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Lv, ZY; Huang, Y; Li, Y.

**Corresponding author:**

Xinrong Li

792479470@qq.com

**Author Affiliation:**

Chengdu University of Traditional Chinese Medicine.

**ADMINISTRATIVE INFORMATION****Support** - None.**Review Stage at time of this submission** - Data analysis.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202540003**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 1 April 2025 and was last updated on 1 April 2025.**INTRODUCTION**

**Review question / Objective** This systematic review and meta-analysis aims to evaluate the effect of quercetin treatment compared with untreated controls on therapeutic outcomes (e.g., symptom alleviation, inflammatory biomarkers, or immune response modulation) in allergic model animals, based on data from experimental studies.

**Condition being studied** Allergic diseases are immune-mediated disorders triggered by hypersensitivity to harmless environmental allergens (e.g., pollen, dust mites, foods). These conditions, affecting millions globally, manifest as allergic asthma, rhinitis, atopic dermatitis, food allergies, or life-threatening anaphylaxis. Prevalence has surged in recent decades, particularly in urban areas, driven by genetic predisposition, environmental factors (e.g., pollution, dietary changes), and reduced microbial

exposure (“hygiene hypothesis”). Chronic symptoms impair quality of life and impose significant healthcare burdens.

The pathophysiology involves a dysregulated type 2 immune response. In sensitized individuals, allergens activate Th2 cells, prompting IgE antibody production. Subsequent allergen exposure triggers IgE-bound mast cells and basophils to release histamine, leukotrienes, and cytokines, causing acute inflammation (itching, swelling, bronchoconstriction). Chronic inflammation may lead to tissue remodeling (e.g., airway thickening in asthma) and persistent symptoms.

While allergies often begin in childhood (e.g., eczema in infancy, asthma in adolescence), they can develop at any age. Current management includes allergen avoidance, antihistamines, corticosteroids, leukotriene inhibitors, and biologics (e.g., anti-IgE antibodies). However, most therapies alleviate symptoms rather than cure the

disease, underscoring the need for novel treatments targeting underlying mechanisms.

Animal models (e.g., murine asthma, dermatitis, or food allergy models) are vital for studying allergic pathways and testing therapies like quercetin. These models mimic human IgE-mediated inflammation, eosinophil activity, and tissue hyperreactivity, enabling controlled exploration of interventions. Preclinical research bridges mechanistic insights to clinical solutions, offering hope for therapies that modify disease progression rather than merely mitigating symptoms.

## METHODS

**Participant or population** Allergic animal models.

**Intervention** Animals that were created as allergic models were treated with quercetin.

**Comparator** Animals that were created as allergic models were not treated.

**Study designs to be included** 1. Controlled Experimental Studies 1.1 Randomized Controlled Trials (RCTs): Studies where allergic model animals (e.g., mice, rats) are randomly assigned to quercetin-treated or untreated control groups. 1.2 Non-Randomized Controlled Trials: Studies with clear treatment and control groups, even if randomization is not explicitly stated (common in preclinical research). 2. Parallel-Group Designs Direct comparison of quercetin-treated and untreated groups within the same experiment. 3. Crossover Studies (if applicable) Studies where animals serve as their own controls (e.g., baseline vs. post-t).

**Eligibility criteria** The exclusion criteria encompassed: (1) duplicate publications; (2) review articles, clinical trials, or in vitro studies; (3) studies meeting inclusion criteria but with unavailable full texts; (4) studies lacking control groups, quercetin intervention, or employing combined interventions; (5) non-allergic disease models; and (6) studies failing to report predetermined primary outcomes or lacking key data such as standard deviation (SD) or standard error of the mean (SEM).

**Information sources** PubMed, Web of Science, and Embase.

**Main outcome(s)** Including serum total immunoglobulin E (Total IgE), ovalbumin-specific IgE (OVA-IgE), cytokine levels (IL-4, IL-5, IL-10), and immune cell counts (macrophages [M $\phi$ ], lymphocytes [Lym], eosinophils [EOS], neutrophils [NE]), TNF- $\alpha$ , IFN- $\gamma$ , and histamine.

## Quality assessment / Risk of bias analysis

Follow the following 10 aspects: sequence generation bias; baseline characteristics bias; allocation concealment bias; random housing bias; blinding of personnel bias; random outcome assessment bias; blinding of outcome assessors bias; incomplete data reporting bias; selective outcome reporting bias; and other potential confounding biases.

**Strategy of data synthesis** The data extraction process encompassed: (1) Bibliographic information (title, first author, and publication year); (2) Animal characteristics (species, sex, and sample size); (3) Modeling methodology (sensitization dose, administration route, and model validation criteria); (4) Intervention protocols (administration method, dosage, and duration); (5) Outcome measures.

**Subgroup analysis** If necessary, subgroup analyses will be used using a dose modelling method.

**Sensitivity analysis** If necessary, a sensitivity analysis will be used on a case-by-case basis.

**Country(ies) involved** China.

**Keywords** Allergic diseases; Quercetin; Animal model; Meta-analysis.

## Contributions of each author

Author 1 - Zeyi Lv.

Email: 792479470@qq.com

Author 2 - Yue Huang.

Author 3 - Yu Li.