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Review Article

The Efficacy of Quercetin in Attenuating Oxidative Stress and Clinical Symptoms in Allergic Rhinitis: A Systematic Review

Niken Dyah Aryani K[1]*, Harijono Kariosentono[2], Bambang Purwanto[3], Made Setiamika[4], Eti Poncorini[5], Paramasari Dirgahayu[6], Risya Cilmiaty[7] and Teti Madiadipoera[8]

[1]Doctoral Program of Medical Sciences, Sebelas Maret University, Surakarta, Indonesia

[2]Department of Otorhinolaryngology Head and Neck Surgery, Faculty of Medicine, Sebelas Maret University, Surakarta, Indonesia

[3]Department of Dermatology and Venerology, Faculty of Medicine, Sebelas Maret University, Surakarta, Indonesia

[4]Department of Internal Medicine, Faculty of Medicine, Sebelas Maret University Surakarta, Indonesia

[5]Department of Public Health, Faculty of Medicine, Sebelas Maret University, Surakarta, Indonesia

[6]Department of Parasitology, Faculty of Medicine, Sebelas Maret University, Surakarta, Indonesia

[7]Department of Oral and Maxillofacial Medicine, Faculty of Medicine, Sebelas Maret University, Surakarta, Indonesia

[8]Department of Otorhinolaryngology Head and Neck Surgery, Faculty of Medicine, Padjadjaran University, Bandung, Indonesia

More Information

***Corresponding author:**
Niken Dyah Aryani K, Department of Otorhinolaryngology Head and Neck Surgery, Faculty of Medicine, Universitas Sebelas Maret, Jl. Ir. Sutami No. 36A, Surakarta 57126, Indonesia, Email: docternikentht@student.uns.ac.id

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Keywords: Quercetin; Allergic rhinitis; Oxidative stress; Malondialdehyde; Systematic review

Abstract

Background: Allergic rhinitis (AR) affects approximately 10% - 30% of the global population and represents a significant healthcare burden. The condition involves complex inflammatory pathways where oxidative stress plays a crucial role, with malondialdehyde serving as a key biomarker of cellular damage. Quercetin, a naturally occurring flavonoid, demonstrates promising antioxidant and anti-inflammatory properties that may benefit allergic rhinitis management.

Methods: We conducted a systematic review following PRISMA 2020 guidelines. Four electronic databases (PubMed, Google Scholar, SagePub, and Semantic Scholar) were searched for studies published between 2000 and 2024. The PICO framework guided study selection, focusing on quercetin intervention in allergic rhinitis models. Both preclinical and clinical studies measuring malondialdehyde levels or clinical symptom improvement were included.

Results: Eighteen studies met our inclusion criteria, comprising 14 animal studies and four human clinical trials. Preclinical evidence consistently demonstrated quercetin's ability to reduce malondialdehyde levels across various tissues, including serum, lung, and liver samples. Human studies showed superior symptom improvement when quercetin-containing supplements were added to standard therapy compared to conventional treatment alone.

The primary mechanism involves nuclear factor erythroid 2-related factor 2 pathway activation, enhancing endogenous antioxidant enzyme production.

Conclusion: Current evidence supports quercetin's effectiveness in reducing oxidative stress and improving clinical outcomes in allergic rhinitis through dual antioxidant and anti-inflammatory mechanisms. While most evidence derives from animal studies, quercetin Shows promise as safe adjuvant therapy. Large-scale human clinical trials using high- high-bioavailability formulations are needed to establish standardized clinical protocols.

Key messages:

- Quercetin consistently reduces oxidative stress markers in allergic rhinitis models.
- Clinical symptoms improve significantly when quercetin supplements are added to standard therapy.
- The therapeutic mechanism involves both direct antioxidant activity and endogenous defense system enhancement.
- High-quality human clinical trials are needed to establish definitive treatment guidelines.

Introduction

Allergic rhinitis (AR) affects millions worldwide as an IgE-mediated inflammatory condition triggered by environmental allergens [1]. The disease involves complex pathways where oxidative stress plays a central role, with malondialdehyde serving as a key damage marker [2,3]. Quercetin, a natural flavonoid found in common foods, demonstrates promising antioxidant and anti-inflammatory properties [4,5]. This systematic review evaluates scientific evidence regarding quercetin's effectiveness in reducing oxidative stress markers and improving clinical symptoms in allergic rhinitis management [6].

Methods

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement guidelines. We developed a comprehensive protocol before initiating the search to ensure transparent and reproducible methodology.

Data sources and search strategy

Four electronic databases were systematically searched: PubMed, Google Scholar, SagePub, and Semantic Scholar. Our search covered publications from January 2000 through December 2024 to capture contemporary evidence while maintaining relevance. The search strategy utilized the PICO (Population, Intervention, Comparison, Outcome) framework (Table 1). We combined relevant Medical Subject Headings terms with text keywords using Boolean operators. The search string included: ("Allergic Rhinitis" OR "Nasal Allergy" OR "Hay Fever") AND ("Quercetin" OR "Oral Quercetin") AND ("Malondialdehyde" OR "Clinical Improvement" OR "Symptom Severity").

Study selection process

Two independent reviewers (N.D.A.K. and H.K.) conducted the study selection process in multiple phases. Initially, we removed duplicate records using reference management software. Subsequently, we screened titles and abstracts against predetermined inclusion criteria. Full-text articles were then retrieved and assessed for final eligibility.

Inclusion and exclusion criteria

Studies were included if they met the following criteria: experimental studies (*in vivo* human or animal models, relevant in vitro studies), participants with diagnosed allergic rhinitis or established experimental models, quercetin intervention as single compound or plant extract, outcome measures including malondialdehyde levels or allergic rhinitis symptoms, and peer- reviewed publications in English or Indonesian.

We excluded narrative reviews, editorials, observational studies without control groups, studies on conditions other than allergic rhinitis, interventions combining quercetin with other compounds without separate controls, and abstract-only publications.

Data extraction process

Structured data extraction forms were developed and piloted before use. Two reviewers independently extracted information, including: author details, publication year, study design, population characteristics, intervention specifics (dose, duration, route), comparison groups, outcome measures, and key findings. Discrepancies were resolved through discussion with a third reviewer (B.P.).

Quality assessment methods

Methodological quality was evaluated using appropriate tools for different study designs. Randomized controlled trials were assessed using the Cochrane Risk of Bias Tool, while observational and quasi-experimental studies were evaluated using the Newcastle-Ottawa Scale. Each reviewer independently scored studies, with disagreements resolved through consensus discussion.

Data synthesis approach

Due to significant heterogeneity in study populations (animal versus human), interventions (pure quercetin versus extracts, varying doses), and outcome measurements, quantitative meta-analysis was not feasible. We employed narrative synthesis methodology, organizing findings thematically by primary outcomes: effects on malondialdehyde levels and clinical symptom improvements.

Results

The systematic search initially identified 5,757 records. After removing duplicates and ineligible records, 3,416 records were screened by title and abstract. Following full-text assessment of 1,920 reports, 18 studies met all eligibility criteria and were included in this systematic review (Figure 1). The included studies comprised 14 animal experimental studies and 4 human clinical trials. Study populations ranged from 18 to 100 participants in human studies, while animal studies included 24 to 70 subjects (Table 2). Quercetin doses

Table 1: PICO Framework and Search Keywords.

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Allergic Rhinitis	Nasal Allergy	Nasal Hypersensitivity	Hay Fever
Intervention (I)	Oral Quercetin	Intranasal Quercetin	Injection Quercetin	Quercetin
Comparison (C)	Placebo	Conventional Therapy	Antihistamine	Corticosteroids
Outcome (O)	Malondialdehyde	Clinical Improvement	Nasal Symptom	Symptom Severity

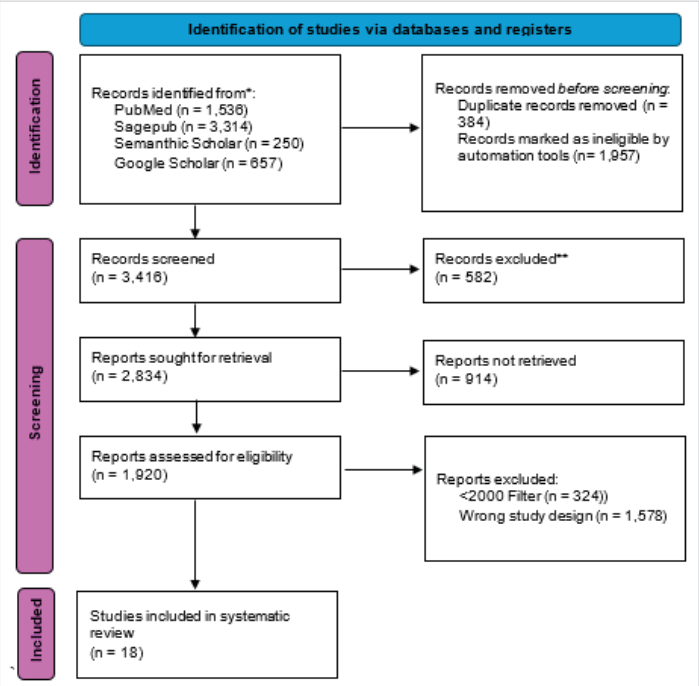

Figure 1: PRISMA 2020 Flow Diagram for Study Selection. Systematic literature search and selection process showing progression from 5,757 initial database records through screening phases to final inclusion of 18 studies meeting eligibility criteria for this systematic review.

Table 2: Summary of Database Search Results.

Database	Hits
PubMed	1,536
SagePub	3,314
Semantic Scholar	250
Google Scholar	657

varied from 4 mg/200g to 200 mg/kg in animal studies, and intervention durations ranged from 3 days to 8 weeks.

Quality assessment results

Methodological quality assessment revealed moderate to high quality across included studies. Animal studies were generally well-designed with clear descriptions of randomization, control groups, and outcome assessment (Table 3). However, several limitations were identified: some animal studies measured malondialdehyde in contexts other than allergic rhinitis, and human clinical trials often utilized multi-component formulations, making it challenging to isolate quercetin's specific effects.

Effects on malondialdehyde levels

Animal studies consistently demonstrated quercetin's ability to reduce malondialdehyde concentrations across various tissues. Bidian, et al. [11] showed that oral quercetin administration (50 mg/kg/day) for four days significantly decreased serum and lung malondialdehyde levels ($p < 0.001$) in allergic rhinitis rat models compared to untreated controls. Additional investigations confirmed these antioxidant effects across different contexts. Helianti, et al. [12] demonstrated that quercetin-rich onion peel infusions significantly lowered serum malondialdehyde in cigarette smoke-exposed rats. Similar protective effects were observed in liver and muscle tissues of hyperthyroid rats [13], kidney tissues following pesticide exposure [14], and cardiac tissues after aluminum intoxication [15]. The consistency of malondialdehyde reduction across diverse tissues and oxidative. Stress conditions indicate quercetin's fundamental cytoprotective mechanisms against lipid peroxidation. This systemic antioxidant capacity appears to be a core biochemical property applicable to allergic rhinitis pathophysiology (Table 4).

Clinical symptom improvements

Human clinical trials demonstrated significant therapeutic benefits when quercetin supplementation was added to standard treatments. Marogna and Ciprandi [16] investigated adults with grass pollen-induced allergic rhinitis, finding that multicomponent nutraceuticals containing quercetin, perilla, and vitamin D3 added to standard therapy produced 39% greater symptom improvement compared to conventional treatment alone. Gori, et al. [17] conducted randomized controlled trials in children with allergic rhinitis, reporting that quercetin-based nutraceutical (Quertal®) combined with antihistamines resulted in significantly superior symptom resolution versus antihistamine monotherapy. These clinical improvements were sustained throughout three-month treatment periods. Animal studies provided additional mechanistic support. Ravikumar and Kavitha [18] demonstrated that oral quercetin significantly reduced nasal hyperresponsiveness in mouse allergic rhinitis models. Sutanegara and Fredlina [19] found that flavonoid-rich Eugenia uniflora leaf extracts were equally effective as corticosteroids in reducing nasal symptom scores in rat models (Tables 5,6).

Mechanistic insights

Evidence indicates quercetin exerts therapeutic effects through multiple complementary mechanisms. Primary actions include direct antioxidant activity via free radical scavenging and transition metal chelation [20]. Additionally, quercetin activates nuclear factor erythroid 2 2-related factor 2 (Nrf2) signaling pathways, enhancing endogenous antioxidant enzyme production, including superoxide dismutase, catalase, and glutathione peroxidase [21].

Anti-allergic properties involve mast cell membrane stabilization, reducing histamine and inflammatory mediator release [22]. Quercetin also modulates immune responses by suppressing Th2 cytokine production and inhibiting immunoglobulin E synthesis, targeting allergic cascades at fundamental levels [23].

Discussion

This systematic review presents robust evidence demonstrating quercetin's therapeutic potential in allergic

Table 3: Characteristics of Included Studies.

Study	Design	Population	Intervention Details	Primary Outcomes Measured
Oremosu, et al. 2018 [7]	Animal Experimental	70 male Wistar rats	Quercetin 50 mg/kg, oral, daily for 56 days	Cerebellar MDA, antioxidant enzymes
Wahdaningsih & Untari, 2021 [8]	Animal Quasi-experimental	35 rats	Quercetin 4 mg/200g (as positive control)	MDA, catalase
El Gezery & Sheha, 2021 [9]	Animal Experimental	40 male Sprague Dawley rats	Quercetin 50-200 mg/kg, oral, daily for 28 days	MDA, organ function markers
Helianti, et al. 2024 [10]	Animal Quasi-experimental	24 male Wistar rats	Onion peel infusion (quercetin-rich), 125-2000 mg/kg for 28 days	Serum MDA, lung histology
Shebl, et al. 2018 [11]	Animal Quasi-experimental	40 male albino rats	Quercetin 25 mg/kg, oral, alternate days for 3 weeks	Liver & muscle MDA, exercise tolerance
Sutanegara & Fredlina, 2022 [12]	Animal RCT	28 male Wistar rats	*Eugenia uniflora* leaf extract (flavonoid-rich), 100/200 mg/kg	AR symptoms, IgE
Yusin, et al. 2021 [13]	Human RCT	47 adults with AR	Broccoli sprout extract (sulforaphane), 3 weeks	AR symptoms (TNSS, PNIF)
Paunović, et al. 2016 [14]	Animal Quasi-experimental	18 male Wistar rats	Quercetin 40 mg/kg, intraperitoneal, daily for 3 days	Erythrocyte MDA, lipid profile
Handayani, et al. 2023 [15]	Animal Experimental	Rats	Cinnamon bark extract (contains quercetin), 125-500 mg/kg	Tissue MDA, lipid profile
El-khateeb, et al. 2020 [16]	Animal Quasi-experimental	30 male Wistar rats	Quercetin 50 mg/kg, oral, daily for 8 weeks	Hippocampal MDA, histology
Chauhan, et al. 2016 [17]	Human RCT	61 adults with AR	Antioxidant mix (not quercetin) + fluticasone, 6 weeks	AR symptoms
Bidian, et al. 2020 [18]	Animal Quasi-experimental	64 male Wistar rats	Quercetin 50 mg/kg/day, oral, for 4 days	Serum & lung MDA, antioxidant enzymes
Asih, et al. 2021 [19]	Animal RCT	Wistar rats	Flavonoid glycoside extract, 50 mg/kg	Liver MDA, SOD
Khoiruddin, et al. 2022 [20]	Animal RCT	28 Wistar rats	Onion peel extract (quercetin-rich), 300-2400 mg/kg	Kidney MDA
Yiga & Samuel, 2024 [21]	Animal Experimental	36 Wistar albino rats	Quercetin 100 mg/kg, intraperitoneal, daily for 30 days	Heart MDA (TBARS), antioxidant enzymes
Gori, et al. 2025 [22]	Human RCT	100 children with AR	Quertal® (quercetin, perilla, vit. D3) + antihistamine, 3 months	AR symptoms, inflammatory markers
Marogna & Ciprandi, 2023 [23]	Human RCT	90 adolescents/adults with AR	Nutraceutical (quercetin, perilla, vit. D3) + standard therapy, 3 months	AR symptoms, spirometry, nasal eosinophils
Ravikumar & Kavitha, 2020 [8]	Animal RCT	Male Balb/c mice	Quercetin 10-30 mg/kg, oral, daily for 13 days	Nasal hyperresponsiveness, Th1/Th2 cytokines

Table 4: Critical Appraisal of Included Studies.

Ref.	Study Design	Population	Intervention	Outcome	Quality	Key Findings	Limitations
Oremosu, et al. 2018 [16]	Animal Exp.	70 male Wistar rats	Quercetin 50 mg/kg, oral, 56 days	Cerebellar MDA	High (8/9 Cochrane)	Significant decrease in cerebellar MDA ($p < 0.05$).	Animal study; outcome measured in brain tissue, not directly related to AR.
Wahdaningsih dan Untari, 2021 [8]	Animal Quasi-exp.	35 rats	Quercetin 4 mg/200g	MDA, catalase	High (8/9 Cochrane)	Decreased MDA levels.	Intervention details (route, duration) and MDA sample source are not specified.
El Gezery dan Sheha, 2021 [9]	Animal Exp.	40 male Sprague Dawley rats	Quercetin 50-200 mg/kg, oral, 28 days	MDA, organ function	High (8/9 Cochrane)	Lowered acrylamide-induced MDA levels.	Context is chemical toxicity, not AR; MDA sample source is non-specific.
Helianti, et al. 2024 [24]	Animal Quasi-exp.	24 male Wistar rats	Onion peel infusion, 125-2000 mg/kg, 28 days	Serum MDA, lung histology	Mod-High (7/8 NOS)	Decreased serum MDA levels.	Animal study; used an unstandardized extract, not pure quercetin.
Shebl, et al. 2018 [22]	Animal Quasi-exp.	40 male albino rats	Quercetin 25 mg/kg, oral, 3 weeks	Liver & muscle MDA	High (8/9 Cochrane)	Decreased MDA in liver and muscle.	Animal study; context is exercise tolerance in hyperthyroidism, not AR.

Sutanegara dan Fredlina, 2022 [23]	Animal RCT	28 male Wistar rats	*Eugenia uniflora* extract, 100/200 mg/kg	AR symptoms, IgE	Mod-High (7/8 NOS)	Significant reduction in nasal symptom scores, comparable to corticosteroids.	Animal study; used an unstandardized extract; duration not specified.
Yusin, et al. 2021 [25]	Human RCT	47 adults with AR	Broccoli sprout extract, 3 weeks	AR symptoms	Moderate (6/7 NOS)	Improved peak nasal inspiratory flow; temporary symptom score improvement.	Intervention was not quercetin; symptom improvement was not sustained.
Paunović, et al. 2016 [17]	Animal Quasi-exp.	18 male Wistar rats	Quercetin 40 mg/kg, IP, 3 days	Erythrocyte MDA	Moderate (6/7 NOS)	Measured MDA in erythrocytes (specific values not reported).	Animal study; non-oral route (intraperitoneal); very short duration.
Handayani, et al. 2023 [26]	Animal Exp.	Rats	Cinnamon bark extract, 125-500 mg/kg	Tissue MDA	Mod-High (7/8 NOS)	Decreased MDA at 500 mg/kg dose ($p < 0.05$).	Used an extract; rat strain and sex not specified.
El-khateeb, et al. 2020 [27]	Animal Quasi-exp.	30 male Wistar rats	Quercetin 50 mg/kg, oral, 8 weeks	Hippocampal MDA	Mod-High (7/8 NOS)	Decreased MDA levels in the hippocampus.	Animal study; outcome measured in brain tissue.
Chauhan, et al. 2016 [5]	Human RCT	61 adults with AR	Antioxidant mix + fluticasone, 6 weeks	AR symptoms	Mod-High (7/8 NOS)	Combination therapy was superior to fluticasone alone ($p < 0.05$).	Intervention was not quercetin, limiting direct relevance.
Bidian, et al. 2020 [4]	Animal Quasi-exp.	64 male Wistar rats	Quercetin 50 mg/kg/day, oral, 4 days	Serum & lung MDA	High (8/9 Cochrane)	Significant decrease in serum and lung MDA ($p < 0.001$).	Animal study; effect on lung MDA was not significant after 24 hours.
Asih, et al. 2021 [28]	Animal RCT	Wistar rats	Flavonoid glycoside extract, 50 mg/kg	Liver MDA	Mod-High (7/8 NOS)	14.71% decrease in liver MDA.	Animal study; used a flavonoid extract; incomplete intervention details.
Khoiruddin, et al. 2022 [14]	Animal RCT	28 Wistar rats	Onion peel extract, 300-2400 mg/kg	Kidney MDA	High (8/9 Cochrane)	Decreased kidney MDA levels.	Animal study; used an unstandardized extract; duration not specified.
Yiga dan Samuel, 2024 [15]	Animal Exp.	36 Wistar albino rats	Quercetin 100 mg/kg, IP, 30 days	Heart MDA (TBARS)	Mod-High (7/8 NOS)	Produced the lowest levels of TBARS in the heart.	Animal study; non-oral route; outcome measured in heart tissue.
Gori, et al. 2025 [17]	Human RCT	100 children with AR	Quertal® + antihistamine, 3 months	AR symptoms	Mod-High (7/8 NOS)	Significant symptom improvement; combination was superior to antihistamine alone.	Intervention was a multi-component product, not pure quercetin.
Marogna dan Ciprandi, 2023 [13]	Human RCT	90 adolescents/ adults with AR	Nutraceutical + standard therapy, 3 months	AR symptoms	Mod-High (7/8 NOS)	Significant symptom improvement (-39%); combination was superior.	Intervention was a multi-component product.
Ravikumar dan Kavitha, 2020 [19]	Animal RCT	Male Balb/c mice	Quercetin 10-30 mg/kg, oral, 13 days	Nasal hyperresponsiveness	High (8/9 Cochrane)	Significant reduction in nasal hyperresponsiveness.	Animal study.

Table 5: Summary of Quercetin's Effect on MDA Levels.

Study	Pre-treatment MDA	Post-treatment MDA	Route	Duration
Bidian, et al. 2020 [18]	Elevated in AR control	Serum & Lung: Decreased with quercetin ($p < 0.001$)	Oral	4 days
Helianti, et al. 2024 [10]	Elevated by smoke	Serum: Decreased with onion peel extract	Oral	28 days
Shebl, et al. 2018 [11]	Not specified	Liver & Muscle: Decreased with quercetin	Oral	3 weeks
Asih, et al. 2021 [19]	Not specified	Liver: 14.71% decrease with flavonoid extract	Not specified	Not specified
Khoiruddin, et al. 2022 [20]	Elevated by diazinon	Kidney: Decreased with onion peel extract	Oral	Not specified
Yiga & Samuel, 2024 [21]	Elevated by aluminium	Heart: Lowest TBARS with quercetin	Intraperitoneal	30 days
Oremosu, et al. 2018 [7]	Elevated by cART	Cerebellum: Decreased with quercetin ($p < 0.05$)	Oral	56 days

Table 6: Summary of Quercetin's Effect on Clinical Symptoms.

Study	Symptom Type	Severity Change	Duration	Comparative Efficacy
Gori, et al. 2025 [22]	Allergic rhinitis symptoms	Statistically significant improvement	3 months	Quercetin combo > Antihistamine alone
Marogna & Ciprandi, 2023 [23]	Allergic rhinitis symptoms	39% greater improvement	3 months	Quercetin combo > Standard therapy alone
Ravikumar & Kavitha, 2020 [8]	Nasal hyperresponsiveness	Significant decrease	13 days	Quercetin *vs.* vehicle
Chauhan, et al. 2016 [17]	Nasal/ocular symptoms	Significant decrease in scores ($p \leq 0.05$)	6 weeks	Antioxidant combo > Fluticasone alone
Sutanegara & Fredlina, 2022 [12]	Nasal symptoms	Significant decrease in scores	Not specified	Extract was equivalent to corticosteroid
Yusin, et al. 2021 [13]	Nasal congestion, TNSS	PNIF improved; TNSS temporarily improved	3 weeks	Broccoli extract + steroid > Steroid alone

rhinitis management through two primary mechanisms: oxidative stress attenuation and direct anti-inflammatory effects. The consistency of malondialdehyde reduction across 14 animal studies, combined with clinically meaningful symptom improvements in human trials, establishes a compelling case for quercetin as an adjunctive therapeutic agent in allergic rhinitis management. The clinical significance becomes particularly apparent when examining the magnitude of therapeutic benefits observed.

Marogna and Ciprandi's study [16] demonstrated a 39% greater improvement in allergic rhinitis symptoms when quercetin-based nutraceuticals were added to standard therapy compared to conventional treatment alone. This substantial improvement suggests that quercetin addresses pathophysiological mechanisms not adequately targeted by current first-line therapies, specifically the oxidative stress component of allergic inflammation.

Mechanistic insights and pathophysiological relevance

The therapeutic efficacy of quercetin in allergic rhinitis can be understood through its multi-targeted approach to disease pathogenesis. Allergic rhinitis involves a complex interplay between IgE-mediated immune responses, inflammatory cell activation, and subsequent oxidative stress generation [1,2]. Our analysis reveals that quercetin effectively interrupts this pathological cascade at multiple critical points.

Direct Antioxidant Mechanisms: Quercetin's molecular structure, featuring multiple hydroxyl groups in strategic positions, enables efficient free radical scavenging capabilities. The consistent reduction in malondialdehyde levels observed across studies by Bidian, et al. [11], Helianti, et al. [12], and others demonstrates quercetin's ability to prevent lipid peroxidation, a key mechanism of cellular damage in allergic inflammation. This direct antioxidant activity is particularly relevant in allergic rhinitis, where activated eosinophils and neutrophils generate substantial reactive oxygen species burdens that overwhelm endogenous antioxidant defenses [4,5].

Nrf2 Pathway Activation: Perhaps more significantly for long-term therapeutic benefits, quercetin activates the nuclear factor erythroid 2-related factor 2 (Nrf2) signaling pathway [21]. This transcription factor functions as the cellular master regulator of antioxidant responses, controlling the expression of over 200 genes involved in cellular protection.

Quercetin-induced Nrf2 activation leads to increased synthesis of endogenous antioxidant enzymes, including superoxide dismutase, catalase, and glutathione peroxidase. This mechanism explains the sustained protective effects observed in longer-duration studies and suggests that quercetin treatment may provide cumulative benefits over time.

Anti-allergic properties: Beyond its antioxidant effects, quercetin demonstrates direct anti-allergic properties crucial for allergic rhinitis management. The compound stabilizes mast cell and basophil membranes, preventing degranulation and subsequent histamine release [22]. This mechanism directly addresses the immediate hypersensitivity reactions characteristic of allergic rhinitis, explaining the rapid symptom improvements observed in clinical trials.

Additionally, quercetin modulates T-helper cell differentiation, suppressing Th2 responses while promoting Th1 immunity, thereby addressing the fundamental immune dysregulation underlying allergic diseases [23].

Comparative analysis with current therapeutic options

Current allergic rhinitis management relies primarily on antihistamines, intranasal corticosteroids, and leukotriene receptor antagonists [1]. While these treatments effectively control symptoms, they primarily target downstream inflammatory mediators rather than addressing the underlying oxidative stress component of disease pathogenesis. The clinical trials included in our review suggest that quercetin supplementation provides additive benefits when combined with conventional therapies, indicating complementary rather than competitive mechanisms of action. The study by Gori, et al. [17] in pediatric populations is particularly noteworthy,

as it demonstrates superior symptom control when quercetin-based formulations are added to antihistamine therapy compared to antihistamine monotherapy. This finding suggests that quercetin addresses therapeutic gaps in current treatment.

Paradigms, particularly the oxidative stress component that conventional therapies do not adequately target.

Dose-response relationships and bioavailability considerations

Analysis of included studies reveals significant variability in quercetin dosing, ranging from 10 - 200 mg/kg in animal studies and varying formulations in human trials. This variability reflects the ongoing challenge of establishing optimal dosing protocols and highlights the critical importance of bioavailability optimization. Natural quercetin exhibits poor oral bioavailability due to limited water solubility, extensive first-pass metabolism, and rapid elimination [27]. The development of enhanced bioavailability formulations, such as the phytosome technology described by Riva, et al. [28], represents a crucial advancement for clinical applications. These formulations achieve up to 20-fold increases in plasma quercetin concentrations compared to standard preparations, suggesting that many previous studies may have been physiologically under-dosing despite high oral doses administered.

Safety profile and clinical implementation

Quercetin demonstrates an excellent safety profile across all reviewed studies, with no significant adverse effects reported in either animal or human investigations. This safety profile, combined with quercetin's natural occurrence in common dietary sources, supports its potential for long-term use in chronic conditions like allergic rhinitis. The compound's GRAS (Generally Recognized as Safe) status by regulatory authorities further supports its clinical application potential. From a practical implementation perspective, quercetin supplementation offers several advantages: oral administration convenience, absence of significant drug interactions, and compatibility with existing therapeutic regimens. These characteristics make quercetin particularly suitable for patients seeking integrative approaches to allergic rhinitis management or those experiencing inadequate symptom control with conventional therapies alone.

This review acknowledges several limitations. The predominance of animal studies limits direct clinical translation. Multi-component formulations in human trials prevent quercetin-Specific effect determination. Additionally, heterogeneous study designs, populations, and outcome measures precluded quantitative meta-analysis performance.

Future investigations should prioritize large-scale, double-blind, randomized controlled trials in diverse human populations utilizing standardized, high-bioavailability quercetin formulations. Head-to-head comparisons against first-line allergic rhinitis therapies would help establish quercetin's therapeutic positioning. Dose-response relationship studies and optimal treatment duration determination are also essential for clinical guideline development.

Conclusion

Based on systematic evaluation of 18 preclinical and clinical studies, quercetin demonstrates significant therapeutic potential in allergic rhinitis management. The evidence consistently shows quercetin effectively reduces oxidative stress markers, particularly malondialdehyde, and ameliorates clinical symptoms when added to standard therapy. These benefits derive from multifaceted mechanisms, including direct antioxidant actions, enhancement of endogenous defense systems via Nrf2 pathway activation, and direct anti-allergic effects.

Despite promising results, current evidence is limited by the predominance of animal studies and the use of multi-component formulations in human trials. Clinicians may consider recommending high-quality quercetin supplements as safe adjuvant therapy, particularly for patients with inadequate responses to conventional treatments. However, large-scale, rigorously designed human clinical trials utilizing standardized, high-bioavailability formulations are critically needed to establish definitive evidence-based clinical guidelines.

The future of quercetin research may depend more on optimizing delivery systems than proving basic efficacy. Enhanced formulations hold potential to bridge the gap between strong preclinical effects and modest human trial results, paving the way for evidence-based dosing recommendations and standardized clinical protocols.

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Conflicts of interest

The authors declare no conflicts of interest related to this systematic review. All contributions were made independently to advance evidence-based therapeutic approaches for allergic rhinitis management. No financial or material support was received from pharmaceutical companies, nutraceutical manufacturers, or any commercial entities with interests in

quercetin research. The research was conducted with complete academic freedom, ensuring analyses and conclusions were based solely on available scientific evidence.

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Data availability

Data supporting the findings of this systematic review, including search strategies, data extraction forms, and quality assessment scores, are available upon reasonable request from the corresponding author. Access will be provided in accordance with PRISMA guidelines and institutional research policies. Interested researchers seeking data access for validation or further analysis are encouraged to contact the corresponding author with specific requests and intended use descriptions.

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Author contributions

Niken Dyah Aryani K: Has extensive clinical experience in otorhinolaryngology with a specific focus on allergic rhinitis management. Currently pursuing doctoral research on oxidative stress mechanisms in allergic diseases and has published multiple peer-reviewed articles on rhinology and allergy immunotherapy.

Harijono Kariosentono: Expert in dermatology and immunology with significant research experience in allergic diseases and inflammatory conditions. Has supervised numerous systematic reviews and meta-analyses in the field of allergy and immunology.

Bambang Purwanto: Internal medicine specialist with expertise in clinical research methodology and systematic review conduct. Has extensive experience in evidence-based medicine and has mentored multiple doctoral students in clinical research.

Other contributors: All contributing authors have relevant clinical and research experience in their respective fields, contributing to the multidisciplinary expertise required for a comprehensive systematic review of quercetin's therapeutic applications in allergic rhinitis.

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