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The effect of quercetin on interleukin-6 and interleukin-8 levels in reducing the signs and symptoms of allergic rhinitis

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Abstract
Background: Allergic rhinitis is a chronic inflammatory disease of the upper respiratory tract mediated by IgE, characterized by increased levels of pro-inflammatory cytokines such as interleukin-6 (IL-6) and interleukin-8 (IL-8), which contribute to symptom severity and mucosal inflammation. Quercetin is a natural flavonoid known for its anti-inflammatory and immunomodulatory properties through various molecular pathways. Therefore, quercetin is considered a promising adjuvant therapy in the management of allergic rhinitis.
Methods: A systematic literature search was conducted using PubMed, Science Direct, and Google scholar data bases for studies published between 2014 and 2025 investigating the effect of quercetin on IL-6 and/or IL-8 levels and clinical symptoms of allergic rhinitis. Eligible studies included *in vivo* and *in vitro* research on animal models, as well as relevant narrative reviews. Studies were appraised based on study design, population, intervention, main outcomes, and methodological quality using the Newcastle-Ottawa Scale (NOS) or the Cochrane Risk of Bias Tool.
Results: Five studies met the inclusion criteria, including four experimental *in vivo* studies on BALB/c or Wistar mice and one narrative review. Most studies reported a significant reduction in IL-6 levels following quercetin administration; two studies also demonstrated reduced IL-8 levels. Additionally, quercetin improved allergic rhinitis symptoms such as sneezing, mucosal inflammation, and IgE levels. The proposed mechanisms included inhibition of the NF-κB and MAPK signaling pathways, along with increased IL-10 and FOXP3 expression. Most studies showed high methodological quality (NOS 8/9, Cochrane 7/8).
Conclusion: Quercetin shows potential as an adjuvant therapy for allergic rhinitis by modulating IL-6 and IL-8 expression and improving mucosal immune responses. However, further large-scale randomized controlled trials are needed to evaluate its clinical efficacy, safety, and optimal dosage in humans

Keywords: Quercetin, allergic rhinitis, interleukin-6, interleukin-8, inflammation, immunomodulator

Introduction

Allergic rhinitis (AR) is a chronic, IgE-mediated inflammatory disease of the nasal mucosa that arises in response to environmental allergens such as pollen, dust mites, pet dander, and mold. It is characterized by classic symptoms including nasal congestion, sneezing, rhinorrhea, and nasal or ocular pruritus. Globally, AR affects a significant proportion of the population, particularly among children and young adults, and is associated with reduced quality of life, impaired sleep, decreased cognitive performance, and increased healthcare utilization [1, 2].

The immunopathogenesis of AR is complex, primarily involving a dysregulated T helper type 2 (Th2)-dominated immune response. Upon allergen exposure, antigen-presenting cells stimulate naive T cells to differentiate into Th2 cells, which secrete cytokines such as IL-4, IL-5, and IL-13. These cytokines promote class switching to allergen-specific IgE, recruitment of eosinophils, and activation of mast cells, all of which contribute to the clinical manifestations of AR.

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In addition to these classic pathways, increasing evidence indicates that cytokines such as interleukin-6 (IL-6) and interleukin-8 (IL-8) also play pivotal roles in the chronicity and severity of nasal inflammation. IL-6 facilitates Th2 polarization and eosinophil survival, while IL-8 acts as a chemo attractant for neutrophils and eosinophils, enhancing mucosal inflammation and mucus hyper secretion [1-3].

Current therapeutic strategies for AR include antihistamines, intranasal corticosteroids, leukotriene receptor antagonists, and allergen immunotherapy. While generally effective, these treatments are often associated with limitations such as mucosal dryness, systemic side effects, and reduced long-term compliance. Moreover, there is growing concern over corticosteroid resistance and the lack of curative potential in conventional therapies. These limitations have prompted the search for novel adjuvant treatments that are both effective and safe, particularly those derived from natural sources [2].

Quercetin, a polyphenolic flavonoid abundantly found in onions, apples, berries, and tea, has emerged as a promising candidate due to its potent anti-inflammatory, antioxidant, and immunomodulatory properties. Preclinical studies have shown that quercetin can inhibit histamine release, suppress the production of proinflammatory cytokines (including IL-6 and IL-8), modulate Th1/Th2 balance, and stabilize mast cells. In murine models of allergic rhinitis, quercetin has been observed to reduce sneezing frequency, nasal rubbing, eosinophilic infiltration, and serum IgE levels. Furthermore, novel formulations such as quercetin-chitosan nanoparticles (QCS) have demonstrated improved bioavailability and enhanced therapeutic efficacy when administered intranasally [1, 3].

Despite these promising findings, there remains a lack of comprehensive synthesis evaluating the effects of quercetin specifically on IL-6 and IL-8 levels in the context of allergic rhinitis. Understanding this relationship is critical given the central roles of these cytokines in driving inflammation and symptom persistence. Therefore, this systematic review aims to critically assess the available evidence on the impact of quercetin on IL-6 and IL-8 expression and its clinical implications in allergic rhinitis. The findings of this review may contribute to the development of novel, evidence-based adjunct therapies derived from natural compounds for the management of allergic diseases.

Methods

This study employed a systematic review approach guided by the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. The review aimed to evaluate the effect of quercetin on the levels of pro-inflammatory cytokines interleukin-6 (IL-6) and interleukin-8 (IL-8) in the context of allergic rhinitis. The focus was on identifying evidence from experimental *in vivo* and *in vitro* studies, as well as narrative reviews that discussed the therapeutic impact of quercetin on allergic inflammation.

The literature search was performed comprehensively across three electronic databases: PubMed, ScienceDirect, and Google Scholar. The time frame for publication was restricted to studies published between January 2014 and March 2025. The search strategy included a combination of keywords and Boolean operators, such as “quercetin”, “allergic rhinitis”, “interleukin-6”, “interleukin-8”, “cytokines”, and “anti-inflammatory”. To enhance the sensitivity of the search, both Medical Subject Headings (MeSH) and free-text terms were used. In addition, reference lists of relevant articles were manually screened to identify further eligible studies.

The inclusion criteria were defined to select original research articles involving *in vitro* or *in vivo* models of allergic rhinitis that investigated the administration of quercetin and reported outcomes on IL-6 and/or IL-8 levels. Studies published in either English or Indonesian and available in full-text format were considered eligible. Articles were excluded if they were review editorials, conference abstracts, or letters to the editor, as well as if they did not provide primary data or lacked explicit measurements of IL-6 or IL-8. Duplicate articles and studies unrelated to allergic rhinitis were also excluded.

The selection process began with an initial identification of 381 records. After removal of duplicates, title and abstract screening were conducted, followed by full-text assessment of potentially eligible studies. A total of five studies met the predefined inclusion criteria and were subsequently included in the final review. The study selection process was documented and visualized using the PRISMA flowchart to ensure transparency.

Data extraction was carried out systematically using a structured format. Extracted information included the authorship, publication year, study design, animal model or cell line used, dosage and route of quercetin administration, measured outcomes (including IL-6, IL-8, and clinical symptom scores), and the key findings of each study. The extracted data were then analyzed narratively due to the methodological heterogeneity among the included studies, particularly in terms of model systems, dosing regimens, and outcome assessment tools. Descriptive comparisons were made to identify recurring patterns and to summarize the potential therapeutic impact of quercetin on inflammatory pathways in allergic rhinitis.

To assess the quality of the included studies, two standardized tools were utilized. For experimental animal studies, the Newcastle-Ottawa Scale (NOS) was used to evaluate aspects such as selection of study subjects, comparability, and outcome assessment. For any clinical or narrative studies, the Cochrane Risk of Bias Tool was employed to assess potential sources of bias in design and reporting. Studies scoring 7 or higher on either scale were considered high-quality and were prioritized in the interpretation of findings.

As this review was conducted using secondary data extracted from previously published literature, no ethical approval or informed consent was required for this study.

Results

A Comprehensive total of 381 records were initially identified through the electronic database searches. After the removal of duplicates and preliminary screening of titles and abstracts, 23 full-text articles were reviewed for eligibility. Following a thorough assessment based on the inclusion and exclusion criteria, five studies were ultimately included in the final analysis. These consisted of four *in vivo* experimental studies using murine models and one narrative review article. The included studies were published between 2020 and 2025 (Table 1).

Table 1: Critical appraisal of systematic review

No	Reference	Study Design	Population	Intervention	Main Outcome	Methodological Quality	Key Findings	Limitations
1	Okumo *et al*., 2021 [5]	*In vitro* and *in vivo*	Murine cell lines and BALB/c mice (allergic rhinitis model)	Quercetin 1-10 μM (*in vitro*), 25 mg/kg (*in vivo*)	Significant reduction in IL-6, IL-8, VEGF, and TNF-α	NOS 8/9	Demonstrated the potential of quercetin to suppress inflammatory cytokines in AR	Preclinical study; no human trials conduc-ted
2	Ke *et al*., 2023 [6]	*In vivo* (experi-mental)	BALB/c mice with OVA-induced AR model	Oral quercetin 20, 35, and 50 mg/kg for 13 days	Reduction in IL-6, TNF-α, IL-17; increase in IL-10 and FOXP3	NOS 8/9	Showed immunomo-dulatory effects of quercetin in regulating Th1/Th2 and Treg/Th17 balance	IL-8 not assessed; no pharma-cological compari-son group
3	Mu *et al*., 2024 [7]	*In vivo* (experi-mental)	BALB/c mice with OVA-induced AR model	Intranasal quercetin-cross-linked chitosan nanoparticles (QCS)	Reduction in IL-6, TNF-α, IL-17, and IgE	Cochrane 7/8	QCS formulation proved effective in reducing local nasal inflammation	IL-8 not reported; still in early preclinical model
4	Tiboc-Schnell *et al*., 2020 [8]	*In vivo* (experi-mental)	Wistar rats with LPS-induced acute rhinosi-nusitis model	Intranasal quercetin 80 mg/kg for 7 days	Decreased IL-6 levels in nasal mucosa, lung, and brain	Cochrane 7/8	Reduced both systemic and local inflammation	Not specific to allergic rhinitis; IL-8 not examined
5	Naso *et al*., 2025 [9]	Narrative review	Human, animal, and *in vitro* studies	Various quercetin preparations (oral, phytoso-me)	Review concluded IL-6 and IL-8 reduction based on multiple studies	Not assessed	Provided additional theoretical support for quercetin's mechanisms of action	Not a primary study; high hetero-geneity among included references

Discussion

Allergic rhinitis (AR) is a chronic inflammatory disease mediated by IgE, characterized by symptoms such as sneezing, nasal obstruction, rhinorrhea, and nasal itching. Proinflammatory cytokines, particularly interleukin-6 (IL-6) and interleukin-8 (IL-8), play pivotal roles in its pathogenesis by promoting the recruitment and activation of immune cells, thereby exacerbating nasal mucosal inflammation. Elevated levels of IL-6 and IL-8 are also associated with increased disease severity and symptom burden [1-3].

Quercetin, a natural flavonoid found in various fruits and vegetables, exhibits strong anti-inflammatory and antioxidant properties. It modulates immune responses by inhibiting NF-κB and MAPK signaling pathways and upregulating antioxidant enzymes, which may lead to reduced IL-6 and IL-8 expression in inflamed nasal tissue [1, 2]. Several studies have demonstrated the therapeutic potential of quercetin in allergic conditions. Yamada *et al*. (2022) reported that daily supplementation of 200 mg quercetin for four weeks significantly improved quality-of-life scores and reduced nasal and ocular symptoms in AR patients [4]. Similarly, Okumo *et al*. (2021) and Ke *et al*. (2023) showed that oral quercetin administration in OVA-induced murine models significantly decreased IL-6 and IL-8 levels, along with impact allergic symptoms. Similar findings were confirmed by Ke *et al*. (2023), who conducted an *in vivo* study on BALB/c mice in an OVA-induced allergic rhinitis model. Oral administration of quercetin at a dose of 20-50 mg/kg decreased levels of IL-6 and other cytokines such as TNF-α and IL-17. Furthermore, FOXP3 and IL-10 expression increased, suggesting that quercetin also plays a role in enhancing immune regulation by increasing Treg cell activity. Although IL-8 was not evaluated in this study, these data confirm quercetin's role as an immunomodulatory agent [5, 6].

Advancements in quercetin delivery were highlighted by Mu *et al*. (2024), who developed a chitosan-based quercetin nanoparticle for intranasal administration. This formulation effectively reduced IL-6, IL-17, TNF-α, and serum IgE levels in AR mice, with improved local delivery and minimized systemic exposure. While IL-8 was not assessed, the significant reduction in IL-6 supports quercetin's local anti-inflammatory efficacy [7]. Tiboc-Schnell *et al*. (2020) further confirmed systemic IL-6 reduction after intranasal quercetin treatment in a rodent model of acute rhinosinusitis, though its relevance to chronic allergic conditions warrants caution due to model differences [8].

A narrative review by Naso *et al*. (2025) reinforced these findings, emphasizing quercetin's consistent effects in reducing IL-6 and IL-8 across multiple preclinical and clinical studies. The review also highlighted the improved bioavailability of phospholipid-based formulations such as quercetin phytosome [9].

Critical appraisal of the included studies revealed high methodological quality and consistent evidence for IL-6 reduction following quercetin administration. However, only two studies explicitly reported IL-8 outcomes, indicating the need for further research focusing on this cytokine in the context of AR.

Quercetin appears to be a promising adjuvant therapeutic agent for allergic rhinitis, capable of modulating inflammatory responses, reducing IL-6 and IL-8 levels, Tregulator and alleviating clinical symptoms. Further well-designed clinical trials are warranted to confirm its long-term efficacy and safety in human subjects.

Conclusion

The effects of quercetin are based on biological mechanisms such as inhibition of the NF-κB and MAPK pathways, reduced expression of pro-inflammatory cytokines, and increased expression of endogenous antioxidants. Furthermore, quercetin also plays a role in increasing IL-10 and stimulating immune regulation by increasing the activity of T-regulatory cells. Several studies have shown that quercetin use can reduce sneezing frequency, IgE production, and nasal mucosal inflammation, supporting its potential clinical effect in reducing allergic rhinitis symptoms. Significant reductions in quality of life scores and an increase in the proportion of patients reporting mild or no symptoms indicate that quercetin not only reduces symptoms but also provides significant improvements in quality of life, particularly in aspects of sleep and physical health.

Quercetin demonstrates immunomodulatory and anti-inflammatory effects relevant to allergic rhinitis management. It significantly reducing IL-6 and IL-8 levels, alleviating inflammation and clinical symptoms. While

animal studies show strong evidence, human trials are still needed to establish clinical applicability, safety, and dosing guidelines.

Conflict of Interest
Not available

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Not available

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