aqueous extract of HS lowered Tc better than simvastatin and improved antihyperlipidemic activity when co-administered at low doses in an animal model.\textsuperscript{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.\textsuperscript{51} An innovative study showed that co-administration of \textit{Z. officinale} or \textit{H. sabdariffa} with amlodipine increased its pharmacodynamic response.\textsuperscript{52} An original study revealed that the herb-drug interaction between \textit{Z. officinale}-losartan and \textit{H. sabdariffa}-losartan could occur in rats.\textsuperscript{53} In general, the simultaneous use of herbal and synthetic medicines can have either positive or toxic effects (Fig. 3).

The interactions between some antihypertensive medicines and herbal teas are summarized in Table 3.

\textbf{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 Tc better than simvastatin and improved antihyperlipidemic activity                             | 50   |
| Hydrochlorothiazide | Animal | —                                                                                                      | 51   |
| Amlodipine | Human    | Co-administration of \textit{Z. officinale} or \textit{H. sabdariffa} with amlodipine increased its pharmacodynamic response | 52   |
| Losartan   | Rat       | Clinical trial required for further results                                                             | 53   |
The table 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.

6. 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.

Table 4. Antihypertensive drugs and their side effects

| Group               | Drugs                                      | Side effects                                                | Ref |
|---------------------|--------------------------------------------|-------------------------------------------------------------|-----|
| **Diuretics**       | Chlorthalidone, Chlorothiazide             | Increase blood sugar levels; decrease body supply of potassium |     |
|                     | Hydrochlorothiazide, Indapamide, Metolazone|                                                              |     |
| **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 | 54-56 |
| **Alpha-blockers**  | Doxazosin mesylate, Prazosin hydrochloride, Terazosin hydrochloride | Tachycardia, dizziness |     |

(ACE): Angiotensin converting enzyme, (ARBs): Angiotensin II receptor blockers
As shown in Table 4, a variety of drug groups are used for the treatment of HBP. 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.

### 7. 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. 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. 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. Increased flow-mediated dilation (FMD) after consumption of *Camellia sinensis* was investigated. *Coriandrum sativum* is one of

| Central agonists | Alpha methyl dopa, 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 |
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 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.

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

| Plants                | Model     | Mechanism of action                                                                 | Ref  |
|-----------------------|-----------|-------------------------------------------------------------------------------------|------|
| Garlic                | 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 miltiorrhiza** | 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 |

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 sour tea as an herbal remedy for high blood pressure, as discussed below.

**8. Sour tea 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. Leonard T. Skeggs, Jr. discovered this enzyme in 1956. This enzyme converts the hormone angiotensin I to the active vasoconstrictor (angiotensin II). Ultimately, ACE raises blood pressure by constricting vessels. ACE inhibitors are widely used as pharmaceutical drugs in cardiovascular diseases. 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.\textsuperscript{71} Daily consumption of sour tea can effectively treat high blood pressure in stage one hypertension along with dietary and lifestyle modifications.\textsuperscript{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.\textsuperscript{74} Improving a patient’s lipid profile is the main therapeutic effect of sour tea. The anthocyanins in sour tea inhibit low-density lipoprotein oxidation and consequently reduce the atherosclerotic process.\textsuperscript{75} Moreover, \textit{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.\textsuperscript{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.\textsuperscript{76} It has also been exhibited that HS can decrease the systolic and diastolic blood pressure (BP).\textsuperscript{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.\textsuperscript{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.\textsuperscript{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\textsuperscript{2+})-influx into vascular smooth muscle.\textsuperscript{80} Another research showed that continuous consumption of HS calyx extract improved myocardial capillarization in spontaneously hypertensive rats.\textsuperscript{81} In an innovative study, the effects of 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.\textsuperscript{82} The flower of HS presented a beneficial effect in controlling preclinical hypertension through the modulation of some molecular networks.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 \textit{C. Micranthum}, used as brews or tablets, were as effective as the standard treatment, captopril, in controlling hypertension over a 6-month follow-up.\textsuperscript{86} Several studies on the antihypertensive properties of sour tea are summarized in Table 6.

\textbf{Table 6.} Sour tea for hypertension and the relative mechanisms of action

| Used type           | Model   | Mechanisms and potential of actions                                                                 | Ref |
|---------------------|---------|-------------------------------------------------------------------------------------------------------|-----|
| Sour tea            | Human   | -                                                                                                     | 72  |
| \textit{Hibiscus Sabdariffa} Tea | Human   | Effective component in cardiovascular health management and leads to lower blood pressure                | 74  |
| Sour tea            | Human   | Inhibits adipogenesis by regulating adipogenic signaling pathways, modulates gene expression of certain microRNAs, decreases LDL oxidation, and transcription factors | 75  |
| HS extract          | Human   | Inhibits ACE activity                                                                                   | 71  |
Notes of Section 8 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 sour tea 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. Some relevant, critical mechanisms are presented in Fig. 4, adapted from reference 87.

As is illustrated in Fig. 4, sour tea carried out different pathways in lowering blood pressure. 88,89

9. 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 *Hibiscus sabdariffa* 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.

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**Disclosure of conflict of interest**

Authors declare no conflict of interest.

**Authors’ contributions:**

Raha kamyab: Conception or design of the work, Mohammadali Torbati & Morteza Ghojazadeh: the acquisition, analysis, Hossein Namdar & Seyyed Mohammad Bagher Fazljou: interpretation of data for the work, Mostafa Araj-Khodaei: drafting the work or revising it critically for important intellectual content.
References:

1. Naseri M, Ardakani MRS. The school of traditional iranian medicine: The definition, origin and advantages. J Int Soc History Islamic Med 2004;3:17-21.
2. Souri E, Farsam H, Hasani M, Azimi Kheirabadi Z. Evaluation of antioxidant activity of 25 plant seeds used in iranian folk medicine. Journal of Medicinal Plants 2003;4(8):27-34. doi: 10.1001.1.2717204.2003.2.8.3.0
3. Riaz G, Chopra R. A review on phytochemistry and therapeutic uses of hibiscus sabdariffa l. Biomedicine & Pharmacotherapy 2018;102:575-86. doi:10.1016/j.biopharma.2018.03.023
4. Da-Costa-Rocha I, Bonnlaender B, Sievers H, Pischel I, Heinrich M. Hibiscus sabdariffa l.—a phytochemical and pharmacological review. Food chemistry 2014;165:424-43. doi:10.1016/j.fooodchem.2014.05.002
5. Kamyab R, Namdar H, Torbati M, Ghojazadeh M, Araj-Khodaei M, Fazljou SMB. Medicinal plants in the treatment of hypertension: A review. Adv Pharm Bull. doi: 10.34172/apb.2021.090
6. Tahir HE, Xiaobo Z, Jiyong S, Mariod AA, Wiliam T. Rapid determination of antioxidant compounds and antioxidant activity of sudanese karkade (hibiscus sabdariffa l.) using near infrared spectroscopy. Food Analytical Methods 2016;9(5):1228-36. DOI 10.1007/s12161-015-0299-z
7. Carvajal-Zarrabal O, Barradas-Dermitz DM, Orta-Flores Z, Hayward-Jones PM, Nolasco-Hipólito C, Aguilar-Uscanga MG, et al. Hibiscus sabdariffa l., roselle calyx, from ethnobotany to pharmacology. Journal of experimental pharmacology 2012;4:25. doi: 10.2147/JEP.S27974
8. Carvajal-Zarrabal O, Hayward-Jones P, Orta-Flores Z, Nolasco-Hipólito C, Barradas-Dermitz D, Aguilar-Uscanga M, et al. Effect of hibiscus sabdariffa l. Dried calyx ethanol extract on fat absorption-excretion, and body weight implication in rats. Journal of Biomedicine and Biotechnology 2009;2009. doi:10.1155/2009/394592
9. Dini C, Zaro MJ, Viña SZ. Bioactivity and functionality of anthocyanins: A review. Current Bioactive Compounds 2019;15(5):507-23. doi:10.2174/1573407214666180821115312
10. Izquierdo-Vega JA, Arteaga-Badillo DA, Sánchez-Gutiérrez M, Morales-González JA, Vargas-Mendoza N, Gómez-Aldapa CA, et al. Organic acids from roselle (hibiscus sabdariffa l.)—a brief review of its pharmacological effects. Biomedicines 2020;8(5):100. doi:10.3390/biomedicines8050100
11. Singh P, Khan M, Hailemariam H. Nutritional and health importance of hibiscus sabdariffa: A review and indication for research needs. J Nutr Health Food Eng 2017;6(5):00212.
12. Pérez-Torres I, Ruiz-Ramírez A, Baños G, El-Hafidi M. Hibiscus sabdariffa linnaeus (malvaceae), curcumin and resveratrol as alternative medicinal agents against metabolic syndrome. Cardiovascular & Hematological Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Cardiovascular & Hematological Agents) 2013;11(1):25-37.
13. AL SNAFI AE. Pharmacological and therapeutic importance of a review. International Journal of Pharmaceutical Research 2018;10(3).
14. Wahabi H, Alansary L, Al-Sabban A, Glasiuio P. The effectiveness of hibiscus sabdariffa in the treatment of hypertension: A systematic review. Phytomedicine 2010;17(2):83-6. doi:10.1016/j.phymed.2009.09.002
15. Showande JS, Igbinoba SI, Kajula M, Hokkanen J, Tolonen A, Adegbolagun OM, et al. In vitro modulation of cytochrome p450 isozymes and pharmacokinetics of caffeine by extracts of hibiscus sabdariffa linn calyx. Journal of basic and clinical physiology and pharmacology 2019;30(3). doi:10.1515/jbcpp-2018-0206
16. Jung E, Kim Y, Joo N. Physicochemical properties and antimicrobial activity of roselle (hibiscus sabdariffa l.). Journal of the Science of Food and Agriculture 2013;93(15):3769-76. doi:10.1002/jsfa.6256
17. Ahmed WKA, Hudson JB. The fatty acid composition of hibiscus sabdariffa seed oil. *Journal of the Science of Food and Agriculture* 1982;33(12):1305-9.

18. Fasoyiro S, Babalola S, Owosibo T. Chemical composition and sensory quality of fruit-flavoured roselle (hibiscus sabdariffa) drinks. *World Journal of Agricultural Sciences* 2005;1(2):161-4.

19. Hopkins AL, Lamm MG, Funk JL, Ritenbaugh C. Hibiscus sabdariffa l. In the treatment of hypertension and hyperlipidemia: A comprehensive review of animal and human studies. *Fitoterapia* 2013;85:84-94. doi:10.1016/j.fitote.2013.01.003

20. Mahadevan N, Kamboj P. Hibiscus sabdariffa linn.—an overview. 2009.

21. Ali BH, Wabel NA, Blunden G. Phytochemical, pharmacological and toxicological aspects of hibiscus sabdariffa l.: A review. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives* 2005;19(5):369-75. doi:10.1002/ptr.1628

22. Gruenwald J, Brendler T, Jaenicke C. *Pdr for herbal medicines*: Thomson, Reuters; 2007. doi:10.1002/elps.200700819

23. Segura-Carretero A, Puertas-Mejía MA, Cortacero-Ramírez S, Beltrán R, Alonso-Villaverde C, Joven J, et al. Selective extraction, separation, and identification of anthocyanins from hibiscus sabdariffa l. Using solid phase extraction-capillary electrophoresis-mass spectrometry (time-of-flight/ion trap). *Electrophoresis* 2008;29(13):2852-61. doi:10.1002/elps.200700819

24. Serban C, Sahebkar A, Ursoniu S, Andrica F, Banach M. Effect of sour tea (hibiscus sabdariffa l.) on arterial hypertension: A systematic review and meta-analysis of randomized controlled trials. *Journal of hypertension* 2015;33(6):1119-27. doi:10.1097/HJH.0000000000000585

25. Herrera-Arellano A, Miranda-Sánchez J, Ávila-Castro P, Herrera-Álvarez S, Jiménez-Ferrer JE, Zamilpa A, et al. Clinical effects produced by a standardized herbal medicinal product of hibiscus sabdariffa on patients with hypertension. A randomized, double-blind, lisinopril-controlled clinical trial. *Planta medica* 2007;73(01):6-12. DOI: 10.1055/s-2006-957065

26. Herrera-Arellano A, Flores-Romero S, Chavez-Soto M, Tortoriello J. Effectiveness and tolerability of a standardized extract from hibiscus sabdariffa in patients with mild to moderate hypertension: A controlled and randomized clinical trial. *Phytomedicine* 2004;11(5):375-82. doi:10.1016/j.phymed.2004.04.001

27. Salem MA, Zayed A, Beshay ME, Mesih MMA, Khayal RFB, George FA, et al. Hibiscus sabdariffa l.: Phytoconstituents, nutritive, and pharmacological applications. *Advances in Traditional Medicine* 2021;1-11. doi:10.1007/s13596-020-00542-7

28. Ismail A, Ikram EH, Nazri HSM. Roselle (hibiscus sabdariffa l.) seeds nutritional composition protein quality and health benefits. *Food* 2008;2(1):1-16.

29. Nwabufo CK, Olusanya O. Biochemical effect of hibiscus sabdariffa calyx extracts on the reproductive hormones of male wistar rat. *Advances in Applied Science Research* 2017;8(2):38-41.

30. Ali BH, Al-Lawati I, Beegam S, Ziada A, Al Salam S, Nemmar A, et al. Effect of hibiscus sabdariffa and its anthocyanins on some reproductive aspects in rats. *Nat Prod Commun* 2012;7(1):41-4. doi:10.1177/1934578X1200700115

31. Abubakar SM, Ukeyima MT, Spencer JP, Lovegrove JA. Acute effects of hibiscus sabdariffa calyces on postprandial blood pressure, vascular function, blood lipids, biomarkers of insulin resistance and inflammation in humans. *Nutrients* 2019;11(2):341. doi:10.3390/nu11020341

32. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians* 2021;71(3):209-49. doi:10.3322/caac.21660

33. Ferlary J, Colombet M, Soerjomataram I, Mathers C, Parkin D, Piñeros M, et al. Estimating the global cancer incidence and mortality in 2018: Globocan sources and methods. *International journal of cancer* 2019;144(8):1941-53. doi:10.1002/ijc.31937
34. Laskar YB, Mazumder PB. Insight into the molecular evidence supporting the remarkable chemotherapeutic potential of hibiscus sabdariffa l. *Biomedicine & Pharmacotherapy* 2020;127:110153. doi:10.1016/j.biopharma.2020.110153

35. Su C-C, Wang C-J, Huang K-H, Lee Y-J, Chan W-M, Chang Y-C. Anthocyanins from hibiscus sabdariffa calyx attenuate in vitro and in vivo melanoma cancer metastasis. *Journal of Functional Foods* 2018;48:614-31. doi: https://doi.org/10.1016/j.jff.2018.07.032

36. Lim H-W, Seo K, Chon J, Song K-Y, editors. Antimicrobial activity of hibiscus sabdariffa l. (roselle) powder against food-borne pathogens present in dairy products: Preliminary study. 2020. doi:10.22424/jdsb.2020.38.1.37

37. Joshua M, Okere C, O'Donnell Sylvester MY, Precious O, Dluya T, Um J-Y, et al. Disruption of angiogenesis by anthocyanin-rich extracts of hibiscus sabdariffa. *International journal of scientific and engineering research* 2017;8(2):299. doi: 10.14299/ijser.2017.02.009

38. Lin H-H, Huang H-P, Huang C-C, Chen J-H, Wang C-J. Hibiscus polyphenol-rich extract induces apoptosis in human gastric carcinoma cells via p53 phosphorylation and p38 mapk/fasl cascade pathway. *Molecular Carcinogenesis* 2005;43(2):86-99. doi: https://doi.org/10.1002/mc.20103

39. Lin H-H, Chan K-C, Sheu J-Y, Hsuan S-W, Wang C-J, Chen J-H. Hibiscus sabdariffa leaf induces apoptosis of human prostate cancer cells in vitro and in vivo. *Food Chemistry* 2012;132(2):880-91. doi: https://doi.org/10.1016/j.foodchem.2011.11.057

40. Tseng T-H, Kao T-W, Chu C-Y, Chou F-P, Lin W-L, Wang C-J. Induction of apoptosis by hibiscus protocatechuic acid in human leukemia cells via reduction of retinoblastoma (rb) phosphorylation and bcl-2 expression. *Biochemical Pharmacology* 2000;60(3):307-15. doi: https://doi.org/10.1016/S0006-2952(00)00322-1

41. Effects of sour tea (hibiscus sabdariffa) on lipid profile and lipoproteins in patients with type ii diabetes. *The Journal of Alternative and Complementary Medicine* 2009;15(8):899-903. doi: 10.1089/acm.2008.0540

42. Mozaffari-Khosravi H, Jalali-Khanabadi B, Afkhami-Ardekani M, Fatehi F, Noori-Shadkam M. The effects of sour tea (hibiscus sabdariffa) on hypertension in patients with type ii diabetes. *Journal of human hypertension* 2009;23(1):48-54.

43. Lee W-C, Wang C-J, Chen Y-H, Hsu J-D, Cheng S-Y, Chen H-C, et al. Polyphenol extracts from hibiscus sabdariffa linnaeus attenuate nephropathy in experimental type 1 diabetes. *Journal of Agricultural and Food Chemistry* 2009;57(6):2206-10. doi: 10.1021/jf802993s

44. Seung TW, Park SK, Kang JY, Kim JM, Park SH, Kwon BS, et al. Ethyl acetate fraction from hibiscus sabdariffa l. Attenuates diabetes-associated cognitive impairment in mice. *Food Research International* 2018;105:589-98. doi: https://doi.org/10.1016/j.foodres.2017.11.063

45. Ali BH, Al-Lawati I, Beegam S, Zida A, salam SA, Nemmar A, et al. Effect of hibiscus sabdariffa and its anthocyanins on some reproductive aspects in rats. *Natural product communications* 2012;7(1):1934578X1200700115. doi:10.1177/1934578X1200700115

46. Showande SJ, Udoh-Kalu CC, Fakeye TOJWAloP. Pattern of use of water beverage of hibiscus sabdariffa linn in a university community in southwest nigeria. 2017;28(2):102.

47. Paramita S, Isnuwardana RC, Puri P, Jayastri PJJSdK. Pola penggunaan obat bahan alam sebagai terapi komplementer pada pasien hipertensi di puskesmas. 2017;1(7):367-76. doi:10.25026/jsk.v1i7.56

48. Nurfaradilla SA, Saputri FC, Harahap Y. Pharmacokinetic herb-drug interaction between <i>hibiscus sabdariffa</i> calyces aqueous extract and captopril in rats. *Evidence-Based Complementary and Alternative Medicine* 2020;2020:5013898. doi: 10.1155/2020/5013898

49. Lin T-L, Lin H-H, Chen C-C, Lin M-C, Chou M-C, Wang C-JJNr. Hibiscus sabdariffa extract reduces serum cholesterol in men and women. 2007;27(3):140-5. doi:10.1016/j.nutres.2007.01.007
50. Showande SJ, Adegbolagun OM, Igbinoba SI, Fakeye TO. In vivo pharmacodynamic and pharmacokinetic interactions of hibiscus sabdariffa calyces extracts with simvastatin. *Journal of clinical pharmacy and therapeutics* 2017;42(6):695-703. doi: 10.1111/jcpt.12629

51. Ndu OO, Nworu CS, Ehiemere CO, Ndukwu NC, Ochiogu IS. Herb–drug interaction between the extract of hibiscus sabdariffa and hydrochlorothiazide in experimental animals. 2011;14(6):640-4. doi:10.1089/jmf.2010.0117

52. Alam MA, Bin Jardan YA, Alzenaidy B, Raish M, Al-Mohizea AM, Ahad A, et al. Effect of hibiscus sabdariffa and zingiber officinale on pharmacokinetics and pharmacodynamics of amlodipine. *Journal of Pharmacy and Pharmacology* 2021;73(9):1151-60. doi: 10.1093/jpp/rgaa062

53. Ahad A, Raish M, Bin Jardan YA, Alam MA, Al-Mohizea AM, Al-Jenoobi FI. Effect of hibiscus sabdariffa and zingiber officinale on the antihypertensive activity and pharmacokinetic of losartan in hypertensive rats. 2020;50(7):847-57. doi:10.1080/00498254.2020.1729446

54. Laurent S. Antihypertensive drugs. *Pharmacological research* 2017;124:116-25. doi:10.1016/j.phrs.2017.07.026

55. Diaconu CC, Dediu GN, Iancu MA. Drug-induced arterial hypertension– a frequently ignored cause of secondary hypertension: A review. *Acta cardiologica* 2018;73(6):511-7. doi:10.1080/00015385.2017.1421445

56. Cernes R, Zimlichman R. Role of paced breathing for treatment of hypertension. *Current hypertension reports* 2017;19(6):45. DOI:10.1007/s11906-017-0742-1

57. Talha J, Priyanka M, Akanksha A. Hypertension and herbal plants. *Int Res J Pharm* 2011;2(8):26-30.

58. Hodgson JM, Puddey IB, Burke V, Watts GF, Beilin LJ. Regular ingestion of black tea improves brachial artery vasodilator function. *Clinical science* 2002;102(2):195-201. doi:10.1042/cs1020195

59. Qidwai W, Ashfaq T. Role of garlic usage in cardiovascular disease prevention: An evidence-based approach. *Evidence-Based Complementary and Alternative Medicine* 2013;2013. doi:10.1155/2013/125649

60. Ho CS, Wong YH, Chiu KW. The hypotensive action of desmodium styracifolium and clematis chinensis. *Am J Chin Med* 1989;17(3-4):189-202. doi: 10.1142/s0192415x89000280

61. Navarro E, Alonso J, Rodriguez R, Trujillo J, Boada J. Diuretic action of an aqueous extract of lepidium latifolium l. *Journal of ethnopharmacology* 1994;41(1-2):65-9. doi:10.1016/0378-8741(94)90059-0

62. Tenorio F, Del Valle L, González A, Pastelín G. Vasodilator activity of the aqueous extract of viscum album. *Fitoterapia* 2005;76(2):204-9. doi:10.1016/j.fitote.2004.12.013

63. Hall JE. Historical perspective of the renin-angiotensin system. *Molecular biotechnology* 2003;24(1):27-39.
69. Kanakamedala K. Role of angiotensin converting enzymes ace and ace 2 in diabetes induced cardiovascular dysfunction. 2007.
70. Giani JF, Veiras LC, Shen JZ, Bernstein EA, Cao D, Okwan-Duodu D, et al. Novel roles of the renal angiotensin-converting enzyme. Molecular and Cellular Endocrinology 2021;111257. doi:10.1016/j.mce.2021.111257
71. Ojeda D, Jiménez-Ferrer E, Zamplpa A, Herrera-Arellano A, Tortoriello J, Alvarez L. Inhibition of angiotensin convertin enzyme (ace) activity by the anthocyanins delphinidin-and cyanidin-3-o-sambubiosides from hibiscus sabdariffa. Journal of ethnopharmacology 2010;127(1):7-10. doi:10.1016/j.jep.2009.09.059
72. Jalalyazdi M, Ramezani J, Izadi-Moud A, Madani-Sani F, Shahlaei S, Ghiasi SS. Effect of hibiscus sabdariffa on blood pressure in patients with stage 1 hypertension. J Adv Pharm Technol Res 2019;10(3):107-11. doi: 10.4103/japtr.JAPTR_402_18 doi: 10.4103
73. McKay DL, Chen CO, Saltzman E, Blumberg JB. Hibiscus sabdariffa l. Tea (tisane) lowers blood pressure in prehypertensive and mildly hypertensive adults. The Journal of nutrition 2010;140(2):298-303. doi:10.3945/jn.109.115097
74. Obu RN. Observational study of hibiscus sabdariffa tea on blood pressure: The case of nyarkotey tea made with concentrated energized hibiscus sabdariffa. DOI: 10.36349/easjpp.2020.v02i04.05
75. Guardiola S, Mach N. Therapeutic potential of hibiscus sabdariffa: A review of the scientific evidence. Endocrinología y Nutrición (English Edition) 2014;61(5):274-95. doi:10.1016/j.endoen.2014.04.003
76. Alarcon-Alonso J, Zamplpa A, Aguilar FA, Herrera-Ruiz M, Tortoriello J, Jimenez-Ferrer E. Pharmacological characterization of the diuretic effect of hibiscus sabdariffa linn (malvaceae) extract. Journal of Ethnopharmacology 2012;139(3):751-6. doi:10.1016/j.jep.2011.12.005
77. Herrera-Arellano A, Flores-Romero S, Chávez-Soto MA, Tortoriello J. Effectiveness and tolerability of a standardized extract from hibiscus sabdariffa in patients with mild to moderate hypertension: A controlled and randomized clinical trial. Phytomedicine 2004;11(5):375-82. doi:https://doi.org/10.1016/j.phymed.2004.04.001
78. Al-Anbaki M, Nogueira RC, Cavin A-L, Al-Hadid M, Al-Ajouni I, Shuhaiber L, et al. Treating uncontrolled hypertension with hibiscus sabdariffa when standard treatment is insufficient: Pilot intervention. The Journal of Alternative and Complementary Medicine 2019;25(12):1200-5. doi:10.1089/acm.2019.0220
79. Odigie I, Ettarh R, Adigun S. Chronic administration of aqueous extract of hibiscus sabdariffa attenuates hypertension and reverses cardiac hypertrophy in 2k-1c hypertensive rats. Experimental Biology and Medicine 2012;237(5):563-9. doi:10.1258/ebm.2012.011357
80. Ajay M, Chai H, Mustafa A, Gilani AH, Mustafa MR. Mechanisms of the anti-hypertensive effect of hibiscus sabdariffa I. Calyces. Journal of ethnopharmacology 2007;109(3):388-93. doi:10.1016/j.jep.2006.08.005
81. Inuwa I, Ali BH, Al-Lawati I, Beegam S, Ziada A, Blunden G. Long-term ingestion of hibiscus sabdariffa calyx extract enhances myocardial capillarization in the spontaneously hypertensive rat. Experimental Biology and Medicine 2012;237(5):563-9. doi:10.1258/ebm.2012.011357
82. Nurfaradilla SA, Saputri FC, Harahap Y. Effects of hibiscus sabdariffa calyces aqueous extract on the antihypertensive potency of captopril in the two-kidney-one-clip rat hypertension model. Evidence-Based Complementary and Alternative Medicine 2019;2019. doi:10.1155/2019/9694212
83. Micucci M, Angeletti A, Cont M, Corazza I, Aldini R, Donadio E, et al. Hibiscus sabdariffa I. Flowers and olea europaea I. Leaves extract-based formulation for hypertension care: In vitro efficacy and toxicological profile. Journal of medicinal food 2016;19(5):504-12. doi:10.1089/jmf.2015.0072
84. Mojiminiyi F, Dikko M, Muhammad B, Ojobor P, Ajagbonna O, Okolo R, et al. Antihypertensive effect of an aqueous extract of the calyx of hibiscus sabdariffa. Fitoterapia 2007;78(4):292-7. doi:10.1016/j.fitote.2007.02.011
85. Nwachukwu D, Aneke E, Obika L, Nwachukwu N. Investigation of antihypertensive effectiveness and tolerability of hibiscus sabdariffa in mild to moderate hypertensive subjects in enugu, south-east, nigeria. *American Journal of Phytomedicine and Clinical Therapeutics* 2015;19(2):148-52.

86. Bourqui A, Niang EAB, Graz B, Diop EA, Dahaba M, Thiaw I, et al. Hypertension treatment with combretum micranthum or hibiscus sabdariffa, as decoction or tablet: A randomized clinical trial. *Journal of Human Hypertension* 2021;35(9):800-8. doi: 10.1038/s41371-020-00415-1

87. Al Disi SS, Anwar MA, Eid AH. Anti-hypertensive herbs and their mechanisms of action: Part i. *Frontiers in Pharmacology* 2016;6(323). doi: 10.3389/fphar.2015.00323

88. Aritonang TR, Siantar RL, Simanjuntak FM. The effectiveness of steeping rosella (hibiscus sabdariffa) against hypertension in the elderly. *International Journal of Science and Society* 2021;3(1):412-9. doi:10.200609/ijsoc.v3i1.308

89. Al-Anbaki M, Cavin A-L, Nogueira RC, Taslimi J, Ali H, Najem M, et al. Hibiscus sabdariffa, a treatment for uncontrolled hypertension. Pilot comparative intervention. *Plants* 2021;10(5):1018. doi:10.3390/plants10051018
Fig. 1. *Hibiscus sabdariffa* properties

**Pharmacological properties**

- Cytotoxic effect
- Anthelmintic effect
- Antibacterial effect
- Antiulcer effect
- Antidiabetic effect
- Hypolipidemic effect
- Immunological effect

**Composition**

- oxalates
- Proteins
- crude fibre
- lipids
- crude protein
- carbohydrate
- phytic acid
- tannins

**Names**

- *Hibiscus sabdariffa*
- Roselle
- Ambary
- Mesta
- patsan
- Pitwa
- Ambari
- Dekkanhanf
- Gambohanf

**Parts**

- Stalks
- Leaves
- Flowers and Pollination
- Fruit and Seed
- Roots
Fig. 2. The main therapeutic mechanisms of sour tea
Fig. 3. Positive or toxic effects because of simultaneous use of herbal and synthetic medicines
Fig. 4. A schematic diagram representative the favorable effects of plantsherbs on the molecular pathogenesis of hypertension