RESERCH PAPER

Hibiscus sabdariffa (Roselle/Karkade) as a Complementary Antihypertensive Agent: A Narrative Review of Pharmacological Mechanisms, Clinical Evidence, and Public Health Implications for Saudi Arabia

Running title: *Hibiscus sabdariffa and Hypertension in Saudi Arabia*

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Received: 30th May, 2026; **Revised:** 12th June, 2026; **Accepted:** 22nd June, 2026; **Available Online:** 6th July, 2026

ABSTRACT

Background: Hypertension is a major public health burden in Saudi Arabia. Estimates vary by measurement method, age denominator, and survey year: self-reported physician-diagnosed prevalence in adults aged ≥15 years was 9.2% in the 2017 General Authority for Statistics Household Health Survey, whereas measured blood pressure data from the 2019 Kingdom of Saudi Arabia World Health Survey yielded a crude prevalence of 12.7% among adults aged ≥18 years, rising to approximately 22% on age-standardisation. Awareness, treatment, and blood pressure control rates remain suboptimal. *Hibiscus sabdariffa* L. (Hs), known locally as *karkade*, is herbal beverage plant of the Malvaceae family with a longstanding history of traditional use for blood pressure management across the wider Arab region.

Objective: To synthesise the current evidence on the pharmacological mechanisms, clinical efficacy, safety profile, and drug-interaction potential of *Hibiscus sabdariffa* in hypertension management, and to outline a research agenda relevant to the Saudi Arabian context.

Methods: Peer-reviewed literature was identified through PubMed, Scopus, Web of Science, and the Cochrane Database of Systematic Reviews. Priority was given to randomised controlled trials (RCTs), systematic reviews, meta-analyses, and mechanistic studies published between 2004 and 2026. No formal PRISMA screening, duplicate review, or risk-of-bias appraisal was performed; the review is therefore a structured narrative synthesis rather than a systematic review.

Results: Several complementary pharmacological pathways may contribute to Hs antihypertensive activity, including angiotensin-converting enzyme (ACE) inhibition, nitric oxide-mediated vasodilation, calcium channel modulation, diuretic effects, antioxidant activity, and lipid metabolism regulation. Evidence from RCTs and meta-analyses suggests that Hs may reduce systolic and diastolic blood pressure, although estimates vary substantially across preparations, doses, populations, and study designs. The magnitude of pooled reduction reported in recent meta-analyses (systolic blood pressure approximately −6 to −8 mmHg versus placebo) overlaps with the size effect seen with some low-dose antihypertensive interventions, but direct therapeutic equivalence has not been established and an earlier Cochrane review reached more cautious conclusions. The safety profile is generally favourable in short- to medium-term studies, although long-term safety and human pharmacokinetic interaction data remain insufficient.

Conclusion: *Hibiscus sabdariffa* may serve as a culturally familiar adjunct to lifestyle modification in hypertension, but it is not a substitute for guideline-directed pharmacotherapy. Evaluation within structured lifestyle-modification programmes is justified, particularly through locally conducted Saudi clinical trials.

Keywords: *Hibiscus sabdariffa*; karkade; roselle; hypertension; blood pressure; antihypertensive; Saudi Arabia; anthocyanins; complementary medicine

How to cite this article: Mahzari A, Alzahrani W, Alghamdi J, alqarni L, Alghamdi R, Alzhrani J, Almalki SSR. Hibiscus sabdariffa (Roselle/Karkade) as a Complementary Antihypertensive Agent: A Narrative Review of Pharmacological Mechanisms, Clinical Evidence, and Public Health Implications for Saudi Arabia. Int J Drug Deliv Technol. 2026;16(67s):231-240. DOI: 10.25258/ijddt.16.67s.24

1. Introduction

Hypertension is one of the most prevalent and burdensome non-communicable diseases worldwide. The global number of adults living with hypertension rose from approximately 594 million in 1975 to over 1.13 billion by 2015, with projections exceeding 1.5 billion by 2025, predominantly driven by growth in low- and middle-income countries [1,2]. Elevated blood pressure is estimated to account for approximately 13.5% of global all-cause mortality [3] and is the single most important modifiable risk factor for cardiovascular disease, stroke, heart failure, and chronic kidney disease [4].

Saudi Arabia shares this burden. National estimates differ by age denominator, survey methodology, and reporting year; these are reconciled in Section 3. Awareness, treatment, and control rates remain well below recommended targets, highlighting a substantial detection and management gap [5,6]. The cornerstone of hypertension management remains pharmacotherapy, including renin-angiotensin-aldosterone system (RAAS) inhibitors, calcium channel blockers, and diuretics. These medications are associated with adverse effects, long-term adherence challenges, and cost burdens in some settings [7]. Against this background, interest in evidence-based complementary and integrative approaches has grown, both globally and within Middle Eastern populations where herbal medicine use is culturally familiar [8].

Hibiscus sabdariffa L. (family Malvaceae), known in the Arab region as *karkade* and in English as roselle or sour tea, is a herbal plant whose dark-red calyces are consumed as a hot or cold beverage across the Middle East, North Africa, West Africa, and Latin America. Its antihypertensive properties have been studied in formal clinical trials since the early 2000s [9,10]. Several systematic reviews and meta-analyses have examined the blood pressure-lowering effects of Hs; however, this evidence has not been synthesised specifically within the Saudi Arabian public health context, where cultural familiarity with *karkade* in the wider Arab region creates a plausibly favourable environment for evaluation. Saudi-specific consumption data are scarce; this review therefore frames cultural familiarity at the regional rather than national level.

This narrative review aims to: (1) summarise the proposed pharmacological mechanisms through which *Hibiscus sabdariffa* may exert antihypertensive effects; (2) appraise the clinical trial evidence for blood pressure reduction, including the Cochrane review; (3) assess the safety profile, adverse events, and drug interactions, distinguishing human, animal, and theoretical evidence; (4) outline sex-related differential responses as a hypothesis-generating topic; and (5) propose a research agenda relevant to the Saudi Arabian context.

2. Methods

This review was conducted as a structured narrative synthesis following established principles for narrative reviews in biomedical sciences [11]. A literature search was performed in PubMed/MEDLINE, Scopus, Web of Science Core Collection, and the Cochrane Database of Systematic Reviews up to April 2026. Search terms applied individually and in combination included: "*Hibiscus sabdariffa*", "roselle", "karkade", "sour tea", "hibiscus extract", "hypertension", "blood pressure", "antihypertensive", "randomised controlled trial", "meta-analysis", "systematic review", "anthocyanins", "ACE inhibition", "drug interaction", and "Saudi Arabia". No date restriction was imposed on mechanistic and ethnopharmacological studies; clinical evidence was limited to studies published between 2004 and 2026. Reference lists of retrieved systematic reviews were manually searched. Non-English articles were considered where English abstracts were available. Editorials, conference abstracts, and non-peer-reviewed sources were excluded.

This work is explicitly framed as a narrative review. It does not include formal PRISMA-guided screening, duplicate study selection, reproducible search strings with hit counts, or formal risk-of-bias appraisal. Pooled estimates reported in this review are reproduced from previously published meta-analyses rather than newly synthesised.

3. Epidemiology of hypertension in Saudi Arabia

Reported hypertension prevalence in Saudi Arabia varies markedly according to the survey year, age denominator, case definition, and measurement method, and these estimates should not be combined into a single range. Self-reported, physician-diagnosed prevalence from the 2017 General Authority for Statistics Household Health Survey was 9.2% among Saudi nationals aged ≥15 years, with women showing a higher age-adjusted prevalence (10.0%) than men (8.5%) [5]. In contrast, measured blood pressure data from the 2019 Kingdom of Saudi Arabia World Health Survey yielded a crude prevalence of 12.7% in adults aged ≥18 years, an age-

standardised prevalence of approximately 22% in adults aged 30–79 years, and rates exceeding 50% in those aged ≥80 years [6]. Recent regional cross-sectional studies conducted between 2024 and 2025 report figures ranging from 15.2% to 32.6% in selected urban or community samples [12,13]; these higher estimates likely reflect both genuine upward trends and differences in sampling frame, age structure, and measurement technique.

Regional variation across the Kingdom is pronounced, with reported prevalence between approximately 6% and 10% depending on region, likely reflecting differential urbanisation, healthcare access, and lifestyle patterns [5]. Established risk factors associated with hypertension in the Saudi population include obesity (prevalence ratio [PR] = 1.72), dyslipidaemia (PR = 1.57), diabetes (PR = 1.34), and chronic kidney disease (PR = 2.05) [6]. A modest but consistent female excess in age-adjusted prevalence has been attributed to hormonal changes, higher adiposity rates, and lower physical activity among Saudi women [5].

Critically, awareness of diagnosis (34.8%), treatment receipt (47.9%), and blood pressure control (37.0%) remain well below recommended targets [6]. These figures suggest that detection and sustained management, rather than drug availability alone, represent the primary barriers, supporting the relevance of accessible, culturally familiar, and affordable complementary interventions as potential adjuncts to standard care.

4. Botanical profile and traditional use of Hibiscus sabdariffa

Hibiscus sabdariffa L. is an annual or perennial herb belonging to the family Malvaceae, comprising over 300 species worldwide [14]. The plant is widely cultivated in tropical and subtropical regions including Sudan, Egypt, Nigeria, India, China, Malaysia, and Mexico, and is recognised as an important economic crop in several low- and middle-income nations due to its versatility as food, fibre, and medicine [14,15]. Botanical evidence suggests India and Africa as primary centres of domestication [15].

The use of *Hibiscus sabdariffa* is embedded in multiple traditional medicine systems. In Egypt and Sudan, infusions of the dried calyces, known locally as *karkade* or *karkadeh*, have been consumed for centuries to treat cardiac and nervous disorders, reduce body temperature, and promote diuresis [14]. In Iran, sour tea (*chai-e-torsh*) has been used as a traditional remedy for hypertension for generations [15,16]. In West Africa, leaves and calyces are incorporated into food and medicinal preparations for hypotensive, choleretic, and febrifugal purposes [14]. In Mexico and Central America, the aqueous preparation *agua de jamaica* is consumed for cardiovascular health [9]. *Karkade* is consumed across the wider Arab region, including Saudi Arabia, although robust nationally representative data on *karkade* consumption patterns or dose in Saudi adults are not available.

The antihypertensive activity of *Hibiscus sabdariffa* has been attributed to its polyphenolic content, particularly anthocyanins (delphinidin-3-sambubioside and cyanidin-3-sambubioside as the most abundant), along with flavonoids (quercetin, luteolin), organic acids (hibiscus acid, citric acid, malic acid), polysaccharides, and vitamin C [14,15,17]. The precise bioactive combination responsible for antihypertensive effects, and the relative contributions of individual compounds, remain active areas of investigation.

5. Pharmacological mechanisms of antihypertensive action

The antihypertensive activity of *Hibiscus sabdariffa* is multifactorial and proposed to involve six complementary pharmacological pathways. The first five (ACE inhibition, nitric oxide-mediated vasodilation, calcium channel modulation, diuretic effect, and antioxidant activity) act directly on blood pressure regulation and are depicted in Figure 1. The sixth (lipid metabolism regulation) provides indirect cardiovascular protection and is summarised in Table 1 but not illustrated in the schematic.

5.1. ACE inhibition

The renin-angiotensin-aldosterone system is a central regulator of blood pressure. Angiotensin-converting enzyme (ACE) catalyses the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor. Delphinidin-3-sambubioside and cyanidin-3-sambubioside, the dominant anthocyanins in *Hibiscus sabdariffa* calyces, have been shown to competitively inhibit ACE in a dose-dependent manner in vitro [17,18]. Hibiscus acid, a unique compound isolated from Hs calyces, has also been identified as an ACE inhibitor in in vitro and in silico studies [19]. Although mechanistically analogous to ACE inhibitor drugs, this evidence is predominantly preclinical.

5.2. Nitric oxide-mediated vasodilation

Hibiscus sabdariffa anthocyanins have been reported to stimulate nitric oxide (NO) release from vascular endothelium by upregulating endothelial nitric oxide synthase (eNOS) [17,20]. The resulting increase in NO bioavailability activates soluble guanylyl cyclase and the cGMP signalling cascade, inducing smooth muscle relaxation and vasodilation. This endothelium-dependent mechanism may reduce peripheral vascular resistance and is consistent with reported improvements in flow-mediated dilation in some clinical studies [20].

5.3. Calcium channel modulation

Polyphenolic extracts from *Hibiscus sabdariffa* suppress the influx of calcium ions (Ca^{2+}) through L-type voltage-gated calcium channels in vascular smooth muscle cells [16,18]. Reduced intracellular calcium availability dampens the trigger for smooth muscle contraction, contributing to vasodilation and reduced arterial tone. This mechanism is pharmacologically analogous to calcium channel blocker drugs and may act additively with ACE inhibition and NO-mediated vasodilation.

5.4. Diuretic effect

Several preclinical studies have documented natriuretic and diuretic properties of *Hibiscus sabdariffa* extracts, attributed to organic acids and anthocyanins that may increase glomerular filtration rate and promote sodium and water excretion via renal tubular mechanisms [15,16]. This reduction in circulating blood volume could contribute an additional antihypertensive effect complementary to vasodilatation, although robust human data quantifying this effect are limited.

5.5. Antioxidant activity and endothelial protection

Oxidative stress is a recognised contributor to endothelial dysfunction and hypertension. The antioxidant capacity of *Hibiscus sabdariffa*, driven by its anthocyanin and ascorbic acid content, enables scavenging of reactive oxygen species, potentially preserving eNOS activity and endothelial vasodilatory function [15,17]. In human trials, Hs consumption has been associated with reductions in some biomarkers of oxidative stress, although clinical translation of this effect remains to be confirmed [21].

5.6. Lipid metabolism and cardiometabolic effects

Hibiscus sabdariffa polyphenols have been associated with reductions in total and LDL cholesterol, possibly through inhibition of LDL oxidation and modulation of hepatic lipogenesis [22]. While these lipid effects do not directly lower blood pressure, they may confer independent cardiovascular benefit. This sixth mechanism is included in Table 1 but is not depicted in Figure 1, which is restricted to mechanisms with direct vascular or renal effects on blood pressure regulation.

6. Clinical evidence for blood pressure reduction

6.1. Randomised controlled trials

The clinical evidence base for *Hibiscus sabdariffa* as an antihypertensive agent has expanded over the past two decades, with trials varying considerably in preparation, dose, duration, and comparator. A selection of representative trials is summarised in Table 2.

6.2. Cochrane review

A Cochrane systematic review by Wahabi et al. evaluated the effect of Roselle (*Hibiscus sabdariffa*) for hypertension in adults, identifying only a small number of eligible RCTs with limited sample sizes and methodological heterogeneity [23]. The review concluded that the evidence available at that time was insufficient to support the use of Hs for the treatment of primary hypertension. This Cochrane assessment remains methodologically important, and subsequent meta-analyses reaching more favourable conclusions have done so largely on the basis of additional trials and broader inclusion criteria; their methodological quality, control of heterogeneity, and risk-of-bias profiles vary.

6.3. Subsequent systematic reviews and meta-analyses

Four subsequent meta-analyses are summarised in Figure 2. Serban et al. (2015) pooled five RCTs (390 participants) and reported a mean SBP reduction of −7.58 mmHg (95% CI: −9.69 to −5.46) and DBP reduction of −3.53 mmHg (95% CI: −5.16 to −1.89), with effects inversely related to baseline blood pressure [24]. Abdelmonem et al. (2022) pooled 13 RCTs (1,205 participants) in mild-to-moderate hypertension and reported SBP reduction (MD −6.67 mmHg; $p = 0.004$) and DBP reduction (MD −4.35 mmHg; $p = 0.02$) versus placebo [25]. Ellis et al. (2022) included 17 RCTs with trial sequential analysis and reported an SBP reduction of −7.10 mmHg (95% CI: −13.00 to −1.20; $I^2 = 95\%$) versus placebo, with the greatest effect magnitude in participants with elevated baseline blood pressure, and an LDL cholesterol reduction of −6.76 mg/dL versus placebo and other teas [22].

The most comprehensive synthesis to date is the umbrella review and dose-response meta-analysis by Norouzzadeh et al. (2025), which pooled data from 26 RCTs involving 1,797 participants and applied GRADE, AMSTAR-II, and ICEMAN quality frameworks. The review reported dose-dependent reductions in SBP and DBP compared with placebo, with effects most pronounced in adults aged over 50 years and in trials lasting more than four weeks; concomitant improvements in lipid profile, fasting glucose, and HDL-C were also reported alongside a favourable short-term safety profile [26].

Taken together, the more recent meta-analyses suggest a pooled SBP reduction of approximately 6–8 mmHg versus placebo and 12–16 mmHg versus pre-treatment values in open trials. This magnitude overlaps with that seen with some low-dose antihypertensive interventions [27]; however, direct therapeutic equivalence has not been established, statistical heterogeneity is high ($I^2 \approx 91$–95% in most analyses), and the earlier Cochrane assessment urged caution [23]. The evidence base therefore supports the hypothesis of a clinically relevant effect but does not currently justify positioning Hs as a substitute for guideline-directed pharmacotherapy.

7. Safety profile, adverse events, and drug interactions

7.1. General safety and tolerability

Hibiscus sabdariffa has been generally well tolerated in short- to medium-term human studies. The most reported adverse events are mild gastrointestinal symptoms (nausea, constipation, flatulence), with rates comparable to placebo [26,28]. A 2026 scoping review of safety, tolerability, and herb-drug interactions covering 53 clinical studies and 53 preclinical toxicology studies concluded that Hs is generally well tolerated at doses used in clinical practice, with no serious adverse events attributable to the plant reported in human interventional studies [28]. Long-term human safety data (beyond 12 weeks of continuous supplementation) and dose-response safety data above 1000 mg/day of standardised extract remain insufficient. A minor but statistically significant increase in aspartate aminotransferase (AST) has been observed in some trials at higher doses, warranting monitoring during prolonged use [26,28].

7.2. Drug interactions: distinguishing evidence categories

Reported drug-interaction signals for *Hibiscus sabdariffa* derive from heterogeneous sources, and the strength of evidence differs by interaction.

Human evidence. Clinical interactions with antihypertensive medication have not been formally characterised. No serious additive hypotensive events have been reported in published RCTs combining Hs with ACE inhibitors or ARBs [10,29].

Animal pharmacokinetic and pharmacodynamic evidence. In rodent studies, Hs extract has been shown to alter the bioavailability of captopril [29] and to potentiate the hypotensive effect of losartan and amlodipine [30]. Extrapolation of these findings to clinical practice in humans is uncertain.

Theoretical concerns. Given shared mechanisms with ACE inhibitors and the natriuretic activity of Hs, theoretical risks include additive hypotension when co-administered with ACE inhibitors, ARBs, or calcium channel blockers, and additive electrolyte disturbance when co-administered with diuretics. These risks have not been demonstrated in adequately powered human studies. Potential interactions with chloroquine, amoxicillin, and acetaminophen have been suggested by isolated case reports or animal pharmacokinetic data and are of uncertain clinical significance at typical beverage doses [28].

7.3. Contraindications and precautions

Caution is appropriate when *Hibiscus sabdariffa* is used by patients with pre-existing hypotension or those receiving multiple antihypertensive medications; in pregnancy (uterotonic effects have been reported in animal models); in patients with known hepatic dysfunction; and in those receiving immunosuppressant therapy pending further pharmacokinetic characterisation. Clinical supervision is advisable when Hs is used alongside conventional antihypertensive drugs, particularly during dose initiation and titration [26,28].

8. Sex-related differences in antihypertensive response

Subgroup signals from some RCTs and biological plausibility have prompted the hypothesis that women, particularly postmenopausal women, may respond differently to *Hibiscus sabdariffa* than men. Proposed mechanisms include phytoestrogenic engagement of oestrogen receptor alpha (ERα) and downstream upregulation of eNOS activity [25,31]. Oestrogen-related vascular pathways are known to influence NO-mediated vasodilation [32], and endothelial function

declines after menopause when oestrogen-related NO production decreases [33].

However, this remains a hypothesis. No published meta-analysis has formally tested sex as a moderator of the Hs antihypertensive response, and no RCT has been designed specifically with postmenopausal women as the target population. A sex-related differential response is biologically plausible but currently unconfirmed and should be investigated in adequately powered, sex-stratified clinical trials (see Section 12).

9. Laboratory monitoring considerations

In hypertensive patients who choose to use *Hibiscus sabdariffa* as part of a complementary approach, periodic laboratory monitoring as per standard hypertension care guidelines is appropriate, with additional attention to Hs-specific considerations. Recommended baseline and follow-up panels include serum creatinine and estimated glomerular filtration rate (eGFR); serum sodium, potassium, and uric acid as electrolyte and gout-risk markers, particularly given the natriuretic properties of Hs; fasting lipid profile (total cholesterol, LDL-C, HDL-C, triglycerides) given the concurrent hypolipidaemic effects of Hs; alanine aminotransferase (ALT) and aspartate aminotransferase (AST) given the minor hepatic enzyme signal at higher doses; and fasting blood glucose and HbA1c in patients with concurrent diabetes or metabolic syndrome [26,34]. A pragmatic monitoring schedule comprises baseline assessment, 6–8 weeks of supplementation, and 12 weeks if supplementation is continued.

10. Implications and research agenda for Saudi Arabia

10.1. Cultural and behavioural considerations

Karkade is consumed across the Arab region, including in some Saudi households, restaurants, and social gatherings, although robust nationally representative data on consumption frequency, preparation method, and dose in Saudi adults are scarce. Cultural familiarity at the regional level is plausibly favourable for acceptability of *Hibiscus sabdariffa* in structured lifestyle interventions, but acceptability research specific to Saudi populations is needed before broader implementation claims can be made.

10.2. Practical feasibility

Hibiscus sabdariffa calyces are widely and inexpensively available across Saudi Arabia in traditional markets and retail chains. Doses studied in clinical trials include two to three cups of tea per day (approximately 1.25–3 g dried calyces per 240 mL) [35] and standardised extracts at 250–500 mg per day [9,10], with monitoring suggested above 1000 mg per day [26,28]. Trials using doses up to 1000 mg per day have also been published [36]. For consistency, this review refers to standardised consumption doses as 250–500 mg per day of standardised extract, or two to three cups per day of infusion, with doses above 1000 mg per day considered investigational and requiring monitoring.

10.3. A research and implementation pathway

Given low awareness (34.8%) and control rates (37.0%) documented in Saudi Arabia [6], and recognising that lifestyle interventions addressing diet and physical activity can reduce SBP by 4–11 mmHg independently of pharmacotherapy [27,37], evaluation of *Hibiscus sabdariffa* within structured lifestyle-modification programmes may be justified, particularly through locally conducted Saudi clinical trials. The following sequenced research and implementation pathway is proposed.

First, descriptive studies quantifying *karkade* consumption patterns and acceptability among Saudi adults. Second, adequately powered RCTs in Saudi populations with pre-hypertension or Stage 1 hypertension, comparing standardised Hs supplementation alongside lifestyle modification with lifestyle modification alone. Third, pharmacokinetic interaction studies in humans, particularly with ACE inhibitors, ARBs, and diuretics. Fourth, sex-stratified analyses to evaluate the hypothesised differential response in postmenopausal women. Fifth, formal cost-effectiveness and implementation studies before any inclusion in clinical pathways. An ongoing trial registered on ClinicalTrials.gov (NCT03804801) at Sulaiman Al-Rajhi Colleges in the Al-Qassim region is examining the effect of hibiscus tea on blood pressure in a Saudi university population; its results may inform the first stages of this pathway.

The 2024 RCT by Dehkhoda et al. demonstrated significant additive benefit of Hs 350 mg twice daily alongside valsartan in hypertensive patients with chronic kidney disease, including improvements in proteinuria, lipid profile, and blood pressure [38]; however, until comparable evidence is generated in Saudi

populations, such adjunctive use should be considered investigational rather than recommended.

11. Discussion

The evidence reviewed here suggests a potentially clinically relevant antihypertensive effect of *Hibiscus sabdariffa*, mediated through several complementary pharmacological pathways and supported by a growing body of RCTs and meta-analyses. The most comprehensive recent synthesis, by Norouzzadeh et al. (2025), reported dose-dependent reductions in SBP and DBP with effect sizes that overlap with those of some low-dose conventional antihypertensives [26]. The present review extends this global evidence base by contextualising it within the specific epidemiological and cultural landscape of Saudi Arabia and by framing implications as a research agenda rather than clinical recommendation.

Several caveats moderate the strength of this evidence. Clinical trial heterogeneity is substantial (I^2 = 91–95% in most meta-analyses), reflecting variation in Hs preparation (tea, standardised extract, capsule), dose (100–2000 mg/day), duration (2–12 weeks), study populations, and comparators. This heterogeneity limits the precision of pooled estimates and complicates identification of an optimal therapeutic dose. The earlier Cochrane review reached more cautious conclusions [23], and subsequent more favourable meta-analyses depend on additional trials and broader inclusion criteria whose methodological quality varies. Most trials have been conducted in Iran, Mexico, Nigeria, and the United States; data from the Gulf region remain sparse, and extrapolation to Saudi populations should therefore be made cautiously.

The mechanistic multiplicity of Hs, acting on RAAS, NO-mediated vasodilation, calcium channels, diuresis, and oxidative stress, may resemble a multi-drug profile rather than a single pharmacological agent. This is both an advantage (pathway redundancy) and a complication (potential for unpredictable interactions). The sex-differential response hypothesis is biologically plausible but clinically unconfirmed. The hepatic enzyme signal at higher doses, although minor and clinically asymptomatic in reported trials, warrants caution at doses above standard beverage exposure for prolonged periods [26,28].

When considered in aggregate, the risk–benefit profile of *Hibiscus sabdariffa* at standard consumption doses (250–500 mg per day of standardised extract or two to three cups per day of infusion for 4–12 weeks) appears acceptable, but the evidence supports use as a culturally familiar adjunct to lifestyle modification rather than as a substitute for guideline-directed pharmacotherapy.

12. Limitations and future research directions

This work is a narrative review and carries the inherent limitations of that design, including potential selection bias in the inclusion and interpretation of studies, the absence of a formal PRISMA-guided screening process, lack of duplicate study selection, and the inability to generate new quantitative pooled estimates. The literature search was conducted by a single reviewer without formal duplicate screening.

Key research priorities are as follows. First, locally conducted Saudi RCTs are needed, given that baseline dietary intake, preparation methods, and polyphenol bioavailability may differ from previously studied populations. Second, sex-stratified analyses, including individual patient data meta-analysis and trials targeting postmenopausal women, are needed to test the oestrogen-pathway hypothesis. Third, standardisation of preparations across trials is essential, as variable polyphenol content between commercially available products makes dose interpretation difficult. Fourth, long-term safety studies extending beyond 12 weeks are required to characterise the hepatic enzyme signal and establish a safe duration of supplementation. Fifth, human pharmacokinetic interaction studies, particularly with ACE inhibitors, ARBs, and diuretics, are needed to replace current reliance on animal model extrapolation. Sixth, formal cost-effectiveness and implementation analyses in Saudi primary care would provide the health system evidence needed to consider any guideline-level role.

13. Conclusion

Hibiscus sabdariffa (roselle/*karkade*) is a culturally familiar herbal plant with mechanistically coherent and clinically suggestive antihypertensive activity, mediated through six proposed complementary pathways. Evidence from RCTs and recent meta-analyses suggests that Hs may produce modest, clinically relevant reductions in systolic and diastolic blood pressure, although estimates vary across preparations, doses, and populations, and an earlier Cochrane review reached more cautious conclusions. The short- to medium-term safety profile is acceptable, but long-term safety, human pharmacokinetic interaction, and Saudi-specific data remain insufficient.

In the Saudi Arabian context, characterised by a rising hypertension burden, low awareness and control rates, and regional cultural familiarity with *karkade*, *Hibiscus sabdariffa* is a plausible candidate for evaluation within structured lifestyle-modification programmes. It should not be presented as a substitute for guideline-directed pharmacotherapy. Locally conducted RCTs, human pharmacokinetic interaction studies, and sex-stratified analyses are the most pressing research priorities to inform any future role in Saudi clinical practice.

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TABLES

Table 1. Proposed mechanisms of antihypertensive action of *Hibiscus sabdariffa*.

Mechanism	Key bioactive compounds	Physiological effect	Clinical relevance
ACE inhibition	Delphinidin-3-sambubioside, cyanidin-3-sambubioside, hibiscus acid	Blocks conversion of angiotensin I to angiotensin II; reduces vasoconstriction	Analogous to ACE inhibitor drug class (e.g. captopril, lisinopril)
Nitric oxide release and vasodilation	Anthocyanins, flavonoids (quercetin)	Activates eNOS → NO → cGMP pathway in vascular endothelium	Peripheral vasodilation; reduces vascular resistance
Calcium channel modulation	Polyphenolic extracts	Suppresses Ca^{2+} influx into vascular smooth muscle cells	Smooth muscle relaxation; analogous to CCB mechanism
Diuretic effect	Organic acids, anthocyanins	Increases glomerular filtration rate; promotes natriuresis	Reduced circulating blood volume; lowers preload
Antioxidant activity	Anthocyanins, vitamin C, hibiscus acid	Scavenges reactive oxygen species; reduces oxidative stress	Protects endothelial function; reduces vascular inflammation
Lipid metabolism regulation	Polyphenols, hibiscus acid	Inhibits LDL oxidation; reduces total and LDL cholesterol	Attenuates atherosclerosis progression; indirect CV protection

Abbreviations: ACE, angiotensin-converting enzyme; CCB, calcium channel blocker; cGMP, cyclic guanosine monophosphate; eNOS, endothelial nitric oxide synthase; LDL, low-density lipoprotein; NO, nitric oxide. Compiled from references [15,16,17–20].

Table 2. Selected randomised controlled trials of *Hibiscus sabdariffa* for hypertension.

Study	Year	n	Population	Duration	Hs dose	Comp
Herrera-Arellano et al. [9]	2004	75	Stage 1–2 HTN	4 wk	Extract 250 mg/d	Capto
Herrera-Arellano et al. [10]	2007	193	Stage 1–2 HTN	4 wk	Extract 250 mg BID	Lisino
Mozaffari-Khosravi et al. [39]	2009	60	T2DM + HTN	4 wk	Sour tea 2 cups/d	Bla

McKay et al. [35]	2010	65	Pre-HTN/mild HTN	6 wk	Tea 3 cups/d	Placebo tea	−7.2	−3.1
Jalalyazdi et al. [16]	2019	46	Stage 1 HTN	6 wk	Sour tea 2 cups/d	Placebo	−9.3	−4.5
Jiménez-Ferrer et al. [40]	2021	171	Stage 1 HTN	8 wk	NW Roselle	Captopril 25 mg	−16.4	−9.9
Dehkhoda et al. [38]	2024	72	CKD + HTN	90 d	Capsule 330 mg BID + valsartan	Valsartan + HCTZ	−13.9	−8.7
Chaisungnern et al. [36]	2025	108	MetS + obesity	12 wk	Capsule 1000 mg/d	Placebo	−8.4	−5.6

Values represent within-group or between-group mean change from baseline as reported in the source articles. Abbreviations: BID, twice daily; CKD, chronic kidney disease; d, days; DBP, diastolic blood pressure; HCTZ, hydrochlorothiazide; HTN, hypertension; MetS, metabolic syndrome; NS, not statistically significant; NW Roselle, proprietary combination product of Hs and Olea europaea; Pre-HTN, pre-hypertension; SBP, systolic blood pressure; T2DM, type 2 diabetes mellitus; wk, weeks. Readers should consult the original publications for full effect estimates, between-group differences, 95% confidence intervals, and p-values, which differ in their reporting conventions across trials.

FIGURES

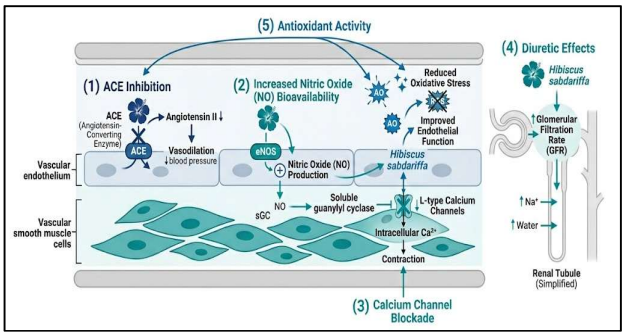

Figure 1. Schematic representation of the proposed pharmacological mechanisms underlying the antihypertensive activity of *Hibiscus sabdariffa*. The diagram illustrates five direct vascular and renal pathways through which *Hibiscus sabdariffa* bioactive compounds may reduce blood pressure: (1) ACE inhibition, (2) increased nitric oxide (NO) bioavailability via endothelial nitric oxide synthase (eNOS) upregulation, (3) calcium channel blockade in vascular smooth muscle, (4) diuretic effects via increased glomerular filtration and natriuresis, and (5) antioxidant activity supporting endothelial protection. A sixth proposed mechanism, lipid metabolism regulation (see Section 5.6 and Table 1), provides indirect cardiovascular protection and is not depicted here because it does not act directly on the vascular or renal pathways shown. Red crosses (×) denote inhibition of the target pathway. AO, antioxidant; sGC, soluble guanylyl cyclase. Compiled from references [15,16,17–20].

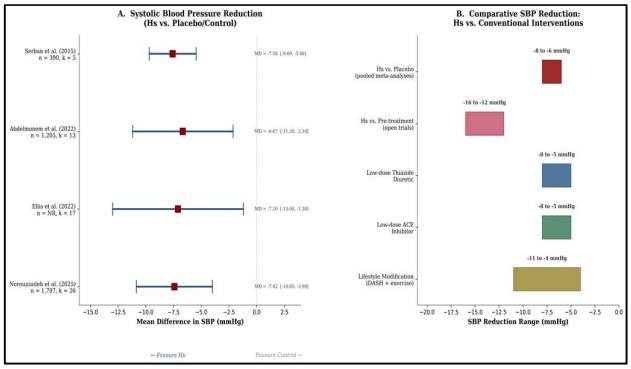

Figure 2. Schematic summary of reported pooled estimates from four meta-analyses examining the antihypertensive effect of *Hibiscus sabdariffa* (Hs). This figure is a graphical summary of previously published pooled effect estimates and is not an independent meta-analysis or a forest plot generated from primary trial-level data. (A) Pooled mean differences in systolic blood pressure (SBP) reported by four meta-analyses comparing Hs with placebo or control [22,24,25,26]. Squares represent reported pooled point estimates (mean difference, mmHg); horizontal lines represent reported 95% confidence intervals. (B) Schematic comparison of the SBP reduction range reported with Hs alongside ranges reported for low-dose thiazide diuretics, low-dose ACE inhibitors, and lifestyle modification combining DASH-style diet with exercise [27,37]. The figure should not be interpreted as an indication of therapeutic equivalence between Hs and conventional antihypertensive agents. k, number of included randomised controlled trials; MD, mean difference; n, pooled sample size; NR, not reported.