INPLASY

Preclinical Evidence for Quercetin in Oral Cancer: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 April 2026 and was last updated on 18 April 2026.

INTRODUCTION

Review question / Objective P: Oral cancer (OSCC) in vitro models, in vivo animal models, and human patients with oral cancer or premalignant lesions.
I: Quercetin administration, alone or in combination with other anti-cancer treatments.
C: Control conditions (no treatment, placebo, or standard therapies).
O: Anti-tumour effects (proliferation, apoptosis, metastasis, tumour growth), mechanism of action, and safety outcomes.
S: Preclinical and clinical studies investigating quercetin in oral cancer.

Condition being studied Oral cancer is the sixth most common malignancy worldwide. In 2022, there were approximately 390,000 new cases and 190,000 deaths globally, with a 5-year survival rate of only 40%–60%. Current treatment modalities, mainly surgery, radiotherapy, and chemotherapy, are limited by significant toxicity and the development of drug resistance, highlighting an urgent need for safer and more effective adjuvant strategies. This study systematically evaluates the preventive and therapeutic effects of the natural flavonoid quercetin on oral cancer using animal models.

METHODS

Participant or population Animal models of oral cancer (e.g., hamster buccal pouch model, mouse xenograft model).

Intervention Quercetin (any dose, route of administration, frequency, or formulation) administered to animal models of oral cancer.

Comparator Control group without quercetin treatment (e.g., vehicle control, solvent control, or no treatment).

Study designs to be included Original in vivo animal studies (including randomized and non-randomized controlled designs) that evaluate the effects of quercetin in oral cancer models. Studies

with clearly defined control groups (vehicle or no treatment) and sufficient quantitative data for effect size extraction are included."

Eligibility criteria Inclusion criteria: (1) Original animal studies; (2) Animal models of oral cancer or OSCC; (3) Quercetin as the primary intervention; (4) Clearly defined control group without quercetin; (5) Reported at least one tumor-related outcome suitable for quantitative synthesis; (6) Sufficient data to calculate effect sizes.
Exclusion criteria: (1) Reviews, conference abstracts, protocols, commentaries; (2) In vitro or human studies; (3) Animal models not representing oral cancer; (4) Complex interventions where quercetin's independent effect cannot be isolated; (5) Unclear or incompatible control group; (6) Insufficient or unobtainable data; (7) Duplicate publications.

Information sources PubMed, Embase, Web of Science, Cochrane Library, and Google Scholar, supplemented by manual reference checking of included studies.

Main outcome(s) Tumor incidence, tumor volume, tumor weight, and expression of Bcl-2, Bax, NF-κB p50/p65, and caspase-3 (mRNA and/or protein).

Quality assessment / Risk of bias analysis The methodological quality and risk of bias of the animal studies were assessed using the SYRCLE's Risk of Bias Tool, a validated instrument specifically designed for animal intervention research. This tool evaluates 10 key items across 6 core bias domains: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases.
Two independent reviewers conducted the assessment independently. Each item was rated as "Low risk", "High risk", or "Unclear risk" based on the detailed description in the original manuscripts. Disagreements between reviewers were resolved through discussion, and a third senior reviewer was consulted to arbitrate if consensus could not be reached. No studies were excluded based solely on their risk of bias, and the impact of bias on pooled results was evaluated via sensitivity analyses.

Strategy of data synthesis Risk of bias was assessed using a tailored tool for animal studies, covering the following domains: random sequence generation, allocation concealment, baseline comparability, blinding, incomplete outcome data, selective reporting, and other sources of bias. Two independent reviewers performed the assessment. Disagreements were resolved through discussion or by a third reviewer.

Subgroup analysis No subgroup analyses were performed due to the limited number of included studies.

Sensitivity analysis Leave-one-out sensitivity analysis was performed to assess the robustness of the pooled results from this meta-analysis. For all primary and secondary outcomes, individual studies were sequentially excluded one by one, and the pooled effect size (odds ratio [OR] for dichotomous outcomes, standardized mean difference [SMD] for continuous outcomes) with 95% confidence interval (CI) was recalculated using the random-effects model. Changes in the magnitude, direction, and statistical significance of the pooled effect size, as well as alterations in between-study heterogeneity (quantified by the I^2 statistic), were evaluated to identify any study that might disproportionately influence the overall findings.

Country(ies) involved All authors of the 5 included studies are affiliated with institutions in China. No studies from other countries or regions were included.

Keywords Quercetin; Oral cancer; Systematic review; Meta-analysis.

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