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INPLASY

Effects and Mechanisms of Quercetin in Sepsis: A Systematic Review and Preclinical Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Review stage at the time of initial registration - Preliminary searches.

Conflicts of interest - The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

INPLASY registration number: INPLASY2026110073

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 November 2026 and was last updated on 21 November 2026.

INTRODUCTION

Review question / Objective Inclusion criteria were established based on the PICOS framework: Population (P): A validated sepsis model in experimental animals is required. Intervention (I): The treatment group must receive quercetin alone, with no restrictions on the route of administration (e.g., intraperitoneal injection, oral administration, or incorporation into feed), dosage, or duration of treatment. Control (C): The control group must receive an equivalent volume of a solvent (e.g., saline or dimethyl sulfoxide) or no additional intervention. Outcomes (O): The study must quantitatively assess the protective effects of quercetin, with primary endpoints including levels of TNF-α, IL-1β, and IL-6. Secondary endpoints will encompass markers of oxidative stress (MDA, ROS, SOD, CAT, GSH), tissue injury scores (Lung Injury Score), MPO activity, NO levels, as well as mRNA expression levels of TNF-α and IL-1β. Study Design (S): This research is restricted to randomized controlled animal studies, incorporating both prophylactic administration (prior to model induction) and therapeutic administration (following model induction). Original research is prioritized; thus, reviews, abstracts, conference communications, in vitro studies, and research lacking a control group will be excluded.

Condition being studied Sepsis is a life-threatening organ dysfunction caused by the body's dysregulated response to infection. With persistently high mortality rates in intensive care

units (ICUs), sepsis remains a major public health challenge that urgently needs to be addressed worldwide. The pathophysiology of sepsis is complex, involving the interaction of multiple pathways related to inflammation, immunity, and multi-organ injury. Despite ongoing updates to diagnostic and treatment guidelines, as well as bundled care protocols, the fundamental causes of sepsis are still not fully understood. Current treatment options provide limited clinical benefits; therefore, there is a critical need for the development of safe, effective, and well-targeted therapeutic agents, along with an understanding of their mechanisms of action. Natural products offer significant advantages and show great promise in the prevention and treatment of inflammatory diseases. Among these, the natural flavonoid quercetin stands out due to its well-established anti-inflammatory and protective effects, making it a focal point in sepsis research.

METHODS

Participant or population The study subjects consisted of experimental rats and mice used for sepsis model construction. No human participants were involved, and no experiments with human subjects were conducted.

Intervention After successfully inducing a sepsis model in laboratory animals, quercetin was administered as a therapeutic intervention.

Comparator Sepsis model controls received normal saline/DMSO with the matched dosing regimen, or no additional treatment.

Study designs to be included This review focuses exclusively on preclinical randomized controlled in vivo animal studies examining quercetin interventions in sepsis models, while excluding in vitro cell experiments, clinical studies, reviews, conference abstracts, and non-experimental research.

Eligibility criteria Additional inclusion criteria: ① Studies are limited to Chinese and English languages; ② Extractable data of at least one core outcome (myocardial infarct size, myocardial enzymes, cardiac function) is provided. Additional exclusion criteria: ① Duplicate publications; ② Studies with missing or unextractable key data.

Information sources The databases to be searched include PubMed, Embase, the Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), Wan Fang Database, and the Chinese Scientific Journal Database.

Main outcome(s) This study aims to quantitatively evaluate the protective effects of quercetin in animals with sepsis. The primary endpoints will include levels of TNF-α, IL-1β, and IL-6. Secondary endpoints will assess markers of oxidative stress, such as MDA, ROS, SOD, CAT, and GSH, in addition to tissue injury scores (Lung Injury Score), MPO activity, NO levels, and the mRNA expression of TNF-α and IL-1β.

Quality assessment / Risk of bias analysis The methodological quality of the included studies was systematically evaluated using the SYRCLE tool, which assesses the risk of bias in animal studies. To evaluate publication bias, we used funnel plots for a qualitative assessment. For outcome measures that included ten or more studies, we conducted a quantitative analysis using Egger's regression test and the trim-and-fill method. For outcome measures with fewer than ten studies, we performed only a visual assessment using funnel plots.

Strategy of data synthesis For continuous outcomes, we used the standardized mean difference (SMD) adjusted for small sample sizes with Hedges' g as the pooled effect size, reporting the corresponding 95% confidence interval (CI). Random-effects models were fitted using the restricted maximum likelihood (REML) method, and the confidence intervals for the pooled effect sizes were corrected with the Hartung-Knapp (HK) method. To evaluate heterogeneity among the studies, we used the I^2 statistic. A p-value of less than 0.05 was considered statistically significant.

Subgroup analysis Subgroup analyses will be performed to investigate potential sources of heterogeneity. The prespecified stratification factors include the following: language (English, Chinese), year of publication (pre-2020, post-2020), animal species (rats, mice), modeling method (cecal ligation and puncture (CLP), lipopolysaccharide (LPS)), LPS dosage (10 mg/kg, other dosages), timing of administration (before or after model induction), route of administration (intraperitoneal injection, oral administration), dosage (greater than 50 mg/kg, less than 50 mg/kg), frequency of administration (single dose versus repeated doses), and duration of administration (long-term (≥7 days) versus short-term (3–5 days)).

Sensitivity analysis A stepwise elimination approach will be employed to perform sensitivity

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analyses and assess the influence of studies with extreme effect sizes on the combined results.

Country(ies) involved China.

Other relevant information Current review status: Ongoing.

Keywords Quercetin; Sepsis; Systematic Review; Preclinical Meta-Analysis.

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