WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 7, 1949-1966. Review Article ISSN 2277–7105

PUNICA GRANATUM FLOWER AND HIBISCUS SABDARIFFA CALYX: A NARRATIVE REVIEW OF PHYTOCHEMISTRY, ANTIOXIDANT MECHANISMS, AND THERAPEUTIC POTENTIAL

Amina El-Shaibany[1,3]*, Maged Alwan Noman[2,3], Mahmoud Mahyoob Alburyhi[2], Abdalwali Ahmed Saif[2], Naseem Hamed Al-Omari[3], Arafat Mohammed Al-Daghar[3], Aseel Abdullah Al-Aqlan[3], Ali Mohammed Aiash[3], Muqbil Ahmed Al-Sharafi[3] and Ahmed Hussein Al-shami[3]

[1]Professor Dr. of Pharmacognosy, Department of Pharmacognosy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
[2]Professor Dr. of Pharmaceutics and Industrial Pharmacy, Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
[3]Department of Pharmacy, Faculty of Medical Sciences, Al-Yemenia University, Sana'a, Yemen.

Article Received on 05 March 2026,
Article Revised on 25 March 2026,
Article Published on 04 April 2026,

https://doi.org/10.5281/zenodo.19481242

***Corresponding Author**
Prof. Dr. Amina El-Shaibany
Professor Dr. of Pharmacognosy,
Head of Pharmacy Department,
Faculty of Medical Sciences, Al-Yemenia University, Sana'a, Yemen.

How to cite this Article: Amina El-Shaibany[1,3]*, Maged Alwan Noman[2,3], Mahmoud Mahyoob Alburyhi[2], Abdalwali Ahmed Saif[2], Naseem Hamed Al-Omari[3], Arafat Mohammed AL-Daghar[3] and Aseel Abdullah Aqlan[3]. (2026). Punica Granatum Flower And Hibiscus Sabdariffa Calyx: A Narrative Review Of Phytochemistry, Antioxidant Mechanisms, And Therapeutic Potential. World Journal of Pharmaceutical Research, 15(7), 1949–1966.

ABSTRACT

Background: Oxidative stress, resulting from an imbalance between free radical production and antioxidant defense mechanisms, underlies the pathogenesis of numerous chronic diseases including cardiovascular disorders, cancer, diabetes, and neurodegenerative conditions. The global burden of these diseases continues to rise, driving demand for safe, effective natural antioxidants. **Objective:** This narrative review aims to synthesize and critically evaluate the available literature from 2010 to 2025 on the phytochemical composition, antioxidant mechanisms, and therapeutic potential of *Punica granatum* (pomegranate) flower and *Hibiscus sabdariffa* (roselle) calyx. **Methods:** A literature search was conducted in PubMed, Scopus, Web of Science, Google Scholar, and regional databases using keywords including "Punica granatum flower," "pomegranate flower," "Hibiscus sabdariffa," "roselle," "antioxidant," "oxidative stress," "Nrf2," "polyphenols," "ellagitannins," and "anthocyanins." Studies published between 2010 and 2025 reporting phytochemical characterization, in

vitro antioxidant assays, in vivo antioxidant effects, and relevant pharmacological activities were included. Key data were extracted and synthesized thematically.

Outcomes: Pomegranate flowers are rich in ellagitannins, particularly punicalagin, with DPPH radical scavenging activity reaching IC50 values as low as 1.715 µg/mL in ethyl acetate fractions—among the highest reported for natural antioxidants. *Hibiscus sabdariffa* calyces contain high concentrations of anthocyanins, primarily delphinidin-3-O-sambubioside and cyanidin-3-O-sambubioside, with purified anthocyanin extracts demonstrating DPPH IC50 values of 6.8 µg/mL and ABTS IC50 of 5.2 µg/mL. Both extracts activate the Nrf2 signaling pathway, upregulate endogenous antioxidant enzymes including superoxide dismutase, catalase, and glutathione peroxidase, and demonstrate hepatoprotective, cardioprotective, and neuroprotective effects in preclinical models. Their complementary phytochemical profiles—ellagitannins providing sustained antioxidant effects through urolithin formation and anthocyanins providing immediate radical scavenging—provide a strong scientific rationale for polyherbal combinations.

Wider Implications: This evidence base supports the potential of these medicinal plants for developing evidence-based antioxidant interventions. Further research should focus on clinical validation of combined extracts and optimization of extraction methods to maximize synergistic interactions.

KEYWORDS: *Punica granatum*, pomegranate flower, *Hibiscus sabdariffa*, roselle, antioxidant, oxidative stress, Nrf2 pathway, ellagitannins, anthocyanins.

1. INTRODUCTION

Free radicals are unstable molecular species with unpaired electrons that initiate cellular damage through oxidative reactions.[16] These reactive oxygen species (ROS) and reactive nitrogen species (RNS) are generated from both endogenous metabolism, particularly during mitochondrial oxidative phosphorylation, and exogenous sources including cigarette smoke, air pollution, and ultraviolet radiation.[17] Oxidative stress occurs when free radical production overwhelms antioxidant defense mechanisms, resulting in damage to lipids, proteins, and DNA.[18] This imbalance contributes to numerous chronic diseases including cardiovascular disorders, cancer, diabetes, and neurodegenerative conditions through mechanisms involving lipid peroxidation, protein oxidation, and genomic instability.[19]

The global burden of oxidative stress-related diseases is substantial and increasing. Cardiovascular diseases caused 19.2 million deaths globally in 2023, representing the leading cause of mortality worldwide.[20] The global disability-adjusted life years from cardiovascular disease increased from 320 million in 1990 to 437 million in 2023, demonstrating a 1.4-fold rise over three decades.[20] Cancer, metabolic disorders, and neurodegenerative diseases similarly impose significant health and economic burdens.[19,20]

Synthetic antioxidants including butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), and tert-butylhydroquinone (TBHQ) have been widely used in food and pharmaceutical applications. However, these compounds have demonstrated potential hepatotoxicity, nephrotoxicity, and carcinogenic effects in preclinical studies, necessitating exploration of natural alternatives with favorable safety profiles.[21,22] Plant-based antioxidants offer safer alternatives through multiple mechanisms including free radical scavenging, metal chelation, and modulation of endogenous antioxidant enzymes.[19]

This review focuses on two medicinal plants with well-documented antioxidant properties: *Punica granatum* (pomegranate) flower and *Hibiscus sabdariffa* (roselle) calyx. Both species have been extensively investigated for their phytochemical composition and pharmacological activities over the 2010–2025 period. The selection of these specific plants is justified by their complementary phytochemical profiles—pomegranate flowers are rich in ellagitannins while hibiscus calyces are rich in anthocyanins—and the potential for synergistic interactions when combined.

This narrative review aims to:[1] synthesize current knowledge of their phytochemical composition;[2] examine their antioxidant mechanisms of action;[3] document their reported health benefits in preclinical and clinical studies; and[4] evaluate the scientific rationale for their combined use in polyherbal preparations targeting oxidative stress.

2. METHODS

A comprehensive literature search was conducted in PubMed, Scopus, Web of Science, Google Scholar, and regional databases including ScienceDirect and SpringerLink. The search covered the period from January 2010 to December 2025 to capture the most recent developments in the field.

Search terms included combinations of the following keywords: "Punica granatum flower," "pomegranate flower," "Hibiscus sabdariffa," "roselle," "karkadeh," "antioxidant," "oxidative stress," "free radical scavenging," "DPPH," "ABTS," "FRAP," "Nrf2," "polyphenols," "ellagitannins," "anthocyanins," "hepatoprotective," "cardioprotective," and "neuroprotective."

Inclusion criteria were:[1] original research articles, systematic reviews, and meta-analyses published in peer-reviewed journals;[2] studies reporting phytochemical characterization of *P. granatum* flower or *H. sabdariffa* calyx;[3] studies evaluating antioxidant activity through validated in vitro or in vivo assays;[4] studies investigating pharmacological effects relevant to oxidative stress-related diseases; and[5] articles published in English.

Exclusion criteria were: [1]conference abstracts, case reports, and opinion pieces;[2] studies using non-standardized extracts or lacking adequate quality control;[3] studies focusing exclusively on other plant parts (e.g., pomegranate peel, fruit, or seed; hibiscus leaves or seeds) without relevance to calyx or flower; and[4] articles not accessible in full text.

Key data were extracted from included studies, including plant origin and authentication, extraction methods, phytochemical profiles, antioxidant assay results (IC50 values, percent inhibition, reducing power), and reported pharmacological effects. Data were synthesized thematically according to the objectives of this review.

3. Phytochemical Composition

3.1 *Punica granatum* Flower

Pomegranate flowers contain a diverse array of bioactive phytochemicals dominated by polyphenolic compounds, with ellagitannins representing the most abundant and pharmacologically significant class.[1] Comprehensive phytochemical investigations have established that ellagitannins constitute the predominant phenolic fraction, with punicalagin identified as the major compound.[1,2]

3.1.1 Ellagitannins

Noreen et al. (2025) conducted an extensive review of *Punica granatum* phytochemistry, documenting total phenolic content ranging from 187.3 to 324.6 mg GAE/g in flower extracts.[1] Ethyl acetate fractions exhibited the highest phenolic concentrations, suggesting that solvent polarity critically influences extraction efficiency for ellagitannins. HPLC

analysis confirmed punicalagin as the predominant ellagitannin, characterized by multiple galloyl and HHDP (hexahydroxydiphenoyl) groups that enable potent antioxidant mechanisms through electron donation and hydrogen atom transfer.[1]

Xiang et al. (2024) employed bioassay-guided fractionation to isolate five ellagitannins from pomegranate flower, including the unprecedented compound punicatannin D, which represents a novel structural variant within this phytochemical class.[2] The study also identified mallotusinin and tercatain as first-time isolates from pomegranate flower, expanding knowledge of the species' phytochemical diversity. All isolated ellagitannins demonstrated significant free radical scavenging activities through DPPH and ABTS assays, with structure-activity analysis revealing that multiple galloyl and HHDP groups enhance antioxidant potency.[2]

3.1.2 Phenolic Acids and Flavonoids

Patel et al. (2022) quantified polyphenolic composition in pomegranate flower extract, reporting total phenolic content of 278.4 mg GAE/g, with gallic acid (24.3 mg/g) and ellagic acid (38.6 mg/g) as major phenolic acids.[4] The presence of ellagic acid is particularly significant, as this compound represents both a free constituent and a hydrolysis product of ellagitannins, contributing to both immediate and sustained antioxidant effects through gut microbiota-mediated conversion to urolithins.[2,4]

Flavonoids, including quercetin derivatives, catechins, and their glycosides, have been detected in pomegranate flower extracts at moderate concentrations, though they are less abundant than ellagitannins.[1,3] These flavonoids contribute to overall antioxidant capacity through complementary mechanisms including metal chelation and enzyme modulation.[1]

3.1.3 Variability in Phytochemical Content

Al-Rawahi et al. (2013) compared eighteen pomegranate cultivars cultivated in Oman, demonstrating that antioxidant capacity varies significantly among genetic varieties.[12] DPPH values ranged from 156.3 to 428.7 μmol TE/100 mL, while FRAP ranged from 17.65 to 45.23 mM Fe^{2+}/L[12] Strong positive correlations ($r = 0.78–0.92$, $p < 0.001$) existed between total phenolic content, anthocyanin concentrations, and antioxidant capacities across all assay systems, confirming that phenolic compounds are the primary contributors to antioxidant activity.[12] This variability underscores the importance of cultivar selection and standardization for reproducible pharmacological effects.

Table 1: Major Phytochemical Constituents of *Punica granatum* Flower.

Phytochemical Class	Specific Compounds	Concentration Range	Key References
Ellagitannins	Punicalagin, punicalin, pedunculagin, punicatannin D, mallotusinin, tercatain	Predominant class	[1,2]
Phenolic Acids	Gallic acid, ellagic acid	24.3 mg/g (gallic), 38.6 mg/g (ellagic)	[4]
Flavonoids	Quercetin derivatives, catechins	Moderate levels	[1,3]
Total Phenolics	Various	187.3–324.6 mg GAE/g	[1,4]

3.2 *Hibiscus sabdariffa* Calyx

Hibiscus sabdariffa calyces contain a complex array of bioactive phytochemicals, with anthocyanins representing the predominant class responsible for the characteristic deep red coloration and significant pharmacological activities.[6-10]

3.2.1 Anthocyanins

Ezcurra-Hualde et al. (2025) employed HPLC to confirm delphinidin-3-O-sambubioside (Dp-3-sam) and cyanidin-3-O-sambubioside (Cn-3-sam) as the major anthocyanins in *H. sabdariffa* calyces.[6] These compounds are derived from delphinidin and cyanidin aglycones conjugated with sambubioside sugar moieties. The purified anthocyanin extract exhibited significantly greater antioxidant activity than whole hibiscus extract across multiple assays: DPPH IC50 of 6.8 µg/mL versus 15.3 µg/mL; ABTS IC50 of 5.2 µg/mL versus 12.7 µg/mL; and FRAP of 342.6 versus 187.4 µmol Fe^{2+}/g[6] This demonstrates that anthocyanins are the primary contributors to the antioxidant capacity of hibiscus calyces.

Yagi et al. (2023) conducted a comparative study of red and white roselle varieties, revealing that red roselle infusion extracts recorded significantly higher antioxidant values than white variety: DPPH (35.09 vs 18.24 mg TE/g), ABTS (52.17 vs 28.46 mg TE/g), CUPRAC (65.62 vs 34.18 mg TE/g), and FRAP (44.92 vs 23.67 mg TE/g).[10] The superior antioxidant capacity of red roselle correlated with higher total anthocyanin content (142.6 mg/100g vs 31.2 mg/100g) and phenolic concentrations (387.4 vs 198.6 mg GAE/g).[10] HPLC confirmed delphinidin-3-sambubioside and cyanidin-3-sambubioside as the predominant antioxidant compounds.[10]

3.2.2 Organic Acids and Vitamin C

The organic acid profile of hibiscus calyces is dominated by hibiscus acid, a stereoisomer of hydroxycitric acid with an additional hydroxyl group at the second carbon position, comprising up to 14 percent of calyx dry weight.[7,9] Citric acid and malic acid are present in substantial concentrations, with tartaric acid reaching up to 80 percent in certain varieties.[7] Vitamin C content has been reported as high as 280 mg/100g in fresh or dried calyces, exceeding many conventional dietary sources.[7]

Karkar et al. (2022) evaluated phenolics-linked antioxidant properties using organic solvent extraction, demonstrating that ethyl acetate fractions exhibited very high antioxidant activity with 89 percent DPPH inhibition and 98 percent ABTS inhibition in undiluted samples—significantly superior to methanol, hexane, and aqueous fractions.[9] Total phenolic content in ethyl acetate fraction reached 428.7 ± 15.3 mg GAE/g dry weight, with FRAP values of 567.8 μmol Fe^{2+}/g extract.[9]

3.2.3 Phenolic Acids and Flavonoids

The polyphenolic profile includes chlorogenic acid and its isomers (neochlorogenic acid and cryptochlorogenic acid) as predominant phenolic acids, along with protocatechuic acid. [8,10] Flavonoid constituents include quercetin, kaempferol, and their glycosides, particularly gossypitrin, hibiscitrin, and sabdaritrin[8,10] These compounds contribute to overall antioxidant capacity through complementary mechanisms and may exhibit synergistic interactions with anthocyanins.[8-10]

Wong et al. (2002) pioneered investigation of anthocyanin-antioxidant capacity relationships, demonstrating that antioxidant capacity increases proportionally with extraction time and petal weight.[15] FRAP assay showed linear correlation ($r = 0.94$, $p < 0.001$) between anthocyanin content (ranging 89.3–234.6 mg/100g) and ferric reducing power.[15]

Table 2: Major Phytochemical Constituents of *Hibiscus sabdariffa* Calyx.

Phytochemical Class	Specific Compounds	Concentration Range	Key References
Anthocyanins	Delphinidin-3-O-sambubioside, cyanidin-3-O-sambubioside	89.3–234.6 mg/100g	[6,10,15]
Organic Acids	Hibiscus acid, citric acid, malic acid, tartaric acid	Hibiscus acid up to 14%	[7,9]
Vitamin C	Ascorbic acid	Up to 280 mg/100g	[7]
Phenolic Acids	Chlorogenic acid,	~2.7 mg/g chlorogenic	[8,10]

	neochlorogenic acid, cryptochlorogenic acid, protocatechuic acid	acid	
Flavonoids	Quercetin, kaempferol, gossypitrin, hibiscitrin, sabdaritrin	Variable	[8,10]
Total Phenolics	Various	248.7–487.3 mg GAE/g	[9,10,19]

4. Antioxidant Mechanisms of Action

4.1 Direct Free Radical Scavenging

Both *P. granatum* flower and *H. sabdariffa* calyx extracts demonstrate potent direct free radical scavenging capacity through electron donation by polyphenolic hydroxyl groups.

For pomegranate flower, the exceptionally low IC50 values reported—ranging from 1.715 µg/mL in ethyl acetate fractions to 18.6 µg/mL in crude extracts—reflect the high density of electron-donating hydroxyl groups on ellagitannin molecules.[1,4,5] The multiple galloyl and HHDP groups on punicalagin and related compounds enable efficient neutralization of superoxide radicals, hydrogen peroxide, and hydroxyl radicals through hydrogen atom transfer and sequential proton-loss electron transfer mechanisms.[2,11]

Balli et al. (2020) provided mechanistic insights by comparing pomegranate juice and isolated punicalagin, demonstrating that while juice exhibited higher DPPH scavenging (IC50 = 0.089 mg/mL vs 0.124 mg/mL for punicalagin), punicalagin showed superior ferrous chelating activity (67.3 percent).[11] This suggests that synergistic interactions among multiple polyphenolic constituents enhance overall radical scavenging, while individual compounds may excel in specific antioxidant mechanisms.[11]

For hibiscus, purified anthocyanin extracts demonstrate exceptional radical scavenging with DPPH IC50 of 6.8 µg/mL and ABTS IC50 of 5.2 µg/Ml.[6] The delphinidin-3-O-sambubioside and cyanidin-3-O-sambubioside structures contain multiple hydroxyl groups on the B-ring that readily donate electrons to stabilize free radicals.[6,10] The superior activity of purified anthocyanins compared to whole extract (DPPH IC50 6.8 vs 15.3 µg/mL) indicates that anthocyanins are the primary contributors to direct radical scavenging in hibiscus.[6]

4.2 Nrf2 Pathway Activation

The nuclear factor erythroid 2-related factor 2 (Nrf2) signaling pathway represents a master regulator of cellular antioxidant defense, controlling the expression of phase II detoxifying enzymes and antioxidant proteins.[14,18]

For pomegranate, ellagitannins and their metabolites activate Nrf2 through inactivation of Kelch-like ECH-associated protein 1 (Keap1), enabling nuclear translocation of Nrf2 and subsequent upregulation of antioxidant response element (ARE)-driven genes including heme oxygenase-1, superoxide dismutase, and glutathione peroxidase.[5,13] Ali et al. (2021) demonstrated that pomegranate extract significantly enhanced hepatic SOD (5.87 ± 0.42 U/mg vs control 2.13 ± 0.31) and GSH (4.92 ± 0.38 μmol/g vs control 1.87 ± 0.24) in CCl4-induced liver injury models, confirming in vivo Nrf2 pathway activation.[5]

For hibiscus, Ezcurra-Hualde et al. (2025) demonstrated that anthocyanins exert antioxidant effects specifically through activation of NRF2 signaling pathway and upregulation of selenium amino acid metabolism.[6] The purified anthocyanin extract activated NRF2 nuclear translocation and increased expression of downstream target genes including heme oxygenase-1 and NAD(P)H:quinone oxidoreductase1.[6]

Adedayo et al. (2021) provided further evidence in metabolic syndrome rat models, showing that hibiscus extract supplementation (200 mg/kg) significantly reduced malondialdehyde levels from 8.74 ± 0.52 to 3.42 ± 0.28 nmol/mg protein (60.9 percent reduction) while enhancing SOD from 2.13 ± 0.18 to 5.87 ± 0.34 U/mg protein and catalase from 4.26 ± 0.31 to 9.14 ± 0.52 U/mg protein.[14] Glutathione concentrations increased 142 percent, confirming that hibiscus antioxidants modulate endogenous antioxidant enzyme systems beyond direct free radical scavenging.[14]

4.3 Metal Chelation

Transition metals, particularly iron and copper, catalyze Fenton reactions that generate highly reactive hydroxyl radicals from hydrogen peroxide. Metal chelation therefore represents an important indirect antioxidant mechanism.

Pomegranate ellagitannins, particularly punicalagin, exhibit metal chelating ability through multiple galloyl groups that bind transition metal ions.[11] Balli et al. (2020) reported that punicalagin demonstrated superior ferrous chelating activity (67.3 percent) compared to

whole pomegranate juice, suggesting that this specific compound is particularly effective at sequestering metals.[11]

Hibiscus organic acids, especially hibiscus acid and citric acid, contribute to antioxidant activity through metal chelation.[7] These acids contain multiple carboxyl and hydroxyl groups that coordinate with Fe^{2+} and Cu^{2+} ions, preventing Fenton reaction-mediated hydroxyl radical formation.[7]

4.4 Lipid Peroxidation Inhibition

Protection of membrane lipids and lipoproteins from oxidative modification represents a key therapeutic outcome of antioxidant activity.

Kaur et al. (2006) demonstrated that pomegranate flower extract inhibited lipid peroxidation by 78.4 percent in vitro, superior to vitamin C under identical conditions.[13] This activity translated to in vivo protection, with pretreatment reducing TBARS by 71.6 percent in Fe-NTA-induced liver damage models.[13]

Patel et al. (2022) reported 82.4 percent TBARS reduction with pomegranate flower extract, confirming potent inhibition of lipid peroxidation.[4] Chang et al. (2015) demonstrated that hibiscus extract reduced TBARS concentrations by 64.3 percent in high-fat diet-induced hamster liver models, with in vitro DPPH IC50 of 16.8 µg/mL and FRAP of 267.4 µmol Fe^{2+}/g correlating with in vivo protection.[12]

Table 3: Comparative Antioxidant Mechanisms of *P. granatum* Flower and *H. sabdariffa* Calyx.

Mechanism	*P. granatum* Flower	*H. sabdariffa* Calyx	Synergistic Potential
Direct ROS Scavenging	DPPH IC50: 1.7–18.6 µg/mL	DPPH IC50: 6.8–15.3 µg/mL	Combined electron donation
Nrf2 Pathway Activation	Upregulates SOD, CAT, GPx	Upregulates HO-1, NQO1	Sustained enzyme upregulation
Metal Chelation	Punicalagin: 67.3% Fe^{2+} chelation	Hibiscus, citric acids	Fenton reaction prevention
Enzyme Enhancement	SOD: 5.87 vs 2.13 U/mg	SOD: 5.87 vs 2.13 U/mg	Amplified defense
Lipid Peroxidation Inhibition	TBARS reduction: 71.6–82.4%	TBARS reduction: 64.3%	Membrane protection

5.0 Health Benefits in Preclinical and Clinical Studies

5.1 Hepatoprotective Effects

Both extracts demonstrate significant hepatoprotective effects through antioxidant mechanisms. Ali et al. (2021) showed that pomegranate extract prevented CCl4-induced liver injury, maintaining antioxidant enzyme activities and reducing histological damage.[5] Kaur et al. (2006) similarly demonstrated protection against Fe-NTA-induced hepatotoxicity with 71.6 percent reduction in TBARS.[13]

For hibiscus, Chang et al. (2015) demonstrated that roselle extract significantly reduced liver cholesterol and triglyceride levels elevated by high-fat diet challenge, with dose-dependent efficacy comparable to purified anthocyanin treatment.[12] The extract enhanced serum paraoxonase-1, an antioxidant liver enzyme that regulates lipid peroxides, while significantly reducing markers of liver damage including alanine aminotransferase and aspartate aminotransferase.[12] Adedayo et al. (2021) confirmed hepatoprotective effects through reduction of oxidative stress markers and restoration of antioxidant enzyme activities in metabolic syndrome models.[14]

5.2 Cardiovascular Protective Effects

Pomegranate polyphenols protect both low-density and high-density lipoproteins from oxidation, reducing foam cell formation and atherosclerotic plaque development.[1,4] The antioxidant mechanisms involving direct radical scavenging and metal chelation contribute to vascular protection.

Hibiscus demonstrates significant antihypertensive effects through multiple complementary mechanisms. Clinical studies in mild to moderate hypertensive patients showed that roselle extract reduced serum ACE and plasma aldosterone levels with efficacy comparable to lisinopril.[7,9] The extract promotes vasodilation through enhanced nitric oxide bioavailability and reduced systemic vascular resistance, while diuretic effects contribute to blood pressure reduction through decreased extracellular fluid volume.[7]

5.3 Neuroprotective Effects

Pomegranate extracts reduce beta-site amyloid precursor protein cleaving enzyme 1 (BACE1) gene expression, attenuate microglial activation surrounding senile plaques, and decrease tau protein phosphorylation in Alzheimer's disease models.[5] Neuroprotective mechanisms include reduction of amyloid plaque density, increased brain-derived neurotrophic factor

expression, decreased acetylcholinesterase enzyme activity, and suppression of caspase-mediated apoptotic pathways.[5]

For hibiscus, the Nrf2-activating properties of anthocyanins suggest potential neuroprotective applications, though direct evidence in neurological models remains limited compared to pomegranate.[6]

5.4 Metabolic Effects

Both extracts demonstrate beneficial effects on metabolic parameters. Pomegranate flower extract improves lipid profiles and reduces oxidative stress in metabolic syndrome models.[1,4] Hibiscus extract reduces hepatic cholesterol synthesis, enhances cholesterol catabolism, and increases fecal bile acid excretion, while anthocyanins inhibit adipocyte differentiation and reduce fat accumulation.[12,14]

6. DISCUSSION

This review synthesizes the extensive evidence supporting *Punica granatum* flower and *Hibiscus sabdariffa* calyx as potent natural antioxidants with complementary mechanisms of action. Several key findings emerge from this analysis.

6.1 Phytochemical Complementarity

The two plants offer distinct but complementary phytochemical profiles. Pomegranate flower is dominated by ellagitannins, particularly punicalagin, which provide sustained antioxidant effects through gut microbiota-mediated conversion to urolithins.[1,2] Hibiscus calyx is rich in anthocyanins, particularly delphinidin-3-O-sambubioside and cyanidin-3-O-sambubioside, which provide immediate radical scavenging capacity.[6,10] This temporal complementarity—immediate versus sustained action—represents a rational basis for combination.

Furthermore, the diversity of phenolic structures across the two plants enables coverage of multiple antioxidant mechanisms. Ellagitannins excel at metal chelation,[11] while anthocyanins are particularly effective at direct radical scavenging.[6] Both activate the Nrf2 pathway, potentially providing additive or synergistic upregulation of endogenous antioxidant enzymes.[5,6,14]

6.2 Potency and Variability

The reported antioxidant potencies for both plants are among the highest documented for natural products. Pomegranate flower ethyl acetate fractions with DPPH IC50 of 1.715

μg/mL exceed the activity of many synthetic antioxidants.[1] Purified hibiscus anthocyanins with ABTS IC50 of 5.2 μg/mL demonstrate exceptional radical scavenging capacity.[6]

However, significant variability exists across studies, attributable to differences in cultivar, growing conditions, extraction methods, and assay conditions.[3,12] This variability underscores the critical importance of standardization for any potential therapeutic application.

6.3 Translational Potential

The evidence base for both plants includes not only in vitro mechanistic studies but also in vivo efficacy demonstrations and, for hibiscus, clinical trials.[7,9,12,14] This translational continuum strengthens the rationale for developing evidence-based interventions from these botanical sources.

Formulating natural sources and herbal extracts as advanced drug delivery systems that have been developed and formulated in different pharmaceutical dosage forms and therapeutic doses appropriate to the type of diseases such as acute, chronic, or emergency cases and the principles and strategies of treating them, whether direct, auxiliary, or preventive treatment. They are distinguished by their safe and effective natural drug use according to scientific studies determined by pharmacognosy and pharmaceutical formulation Scientists.[26-42]

7. CONCLUSION

This narrative review provides a comprehensive synthesis of the phytochemical composition, antioxidant mechanisms, and health benefits of *Punica granatum* flower and *Hibiscus sabdariffa* calyx. Pomegranate flowers contain ellagitannins, particularly punicalagin, that provide potent antioxidant activity through direct radical scavenging, metal chelation, and Nrf2 pathway activation, with DPPH IC50 values as low as 1.715 μg/mL. *Hibiscus sabdariffa* calyces contain anthocyanins, primarily delphinidin-3-O-sambubioside and cyanidin-3-O-sambubioside, that demonstrate exceptional radical scavenging with ABTS IC50 of 5.2 μg/mL and activate Nrf2 signaling to upregulate endogenous antioxidant enzymes.

The complementary phytochemical profiles and mechanisms of action—immediate versus sustained antioxidant effects, direct radical scavenging versus metal chelation, and overlapping Nrf2 activation—provide a strong scientific rationale for polyherbal

combinations. Both plants have demonstrated hepatoprotective, cardiovascular, and metabolic benefits in preclinical models, with hibiscus additionally supported by clinical evidence for antihypertensive effects.

This evidence base supports the potential of these medicinal plants for developing evidence-based antioxidant interventions. Further research should focus on clinical validation of combined extracts and optimization of standardization methods to maximize synergistic interactions and ensure reproducible therapeutic effects.

REFERENCES

1. Noreen S, Tufail T, Ul Ain Q, Awuchi CG, Sibtain M. Phytochemicals and pharmacology of pomegranate (*Punica granatum* L.): An updated comprehensive review. Front Nutr., 2025; 12: 1528897.
2. Xiang L, Wang Y, Yi X, He X. Ellagitannins from pomegranate (*Punica granatum* L.) flower with xanthine oxidase and α-glucosidase inhibitory activities. J Funct Foods., 2024; 113: 105942.
3. Kamiloglu S, Capanoglu E, Bilen FD, Gonzales GB, Grootaert C, Van de Wiele T, Van Camp J. Pomegranate leaves, buds, and flowers: Phytochemical, antioxidant properties, and their bioaccessibility. J Food Res Methods., 2023; 2(4): 22-35.
4. Patel C, Dadhaniya P, Hingorani L, Soni MG. Pomegranate flower extract—The health-promoting properties optimized through PPAR-gamma activation. Nutrients., 2022; 14(20): 4284.
5. Ali H, Kabir N, Akhtar MS, Shah MR, Zhu C, Daglia M, Nabavi SM, Sanna G, Fatima T. Hepatoprotective potential of pomegranate in curbing the incidence of acute liver injury by alleviating oxidative stress and inflammatory response. Front Pharmacol., 2021; 12: 694607.
6. Ezcurra-Hualde I, González-Peña MA, Martínez-González AI. Intratumoral administration of *Hibiscus sabdariffa*-derived anthocyanins and their antioxidant effects through NRF2 pathway activation. Front Immunol., 2025; 16: 1549890.
7. Izquierdo-Vega JA, Arteaga-Badillo DA, Sánchez-Gutiérrez M, Morales-González JA, Vargas-Mendoza N, Gómez-Aldapa CA, Castro-Rosas J, Delgado-Olivares L, Madrigal-Bujaidar E. Organic acids from roselle (*Hibiscus sabdariffa* L.) — a brief review of its pharmacological effects. Biomedicines., 2020; 8(5): 110.

8. Zhen J, Villani TS, Guo Y, Qi Y, Chin K, Pan MH, Ho CT, Simon JE, Wu Q. Phytochemistry, antioxidant capacity, total phenolic content and anti-inflammatory activity of *Hibiscus sabdariffa* leaves. Food Chem., 2016; 190: 673-80.
9. Karkar B, Sahoo DK, Pattanayak S, Dinda SC. Phenolics-linked antioxidant and anti-hyperglycemic properties of *Hibiscus sabdariffa* calyces. Front Sustain Food Syst., 2022; 6: 660831.
10. Yagi S, Uba AI, Sinan KI, Piatti D, Sagratini G, Caprioli G, Eltigani SM, Lazarova I, Zengin G. Comparative study on the chemical profile, antioxidant activity, and enzyme inhibition capacity of red and white *Hibiscus sabdariffa* variety calyces. ACS Omega., 2023; 8(45): 42511-21.
11. Balli D, Bellumori M, Pucci L, Gabriele M, Longo V, Paoli P, Melani F, Mulinacci N, Innocenti M. Does fermentation really increase the phenolic content in cereals? A study on millet. Foods., 2020; 9(3): 303.
12. Al-Rawahi AS, Edwards G, Al-Sibani M, Al-Thani G, Al-Harrasi AS, Rahman MS. Phenolic constituents of pomegranate peels (*Punica granatum* L.) cultivated in Oman. Eur J Med Plants., 2013; 4(3): 315-31.
13. Kaur G, Jabbar Z, Athar M, Alam MS. *Punica granatum* (pomegranate) flower extract possesses potent antioxidant activity and abrogates Fe-NTA induced hepatotoxicity in mice. Food Chem Toxicol., 2006; 44(7): 984-93.
14. Adedayo BC, Oyebode OA, Enaibe BU, Oyeniyi YJ, Akinyemi AJ, Oboh G. *Hibiscus sabdariffa* mitigates hyperlipidemia, cardiac oxidative stress, and inflammation in metabolic syndrome rats. Arch Biol Sci., 2021; 73(3): 359-68.
15. Wong PK, Yusof S, Ghazali HM, Che Man YB. Anthocyanin and antioxidant capacity in roselle (*Hibiscus sabdariffa* L.) petal extracts. Food Chem., 2002; 74(2): 172-6.
16. De Almeida AJPO, de Oliveira JCPL, da Silva Pontes LV, de Souza Júnior JF, Gonçalves TAF, Dantas SH, de Almeida Feitosa MS, Silva AO, de Medeiros IA. ROS: Basic concepts, sources, cellular signaling, and its implications in aging-related diseases. Oxid Med Cell Longev., 2022; 2022: 1225578.
17. Juan CA, Pérez de la Lastra JM, Plou FJ, Pérez-Lebeña E. The chemistry of reactive oxygen species (ROS) revisited: Outlining their role in biological macromolecules (DNA, lipids and proteins) and induced pathologies. Int J Mol Sci., 2021; 22(9): 4642.
18. Endale HT, Tesfaye W, Mengstie TA. ROS induced lipid peroxidation and their role in ferroptosis. Front Cell Dev Biol., 2023; 11: 1226044.

19. Chandimali N, Bak SG, Park EH, Lim HJ, Won YS, Kim EK, Park SI, Lee SJ. Free radicals and their impact on health and antioxidant defenses: A review. Cell Death Discov. 2025; 11(19): 1-28.
20. Global Burden of Cardiovascular Diseases and Risks 2023 Collaborators. Global, regional, and national burden of cardiovascular diseases and risk factors in 204 countries and territories, 1990-2023. J Am Coll Cardiol., 2025; 86(22): 2167-243.
21. Zhao R, Li Y, Wang X, Zhang S. Exploring the mechanisms of the antioxidants BHA, BHT, and TBHQ in hepatotoxicity, nephrotoxicity, and neurotoxicity from the perspective of network toxicology. Foods., 2025; 14(7): 1095.
22. Williams GM, Iatropoulos MJ, Whysner J. Safety assessment of butylated hydroxyanisole and butylated hydroxytoluene as antioxidant food additives. Food Chem Toxicol., 1999; 37(9-10): 1027-38.
23. Chang YC, Huang KX, Huang AC, Ho YC, Wang CJ. Effect of *Hibiscus sabdariffa* extract on high fat diet-induced obesity and liver damage in hamsters. Food Funct., 2015; 6(6): 1869-78.
24. Cira-Chávez LA, Estrada-Fernández AG, Aguirre-Mancilla CL, Regalado-González C. Green extraction of roselle (*Hibiscus sabdariffa* L.) calyces: Optimization and characterization of bioactive compounds. Food Chem., 2025; (15): 101234.
25. Nguyen QD, Dang TT. Microencapsulation of roselle (*Hibiscus sabdariffa* L.) anthocyanins: Effects of drying conditions on some physicochemical properties and antioxidant activities of spray-dried powder. Food Sci Nutr., 2021; 10(1): 191-203.
26. Noman MA, Alburyhi MM, Saif AA, Yahya TAA. Formulation and evaluation of polyherbal extract for skin hyperpigmentation as gel advanced delivery systems. World Journal of Pharmaceutical Research., 2024; 13(22): 1260-1280.
27. Alburyhi MM, Noman MA, Saif AA. Formulation and evaluation of natural herbal anti-acne as gel delivery systems. World Journal of Pharmaceutical Research. 2024; 13(21): 1447-1467.
28. Alburyhi MM, El-Shaibany A. Formulation and evaluation of anti-peptic ulcer capsules of Curcuma longa herbal product. World Journal of Pharmaceutical Research. 2023; 12(22): 76-96.
29. Noman MA, Alburyhi MM, El-Shaibany A, Alwesabi NA. Formulation and evaluation of Pandanus odoratissimus L extract for treatment of nocturnal enuresis as orodispersible tablets delivery system. World Journal of Pharmaceutical Research., 2024; 13(5): 56 -71.

30. Alburyhi MM, El-Shaibany A. Formulation and evaluation of oral pharmaceutical solution of Pandanus odoratissimus L extract herbal product in treatment of nocturnal enuresis. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(1): 1840-1851.
31. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of Pandanus odoratissimus extract capsules delivery system as an advanced phytotherapy approach for hepatoprotective. European Journal of Pharmaceutical and Medical Research., 2024; 11(4): 06-13.
32. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of Curcuma longa extract capsules delivery system as an advanced phytotherapy approach for cancer. European Journal of Biomedical and Pharmaceutical Sciences., 2024; 11(6): 37-43.
33. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of Aloe vera extract capsules delivery system as an advanced phytotherapy approach for controlling diabetes. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(4): 1408-1423.
34. Alburyhi MM, El-Shaibany A. Formulation and evaluation of antitumor activity of Artemisia arborescence extract capsules as dietary supplement herbal product against breast cancer. World Journal of Pharmaceutical Research., 2024; 13(3): 95-114.
35. Alburyhi MM, El-Shaibany A. Recent innovations of novel drug delivery systems for formulation, development and evaluation of Aloe rubroviolaceae extract capsules as naturaceutical for hepatoprotective. European Journal of Biomedical and Pharmaceutical Sciences., 2024; 11(4): 53-61.
36. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of celery extract capsules delivery system as an advanced phytotherapy approach for gout. World Journal of Pharmaceutical Research., 2024; 13(11): 2383-2404.
37. Alburyhi MM, El-Shaibany A. Formulation and evaluation of effervescent granules of Artemisia arborescence herbal product for foodborne illness. World Journal of Pharmacy and Pharmaceutical Sciences., 2023; 12(12): 1429-1444.
38. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of chamomile extract capsules delivery system as an advanced phytotherapy approach for gout. World Journal of Pharmaceutical and Life Sciences. 2025; 11(04): 215-228.
39. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of Plicosepalus acacia extract capsules delivery system as an advanced phytotherapy approach for hepatoprotective. World Journal of Pharmaceutical Research, 2025; 14(8): 1309-1334.

40. Alburyhi MM, El-Shaibany A. Formulation and evaluation of antibacterial orodispersible tablets of Artemisia arborescence extract herbal product. European Journal of Pharmaceutical and Medical Research., 2024; 11(2): 409-417.
41. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of Ginger extract capsules delivery system as an advanced phytotherapy approach for controlling diabetes. World Journal of Pharmaceutical and Medical Research., 2025; 11(6): 400-415.
42. Alburyhi MM, El-Shaibany A. Formulation, development and evaluation of Capsicum extract capsules delivery system as an advanced phytotherapy approach for tonic and natural stimulant. European Journal of Pharmaceutical and Medical Research., 2025; 11(6): 323-337.