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Review Article

Cydonia oblonga Miller (Quince) Leaf: A Comprehensive Review of Phytochemistry, In Vitro Pharmacology, Animal Evidence and Therapeutic Potential

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ABSTRACT

Cydonia oblonga Miller (quince) leaves represent a concentrated, renewable source of bioactive polyphenols, dominated by caffeoylquinic acid isomers and quercetin and kaempferol glycosides, with 5-*O*-caffeoylquinic acid and quercetin-3-*O*-rutinoside as the principal constituents [1, 2]. Phytochemical profiling via RP-HPLC-DAD, UHPLC-QTOF-MS, and elemental analyses reveals total phenolic contents spanning 4.9 to 16.5 g/kg dry matter, alongside notable levels of calcium, magnesium, iron, and α-tocopherol [1, 2]. Preclinical pharmacological evaluations demonstrate robust *in vitro* multi-pathway antioxidant capacity (DPPH, ABTS, FRAP, CUPRAC, metal chelation, and AAPH-induced erythrocyte membrane protection comparable to *Camellia sinensis*), selective acetylcholinesterase and tyrosinase inhibition, growth inhibition against *Staphylococcus aureus* and *Bacillus subtilis*, and concentration-dependent antiproliferative activity against human colon adenocarcinoma cells (IC50 = 239.7 ± 43.2 µg/mL) [1, 3, 4]. In whole-animal models, oral administration of standardized leaf extracts and total flavonoid fractions achieves dose-dependent reductions in systolic blood pressure, suppression of the renin-angiotensin-aldosterone axis, downregulation of pro-inflammatory cytokines (IL-1β, IL-6, TNF-α, CRP), correction of dyslipidemia, protection against hypercholesterolemia-induced renal tubular injury and testicular germinal-epithelium degradation, and potent dose-dependent antithrombotic and thrombolytic effects mediated through the modulation of thromboxane B2 and 6-keto-PGF1α [1, 4, 7, 8]. However, no human randomized controlled trial has evaluated leaf-derived preparations for cardiovascular, metabolic, or nephroprotective indications [1, 4]. This systematic review synthesizes the full spectrum of published phytochemical, analytical, *in vitro*, and *in vivo* pharmacological data on quince leaves, defines critical methodological limitations, highlights safety considerations regarding hemostasis, and establishes a prioritized roadmap toward clinical translation [1].

Keywords: Cydonia oblonga; antioxidant; cardiovascular; thrombosis; lipid metabolism; antihypertensive.

INTRODUCTION

Cydonia oblonga Miller (quince) is the sole member of the monotypic genus *Cydonia* within the family Rosaceae (subfamily Maloideae, tribe Maleae/Pireas) [1, 3, 4]. While the pomaceous fruit of quince has enjoyed extensive culinary and traditional use across the Mediterranean basin, the Middle East, Central Asia, and Southwest Europe, its foliage has historically served as an important yet underutilized bioresource in traditional pharmacopeias [1, 3, 5]. In traditional Iranian, Unani-Tibb, and Mediterranean folk medicine systems, infusions and decoctions

prepared from quince leaves have been prescribed to manage cardiovascular complaints, arterial hypertension, dysuria, respiratory distress (cough and bronchitis), nervous tension, insomnia, and gastrointestinal ailments [1, 3, 4].

Recent chemical evaluations have established that quince leaves exhibit a phenolic density that equals or exceeds that of the fruit pulp and peel, with total phenolic content ranging between 4.9 and 16.5 g/kg dry matter (mean: 10.3 g/kg dry matter) across seasonal and geographic variations in Portugal [1, 2]. Unlike the fruit, which requires harvesting during a narrow late-autumn window, foliage represents an abundant, renewable agricultural byproduct available during regular pruning cycles [1, 5].

To critically evaluate the therapeutic potential of *C. oblonga* leaves, this review organizes the available scientific literature across three distinct methodological tiers: 1. **Chemical and analytical identification:** Rigorous chromatographic (HPLC-DAD, UHPLC-QTOF-MS) and spectroscopic identification of secondary metabolites, fatty acids, tocopherols, and elemental constituents [1, 2]. 2. **Mechanistic *in vitro* assays:** Direct radical scavenging, erythrocyte antihemolytic protection, isolated enzyme kinetics (AChE, BChE, tyrosinase, α-amylase, α-glucosidase), antibacterial disk diffusion, and cellular cytotoxicity in malignant cell lines [1, 3, 4]. 3. **Whole-animal *in vivo* pharmacology:** Preclinical evaluations in validated models of renovascular and genetic hypertension, diet-induced hyperlipidemia, experimentally induced thrombosis, hypercholesterolemic organ damage (kidney and testes), and streptozotocin-induced diabetes [1, 4, 7, 8].

Crucially, this review explicitly separates preclinical animal and cellular findings from clinical efficacy claims, addressing the persistent absence of human interventional trials [1, 4].

Review Scope and Literature Approach

This comprehensive review was conducted through structured electronic searches across PubMed/MEDLINE, Web of Science, Scopus, Google Scholar, and institutional repositories [1, 4]. The search encompassed all literature published through late 2026, utilizing controlled terms including "*Cydonia oblonga*", "quince leaf", "foliage", "phytochemistry", "polyphenols", "caffeoylquinic acids", "antioxidant", "cardiovascular", "antihypertensive", "thrombosis", "platelet", "renal protection", "hepatoprotective", "antimicrobial", and "toxicology" [1, 4].

Inclusion and Exclusion Boundaries

- **Inclusion criteria:** Original peer-reviewed investigations and systematic datasets specifically evaluating extracts, fractions, or isolated pure constituents derived from the leaves (*folia*) of *Cydonia oblonga* Mill. [1].
- **Exclusion criteria:** Studies focusing exclusively on related taxa (*Chaenomeles speciosa*, *Chaenomeles japonica*, *Pseudocydonia sinensis*) or solely on quince fruit pulp, peel, or seeds, unless incorporated as direct experimental comparators to leaf-derived samples [1, 5].

Synthesis Framework

Because existing animal and *in vitro* studies exhibit substantial heterogeneity in extraction solvents, dosing regimens, animal strains, and disease induction protocols, a formal quantitative meta-analysis was neither feasible nor methodologically valid [1]. Instead, this review implements a qualitative, evidence-tiered narrative synthesis mapped against standard analytical and pharmacological quality benchmarks, identifying points of mechanistic convergence, analytical discrepancies, and translation barriers [1, 4].

Botany, Traditional Medicine and Preparation Formats

Botanical characteristics and preparation practices materially affect the composition of *Cydonia oblonga* leaf extracts and the interpretation of pharmacological findings [1, 3, 4].

Botanical Characteristics

Cydonia oblonga Miller develops as a deciduous, thornless shrub or small spreading tree reaching 4–8 m in height with an equivalent crown spread [1, 3, 4]. Its leaves are alternate, petiolate, ovate to oblong-elliptic (5–12 cm long, 3–7 cm wide), with entire margins, an obtuse to subacute apex, and a rounded base [1, 3]. The adaxial (upper) leaf surface is dark green and glabrescent at maturity, whereas the abaxial (lower) surface is densely covered with white-to-grayish tomentose hairs [1, 3].

Traditional and Ethnomedicinal Applications

In historical ethnomedicinal records across Iran, Turkey, and Central Asia, leaf decoctions have been taken for nervousness, dysuria, insomnia, cough, colds, abdominal cramps, diarrhea, and fever [1, 3]. Cardiovascular use, including traditional use for hypertension, is also described, although such records document cultural practice and do not demonstrate clinical efficacy [4]. Claims of specific dose ranges and topical uses should not be generalized unless linked to a primary ethnobotanical source; the available experimental literature does not establish standardized traditional dosing [1, 3].

Extraction Methodologies and Yield Considerations

The pharmacological profile of quince leaf preparations depends fundamentally on extraction solvent polarity, temperature, and matrix contact time [1].

Matrix / Extraction Approach	Representative Conditions	Target Analytes / Biological Aim	Key Practical Limitation
Aqueous decoction	Boiling-water preparations; rabbit pilot used 4.95 g leaves in 600 mL, boiled for 2 h	Traditional mimic; polar constituents; renal and testicular pilot studies [1]	Batch composition and thermal stability insufficiently standardized [1]
Aqueous-alcoholic (methanol/ethanol)	Laboratory maceration/extraction	Polyphenol recovery; antioxidant and cellular screening [1, 2]	Methanol extracts are not directly suitable for human consumption; solvent removal and residue testing are required [1]
Repeated water extraction	Water extraction at 60 °C in antithrombotic study	Water-soluble leaf fraction tested in thrombosis models [1]	Extraction yield and constituent exposure need replication [1]
Deep eutectic solvents	Choline chloride-based solvent systems described as emerging analytical options	Green extraction of phenolics [1]	Limited biological validation and downstream isolation data [1]

Aqueous and alcoholic extracts are not interchangeable: their chemical composition, extraction yield, and biological activity can differ substantially. Future studies should report authenticated botanical material, voucher specimens, leaf maturity, geographic origin, solvent-to-solid ratio, extraction time and temperature, dry yield, and chromatographic fingerprint [1, 2].

Phytochemical Composition of the Leaf

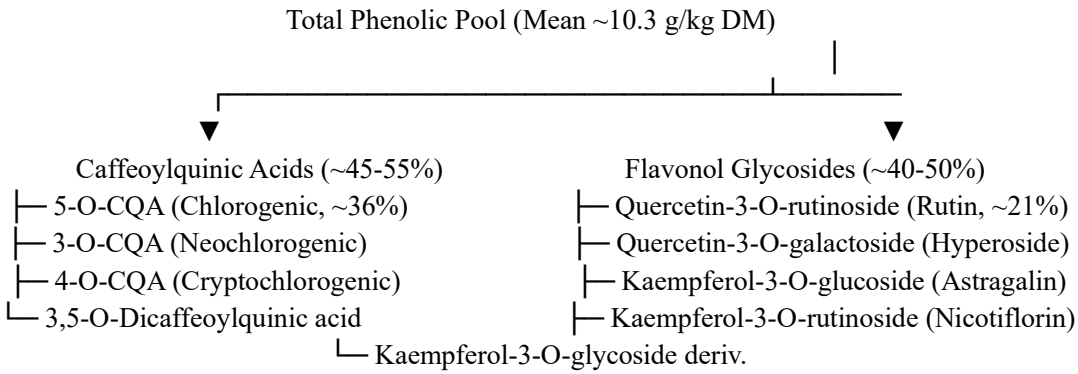
The pharmacological efficacy of *C. oblonga* leaf is anchored in its dense secondary metabolite profile, which consists predominantly of hydroxycinnamic acid derivatives and flavonol glycosides, alongside significant mineral, vitamin, and lipid fractions [1, 2].

Detailed Phenolic Profile and Structural Diversity

Pioneering chromatographic profiling by Oliveira et al. [2] on 36 quince leaf samples collected across three geographic regions in Portugal (Trás-os-Montes, Minho, and Beira Litoral) over three developmental months (June, August, and October) established a conserved chemical fingerprint consisting of nine principal phenolic compounds [1, 2]:

1. **3-*O*-Caffeoylquinic acid (Neochlorogenic acid):** Hydroxycinnamic monoester (MW 354.31 g/mol) [1, 2].
2. **4-*O*-Caffeoylquinic acid (Cryptochlorogenic acid):** Hydroxycinnamic monoester [1, 2].
3. **5-*O*-Caffeoylquinic acid (Chlorogenic acid):** Quantitative dominant monoester; accounts for 36.2% of the total phenolic fraction in representative samples [1, 2].
4. **3,5-*O*-Dicaffeoylquinic acid:** Caffeic acid diester of quinic acid (MW 516.45 g/mol); high antioxidant efficiency [1, 2].
5. **Quercetin-3-*O*-galactoside (Hyperoside):** Flavonol glycoside (MW 464.38 g/mol) [1, 2].
6. **Quercetin-3-*O*-rutinoside (Rutin):** Quantitative dominant flavonoid; accounts for 21.1% of total phenolics [1, 2].
7. **Kaempferol-3-*O*-glucoside (Astragalin):** Flavonol monoglycoside (MW 448.38 g/mol) [1, 2].
8. **Kaempferol-3-*O*-rutinoside (Nicotiflorin):** Flavonol diglycoside (MW 594.52 g/mol) [1, 2].
9. **Kaempferol-3-*O*-glycoside derivative:** Structural isomer identified via HPLC-DAD retention and UV absorption spectra [1, 2].

10.



Quantitative total phenolic concentrations exhibit dynamic seasonal and geographic fluctuation: - **Concentration range:** 4.9 g/kg dry matter (June, lowest region) to 16.5 g/kg dry matter (October, highest region), with an overall mean of 10.3 g/kg dry matter [1, 2]. - **Seasonal trajectory:** Total phenolic content systematically increases from June through August and peaks in October, driven by sunlight exposure and late-season secondary metabolite accumulation [1, 2].

Extended Metabolomics

Subsequent non-targeted metabolomic investigations utilizing ultra-high-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry (UHPLC-QTOF-MS) have expanded the leaf metabolome beyond simple phenolics, identifying [1]: - **Lignan and Stilbene traces:** Low-abundance secoisolariciresinol and resveratrol glucoside derivatives [1]. - **Low-molecular-weight Phenolic Acids:** Vanillic, syringic, ferulic, *p*-coumaric, and gallic acid derivatives [1, 3]. - **Proanthocyanidin oligomers:** Dimeric and trimeric procyanidin B-type linkages detected in aqueous-methanolic extracts [1, 4].

Comparative evaluations across plant organs confirm that *C. oblonga* leaves possess the highest total phenolic content and the strongest radical scavenging capacity relative to fruit peel, pulp, and seed mucilage [1, 3, 4].

Minerals, Lipids, and Lipophilic Micronutrients

Elemental and lipid profiling conducted by Ferreira and colleagues provides quantitative benchmarks for quince leaf nutritional chemistry [1]:

Nutritional / Elemental Fraction	Green Leaves (Harvest Peak)	Brown / Senescent Leaves	Biological Significance
Calcium	≈ 15.00 g/kg DM	≈ 21.48 g/kg DM	Structural cell wall component; accumulates with maturity [1]
Magnesium	≈ 5.50 g/kg DM	≈ 4.35 g/kg DM	Central chlorophyll atom; decreases during foliar senescence [1]
Iron	≈ 119.0 mg/kg DM	≈ 40.0 mg/kg DM	Redox co-factor; mobilized prior to leaf abscission [1]
Potassium	Increasing with maturity	Peak in late autumn	Osmotic regulation and stomatal control [1]
Vitamin E (Tocopherols)	Predominantly tocopherol	Minor tocopherol	Membrane antioxidant protecting photosynthetic lipids [1]
Fatty Acid Profile	Palmitic (16:0) and Linolenic (18:3n-3)	Palmitic (16:0) dominant	Essential polyunsaturated fatty acid donor [1]

These high mineral (Ca, Mg) and lipophilic antioxidant (α-tocopherol, linolenic acid) concentrations reinforce the value of quince foliage as a multi-component botanical matrix [1]

Analytical Methodologies

Rigorous characterization of *Cydonia oblonga* leaf phytochemicals and biological endpoints relies on an array of modern analytical platforms [1].

Analytical Technique	Target Analyte / Biological Parameter	Application in Quince Leaf Literature	Interpretive Caveats & Limitations
RP-HPLC/UV-DAD	9 Major caffeoylquinic acids and flavonol glycosides	Routine qualitative fingerprinting and absolute quantification [1, 2]	Co-elution of isomeric dicaffeoylquinic acids without high-resolution MS [1]
UHPLC-QTOF-MS	Extended phenolic, lignan, and stilbene metabolome	Non-targeted metabolomics, accurate mass elemental composition (< 3 ppm) [1]	Ion suppression; relative peak areas overestimate minor ionizable species [1]
ICP-MS / ICP-OES	Heavy metals macro/micro elements (Ca, Mg, Fe, K)	Elemental profiling, safety threshold screening [1]	Digest matrix effects; requires certified reference materials for accuracy [1]
GC-FID / GC-MS	Fatty acid methyl esters (FAMEs), volatile terpenes	Leaf cuticular wax and fatty acid determination [1]	Derivatization efficiency variations; volatile loss during sample drying [1]
HPLC-DAD-FLD	Tocopherols (isomers)	Lipophilic antioxidant profiling [1]	Light- and oxidation-induced degradation during extraction [1]
Spectrophotometric Assays	Folin–Ciocalteu, DPPH, ABTS, FRAP, CUPRAC	Screening of total reducing capacity and radical scavenging [1, 3]	Non-specific; reducing sugars and proteins inflate "total phenolic" values [1]

Analytical Constraints and Inter-Laboratory Comparability

A significant challenge in the quince leaf literature is the widespread reliance on non-specific spectrophotometric assays (e.g., Folin–Ciocalteu expressed as gallic acid equivalents [GAE]) [1]. Because Folin–Ciocalteu measures total one-electron reducing capacity rather than direct phenolic bonding, non-phenolic leaf constituents (reducing sugars, ascorbic acid, amino acids) introduce upward bias [1]. Quantitative comparisons between different laboratories must prioritize validated chromatographic methods (RP-HPLC-DAD with external reference standards) [1, 2].

In Vitro Antioxidant and Antihemolytic Activity

The radical scavenging, reducing capacity, and biological membrane protection of *Cydonia oblonga* leaf extracts have been characterized across multiple validated *in vitro* models [1, 3, 4].

Multiplatform Radical Scavenging and Reducing Capacity

Comparative studies by Costa and colleagues [1, 4] evaluated methanolic extracts of quince leaves directly against *Camellia sinensis* (green tea), widely regarded as the gold standard botanical antioxidant.

Assay Platform	Quince Leaf Extract Value	*Camellia sinensis* (Green Tea)	Analytical Interpretation
Reducing Power Assay	227.8 ± 34.9 g/kg dry leaf	112.5 ± 1.5 g/kg dry leaf	**Quince leaf exhibited** $> 2\times$ **higher ferric reducing power** (< 0.05) [1]
DPPH Radical Scavenging	21.6 ± 3.5 g/mL	12.7 ± 0.1 g/mL	Potent radical neutralization; slightly higher than pure green tea [1]
AAPH Erythrocyte Hemolysis	30.7 ± 6.7 g/mL	24.3 ± 9.6 g/mL	**No statistically significant difference** in protecting biological membranes [1]
ABTS Scavenging Capacity	High Trolox equivalent capacity	Reference comparator	Rapid quenching of ABTS cation radical [1, 3]
CUPRAC (Cupric Reducing)	Strong dose-dependent reduction	Reference comparator	Electron-transfer mechanism at physiological pH [1]
FRAP (Ferric Reducing)	High Fe^{2+} generation	Reference comparator	Strong single-electron transfer capacity [1]
Metal Chelation	Concentration-dependent binding	EDTA reference	Prevents Fenton-reaction-mediated. generation [1]

Erythrocyte Membrane Antihemolytic Protection

In the biological AAPH (2,2'-azobis(2-amidinopropane) dihydrochloride) assay, thermal peroxyl radicals attack the lipid bilayer of human red blood cells, causing lipid peroxidation and cell lysis [1, 4]. Quince leaf methanolic extract demonstrated powerful, concentration-dependent antihemolytic protection (30.7 ± 6.7 g/mL) [1]. The 5-*O*-caffeoylquinic acid and quercetin-3-*O*-rutinoside molecules insert into the polar head groups of the erythrocyte phospholipid membrane, intercepting propagating lipid peroxyl radicals and preserving membrane structural integrity [1, 4].

Enzyme-Inhibitory and Metabolic Effects (In Vitro)

Beyond direct antioxidant chemistry, *C. oblonga* leaf extracts have shown measurable inhibition of several enzymes relevant to metabolic, dermatological, and neuroactive research [1].

Cholinesterases

In colorimetric assays, methanolic leaf extract produced acetylcholinesterase (AChE) inhibition of 2.37 ± 0.04 mg galantamine equivalents (GALAE)/g dry matter and butyrylcholinesterase (BChE) inhibition of 2.35 ± 0.07 mg GALAE/g dry matter [1]. These findings are preliminary biochemical screening results, not evidence of cognitive benefit; no animal behavioral study or human study of leaf-derived preparations has established such an effect [1].

Tyrosinase

Tyrosinase inhibition was reported as 68.32 ± 0.30 mg kojic acid equivalents (KAE)/g dry matter [1]. This result may justify further investigation of leaf extracts as cosmetic research ingredients, but efficacy, skin penetration, irritation, and formulation stability remain untested. A recent review of quince-derived dermatological applications likewise emphasizes that clinical validation is limited [6].

Carbohydrate-Digesting Enzymes

The reported α-amylase inhibitory capacity was 0.48 ± 0.00 mmol acarbose equivalents (ACAE)/g dry matter; α-glucosidase inhibition was not detected [1]. An independent investigation also reported no significant α-amylase or α-glucosidase inhibition despite measurable antioxidant activity [1]. Thus, the glucose-

lowering result observed in diabetic rats (Section 13) should not be attributed to inhibition of these digestive enzymes without further evidence.

Antimicrobial Activity (In Vitro)

Available leaf-specific antimicrobial evidence is limited to antibacterial screening and does not yet establish clinical or product-level efficacy [1]. A study of clinical bacterial isolates reported inhibition zones of 15 mm for an alcoholic leaf extract against *Staphylococcus aureus*, and 20 mm for an aqueous extract against *S. aureus* and 10 mm against *Bacillus subtilis* [1]. A separate study evaluating aqueous quince leaf extracts in a wool-dyeing context also reported antibacterial activity [1].

These disk-diffusion results are preliminary: inhibition zones depend on extract concentration, diffusion, and assay conditions, and cannot be directly equated with antibiotic potency. The available leaf evidence does not provide a complete minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), or time-kill profile against standardized reference strains [1]. Nor does it establish a leaf-specific antifungal effect; antifungal claims for other quince parts should not be transferred to the leaves [1, 3].

Endpoint	Reported leaf finding	Evidence and qualification
S. aureus	15 mm (alcoholic); 20 mm (aqueous)	Disk-diffusion screening; concentrations and comparators require confirmation [1]
B. subtilis	10 mm (aqueous)	Disk-diffusion screening [1]
Antifungal activity	No leaf-specific result identified in the reviewed evidence	Not established [1, 3]
MIC/MBC	Not reported in the available leaf studies	Required for potency benchmarking [1]

Host-cell cytotoxicity, activity against resistant isolates, formulation stability, and interference with food or topical matrices also require study before practical application can be proposed [1].

Antiproliferative and Cellular Effects

A methanolic quince leaf extract was assessed alongside quince fruit preparations against human cancer-cell models [1, 3]. In a human colon carcinoma cell assay, the extract showed concentration-dependent growth inhibition with an IC50 of 239.7 ± 43.2 µg/mL; HPLC-DAD characterization identified 5-*O*-caffeoylquinic acid among the major phenolics [1]. No comparable inhibitory effect was reported against the tested renal adenocarcinoma cells [1].

This is an initial cell-screening signal, not evidence of cancer treatment. The reported IC_{50} cannot be interpreted as a clinical dose, and the available data do not establish selectivity over non-malignant cells, a molecular mechanism, or efficacy in an animal tumor model [1]. The finding therefore remains at the discovery stage and warrants replication using chemically standardized extracts and validated cell-viability, apoptosis, and selectivity assays [1, 3].

In Vivo Cardiovascular and Metabolic Effects

Animal studies provide the principal whole-organism evidence for quince leaf pharmacology, with reported effects on blood pressure, circulating lipids, inflammatory markers, and hepatic endpoints [1, 4]. These data are preclinical and should not be presented as proof of benefit in people.

Renovascular Hypertension

In a two-kidney, one-clip (2K1C) rat model, an ethanol leaf extract was administered orally at 80 or 160 mg/kg/day for eight weeks. The compiled study report describes systolic blood pressure (SBP) of 193 ± 7 mmHg in untreated model animals and 166 ± 4 mmHg at 160 mg/kg/day, together with lower blood viscosity and improved erythrocyte deformability [1, 7]. A separate renal-hypertensive rat study reported dose-related reductions in blood pressure, angiotensin II, plasma renin activity, aldosterone, and endothelin, with an increase in nitric oxide; the highest dose was described as comparable to captopril [1]. These findings suggest possible effects on vascular tone and the renin–angiotensin–aldosterone system, but require independent replication with standardized extracts and complete dose/exposure reporting [1, 4].

Inflammation in Spontaneously Hypertensive Rats

A 16-week study of total quince-leaf flavonoids in spontaneously hypertensive rats used doses of 40, 80, and 160 mg/kg and reported reductions in IL-1β, IL-6, TNF-α, and C-reactive protein; IL-10 was also measured [1, 8]. This supports a preclinical anti-inflammatory signal in a hypertension model, not a demonstrated anti-inflammatory treatment effect in humans [1, 8].

Hyperlipidemia and Hepatic Measures

In a 56-day study involving 70 Sprague-Dawley rats, with simvastatin as comparator, quince leaf extract was reported to lower total cholesterol, triglycerides, LDL cholesterol, and malondialdehyde, while increasing HDL cholesterol, superoxide dismutase, glutathione peroxidase, lipoprotein lipase, and hepatic lipase [1]. ALT and AST declined, and hepatic steatosis was attenuated in the reported model [1]. The supplied review summarizes these results but does not provide every dose and numerical endpoint; accordingly, effect sizes should not be inferred beyond the reported directions [1].

A 2022 review of quince cardiovascular evidence found that the included studies were animal or *in vitro* investigations and identified no human clinical trial [4]. Its synthesis describes favorable lipid and liver-enzyme findings, while also noting that effects on coronary atherosclerotic plaque were not significantly improved in one comparison [4].

Model	Exposure / duration	Reported outcomes	Interpretation
2K1C hypertensive rats	Ethanol leaf extract, 80/160 mg/kg/day, 8 weeks	SBP 193 ± 7 to 166 ± 4 mmHg at the higher dose; hemorheological changes [1, 7]	Preclinical antihypertensive signal
Renal-hypertensive rats	Leaf extract, 8 weeks; captopril comparator	Lower BP, angiotensin II, renin activity, aldosterone, endothelin; higher NO [1]	Possible vascular/RAAS effects
Spontaneously hypertensive rats	Total flavonoids, 40/80/160 mg/kg, 16 weeks	Lower pro-inflammatory cytokines and CRP [1, 8]	Animal anti-inflammatory signal
Hyperlipidemic rats	Leaf extract, 56 days; simvastatin comparator	Improved lipid, oxidative-stress, and liver-associated endpoints [1]	Needs dose-level replication and full reporting

Antithrombotic and Hemostatic Effects

A leaf-derived preparation was evaluated in mouse and rat thrombosis models after oral administration of 20, 40, or 80 mg/kg/day for 14 days, with aspirin at 5 mg/kg as a comparator [1]. Reported changes were dose-related across several hemostatic endpoints:

Endpoint	20 mg/kg/day	40 mg/kg/day	80 mg/kg/day	Aspirin comparator
Bleeding-time increase	2.17-fold	2.78-fold	3.63-fold	2.58-fold
Clotting-time increase	1.44-fold	2.47-fold	2.48-fold	1.91-fold
Reduction in pulmonary-embolism mortality	27%	40%	53%	—
Increase in reported thrombolysis	45%	55%	63%	—

Arterial and venous thrombus weights were also reported to decline with dose [1]. The study further reported reduced thromboxane B2 (TXB2) and increased 6-keto-prostaglandin F1α, a metabolite used as an index of prostacyclin activity [1]. This pattern is consistent with altered platelet and vascular prostanoid balance, but does not by itself establish the precise molecular target or human clinical effect.

The prolonged bleeding and clotting times are simultaneously a potential safety concern. Until interaction studies are available, concentrated quince-leaf preparations should not be presumed safe alongside aspirin, clopidogrel, anticoagulants, or other medicines affecting hemostasis; perioperative use also warrants particular caution [1]. The underlying animal findings require

replication with blinded assessment, complete extract characterization, and explicit reporting of adverse events.

Renal and Reproductive Tissue Protection

Two small rabbit pilot studies examined quince-leaf decoction in the setting of diet-induced hypercholesterolemia [1]. Their findings are hypothesis-generating because of the very small and unequal group sizes.

Renal Histology

The renal pilot included 11 New Zealand White rabbits: three hypercholesterolemic animals, six hypercholesterolemic animals receiving decoction, and two controls [1]. The protocol included six weeks of a cholesterol diet followed by six weeks on a normal diet. The decoction was prepared from 4.95 g of leaves in 600 mL of boiling water over two hours and administered at 100 mL per rabbit [1]. Histological assessments used H&E, PAS, and Masson staining. Untreated hypercholesterolemic animals showed mild glomerular and moderate tubular damage; among treated animals, two of six showed mild glomerular changes, with milder tubular injury and no reported basement-membrane thickening or fibrosis [1]. The study did not provide a robust functional assessment of renal filtration and is too small to establish renal efficacy.

Testicular Histology

A separate pilot with 11 rabbits used a similar group structure and decoction regimen [1]. The Johnsen score was 4.20 ± 1.92 in untreated hypercholesterolemic animals, 7.33 ± 0.52 in decoction-treated animals, and 7.05 ± 0.07 in controls (P = 0.01) [1]. Untreated animals reportedly showed increased intertubular connective tissue, vascular dilation, and disorganization and thinning of the germinal epithelium [1]. The findings suggest preservation of testicular histology in this model, but the study lacked semen analysis and hormone measurements and cannot establish improved fertility [1].

Pilot model	Main measure	Reported observation	Principal limitation
Hypercholesterolemic rabbit kidney	H&E, PAS, Masson histology	Less severe tubular/glomerular injury in decoction group [1]	n = 11; unequal groups; limited functional biomarkers
Hypercholesterolemic rabbit testis	Johnsen score and tissue morphology	4.20 ± 1.92 untreated vs 7.33 ± 0.52 treated; P = 0.01 [1]	No hormone or semen endpoints; unequal small groups

Antidiabetic Effects

Aslan and colleagues evaluated an ethanol extract of quince leaves in normal and streptozotocin (STZ)-diabetic rats, administering 250 or 500 mg/kg for five days [1]. At 500 mg/kg, blood glucose was reported to fall by 33.8% in diabetic rats [1]. In heart tissue, thiobarbituric-acid-reactive substances (TBARS), a lipid-peroxidation measure, decreased by 45.7%; reduced glutathione was not restored to normal levels [1]. These results suggest partial glycemic and oxidative-stress effects in a short-duration animal model, rather than comprehensive diabetic protection.

The weak α-amylase activity and absence of detected α-glucosidase inhibition in leaf-extract assays argue against assuming that the animal glucose effect is mediated by inhibition of intestinal carbohydrate digestion [1]. Other mechanisms, such as altered oxidative stress or glucose handling, remain hypotheses and require direct testing. The current evidence does not establish efficacy in chronic diabetes, prevention of diabetic complications, or safety with standard glucose-lowering medicines [1, 4].

Additional Reported Activities

Several additional activities have been reported, but the strength and relevance of their evidence vary substantially.

Hepatic Protection

In hyperlipidemic rats, quince-leaf extract was associated with lower ALT and AST, improved antioxidant enzyme measures, and attenuated hepatic steatosis [1]. These outcomes occurred within a dyslipidemia study and do not amount to proof of protection against drug-induced or infectious liver injury. Dedicated hepatotoxicity-challenge models and functional liver outcomes are needed [1].

Enzyme-Based Neuroactive and Cosmetic Leads

The reported AChE and BChE inhibition warrants exploratory biochemical work, but no leaf-specific animal study has shown a cognitive or neurobehavioral benefit [1]. Tyrosinase inhibition may be relevant to cosmetic formulation research; however, enzyme results alone do not establish skin efficacy, tolerability, or consumer safety [1, 6].

Antimicrobial and Antiproliferative Leads

The antibacterial disk-diffusion findings and colon-cell growth-inhibition result are screening signals only [1]. Antimicrobial development requires MIC/MBC, cytotoxicity, resistance-panel, and stability studies. Antiproliferative development requires confirmation across cell lines, normal-cell selectivity, mechanism studies, and appropriate animal models [1]. A recent broad dermatology review also notes that human validation of quince-derived skin applications remains limited [6].

Safety Profile and Toxicological Considerations

The available evidence does not establish a comprehensive safety profile for medicinal use of quince-leaf extracts. The reviewed leaf literature does not provide a sufficient dedicated package of acute and repeated-dose toxicity, genotoxicity, reproductive toxicology, pharmacokinetics, or drug-interaction studies [1].

Hemostatic Interactions

The animal findings of prolonged bleeding and clotting times create a plausible interaction concern for people using aspirin, clopidogrel, anticoagulants, or other medicines that alter coagulation or platelet function [1]. This is a precaution based on preclinical evidence, not a quantified human interaction. Until evaluated, concurrent use of concentrated leaf preparations should be approached cautiously, especially before surgery or in patients with bleeding disorders [1].

Botanical Authentication and Contaminants

Any investigational preparation should be authenticated to species and plant part, supported by a voucher specimen, and screened for microbial contamination, pesticides, and toxic elements such as lead, cadmium, and arsenic using validated elemental methods [1]. Leaf harvest location and maturity may influence constituent profiles, so batch fingerprinting is also essential [1, 2].

Distinguishing Leaf from Seed Safety

A general quince review describes the plant as broadly regarded as safe while noting that large quantities of quince seeds may pose toxic effects because of nitrile constituents [3]. This seed-specific warning should not be represented as evidence that quince leaves contain the same hazard; rather, it reinforces the need to verify plant-part identity and avoid extrapolating safety between fruit, seed, and leaf preparations [3].

Integrated Evidence Map, Limitations and Future Directions

The breadth of reported quince-leaf activity exceeds the depth of validation. A concise evidence map makes clear where findings are consistent and where basic confirmation is still needed.

Domain	Evidence available	Maturity	Main evidence gap
Antioxidant / antihemolytic	Multiple chemical assays and erythrocyte protection [1, 4]	Consistent in vitro signal	Standardized extraction, assay harmonization, biological exposure
Blood pressure	Rodent renovascular and spontaneous-hypertension studies [1, 4, 7, 8]	Moderate preclinical	Independent replication, PK, dose selection, human study
Lipid and liver endpoints	Hyperlipidemic rat studies; statin comparators reported [1, 4]	Moderate preclinical	Full effect-size reporting, plaque outcomes, human validation
Thrombosis / hemostasis	Dose-related animal thrombosis and bleeding-time results [1]	Moderate preclinical, safety-sensitive	Reproducibility and drug-interaction/bleeding-risk assessment
Renal protection	Rabbit histology pilot [1]	Preliminary	Larger randomized study and functional renal markers
Testicular protection	Rabbit histology and Johnsen score pilot [1]	Preliminary	Hormones, semen, fertility, and replication

Domain	Evidence available	Maturity	Main evidence gap
Diabetes	Short STZ-rat study; enzyme assay data [1]	Preliminary	Mechanism, longer duration, medication interaction, replication
Antibacterial	Disk-diffusion findings [1]	Preliminary	MIC/MBC, standardized strains, cytotoxicity
Antiproliferative	Colon-cell screening; no renal-cell effect [1]	Discovery stage	Selectivity, mechanism, replication, animal tumor model
Human efficacy and safety	No leaf-specific clinical trial identified [1, 4]	Not established	Carefully staged clinical research after safety work

Cross-cutting limitations include differences in extraction solvents and dose expressions, incomplete chemical standardization, small animal groups in organ-protection pilots, inconsistent reporting of botanical authentication and blinding, and a shortage of pharmacokinetic and toxicological data [1, 4]. Values from different radical-scavenging assays or total-phenolic methods are not directly interchangeable; Folin–Ciocalteu results represent reducing capacity and not a complete chemical inventory [1].

Priority steps are: (1) define authenticated, reproducible leaf-extract specifications and batch fingerprints; (2) conduct GLP-compliant acute and repeated-dose safety and pharmacokinetic studies; (3) replicate key cardiovascular and metabolic results in adequately powered, blinded animal studies; (4) investigate the hemostatic interaction signal before human dosing; and (5) only then consider a registered, ethically approved early-phase human study with prespecified outcomes and interaction monitoring [1, 4].

CONCLUSION

Quince leaves contain a well-documented phenolic profile dominated by caffeoylquinic acids and flavonol glycosides, with antioxidant activity demonstrated across several chemical assays and erythrocyte protection models [1, 2, 4]. The wider preclinical literature reports enzyme inhibition, antibacterial and cell-screening effects, as well as animal findings involving blood pressure, inflammatory markers, lipids, hemostasis, kidney and testicular histology, and glucose regulation [1, 4, 7, 8]. The depth of evidence is uneven: antioxidant chemistry and cardiovascular animal outcomes are more developed than renal, reproductive, antimicrobial, and anticancer claims.

Most importantly, animal and laboratory outcomes are not clinical proof. No human clinical trial of quince-leaf preparations has established efficacy, and essential safety data—including repeated-dose toxicity, pharmacokinetics, and interactions with antithrombotic medicines—remain unavailable [1, 4]. Quince leaf should therefore be treated as a promising research subject, not a proven treatment. Progress toward clinical use depends on standardized extracts, independent replication, comprehensive safety assessment, and carefully staged human research.

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