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The potential value of quercetin for colorectal cancer: A systematic review and a meta-analysis of preclinical studies

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ADMINISTRATIVE INFORMATION

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INTRODUCTION

Review question / Objective The potential value of quercetin for colorectal cancer: A systematic review and a meta-analysis of preclinical studies. According to PRISMA's recommendation, we selected a specific framework of population (P), intervention (I), comparison (C), outcome (O), and study design (S) (PICOS) to define study eligibility: Population (P) : Healthy mice capable of colorectal cancer induction; Intervention (I) : Only quercetin intervention treatment was carried out; Control (C) : Perform corresponding induction for colorectal cancer; Outcome (O) : Relevant outcome indicators of colorectal cancer in the controlled experiment; Research Design (S) : Randomized controlled trial.

Condition being studied Colorectal cancer is the third most common cancer worldwide, accounting for approximately 10% of all cancer cases. Meanwhile, the global number of deaths caused by colorectal cancer is approximately 940,000, accounting for 9.4% of all cancer deaths, making it the second leading cause of cancer-related deaths. However, we encounter many difficulties in the treatment of colorectal cancer. In addition to the limitations of precise treatment options in the early stage and targeted therapy in the late stage, we will also face many treatment difficulties. For example, the chemotherapy regimen based on 5-FU has poor therapeutic effects due to the problem of drug resistance. Therefore,it is very necessary to seek a new therapeutic drug for colorectal cancer.

Quercetin is a natural flavonoid compound widely present in plants and an effective component of dietary polyphenols. It is regarded as the flavonoid with the highest intake. It has a variety of significant biological activities and plays a remarkable role in anti-inflammation, anti-oxidation, anti-tumor and other aspects. However, in the current animal experimental studies of quercetin in the treatment of colorectal cancer, there is a phenomenon of deviation between the result indicators of different experiments. For example: In the study of Shirin Sadighparvar in

2020, quercetin increased the expression level of β -catenin. However, this result is clearly contradictory to the conclusion drawn by Alpa Shree's study in 2020 that quercetin reduces the expression level of β -catenin. Furthermore, in some animal experiments, it was found that the therapeutic effect of quercetin could not be proved to be statistically significant. Therefore, it is necessary to conduct a statistical analysis of the therapeutic effect of quercetin.
At present, in animal experiments on the treatment of colorectal cancer with quercetin, contradictory conclusions have emerged in outcome indicators.In order to solve this problem, reduce random errors and publication bias, improve statistical power, and further discover potential patterns that individual studies may overlook, it is necessary to conduct a meta-analysis.Therefore, this study aims to conduct a comprehensive analysis of relevant animal experiments, systematically and dynamically evaluate the therapeutic effect of colorectal cancer, and explore the related mechanisms of quercetin, thereby further providing a scientific reference for the clinical practice of quercetin in the treatment of colorectal cancer.

METHODS

Search strategy We selected relevant studies published by April 2025 that were not limited by language by searching databases including Embase,Web of Science, and PubMed. The following search terms were used to search all databases:“Quercetin”“Isoquercitrin”“colorectal cancer” “Colorectal Neoplasms” “Colitis-Associated Neoplasms” “Lynch Syndrome”.The search terms were used in conjunction with the medical subject headings (MeSH).Searches were performed with AND or OR.Additional studies were sourced from the reference lists of relevant studies. Comprehensive and systematic retrieval was conducted according to different database situations. The obtained literature was imported into Endnote software.

Participant or population Healthy mice capable of colorectal cancer induction.

Intervention Only quercetin intervention treatment was carried out.

Comparator Perform corresponding induction for colorectal cancer.

Study designs to be included The animal models met the standards for colorectal cancer treatment.

Eligibility criteria The experimental group was treated with quercetin, and the control group did not receive any treatment. The difference in intervention measures between the experimental and control groups should only be whether quercetin treatment was used.

Information sources Embase,Web of Science, and PubMed.

Main outcome(s) iNOS, COX-2, SOD, GSH, GST, SOD, LPO, CAT, G6PD, CEA, NO, PCNA, BCL-2, IL-2β, ACF,β-catenin, caspase, TNF-α, tumor size, weight.

Quality assessment / Risk of bias analysis The SYRCLE risk of bias tool was used by two researchers to make low-risk, high-risk and unclear judgments for each entry according to the appropriate criteria. The statistical software Review Manager 5.4 was used to create risk of bias plots. The standard lists included sequence generation (selection bias), baseline characteristic (selection bias), allocation concealment (selection bias), random housing (performance bias), blinding (performance bias), random outcome assessment (detection bias), blinding (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), and other sources of bias (other). Any disagreements were resolved by discussion with another researcher.

Strategy of data synthesis The collected data were analyzed using the statistical software Review Manager 5.4. The forest graph is constructed using this software, where the black rhombus represents the combination effect,and its horizontal length represents the confidence interval of the combination result.The horizontal bars represent the range of confidence intervals for the magnitude of the observed effect calculated.For continuous variables, the 95% confidence interval (95%CI) was calculated using the mean difference (MD) or the standardized mean difference (SMD).
Due to the differences in intervention measures such as drug dosage and trial period, we chose the random effects model for analysis. We use funnel plots to test publication bias.Define a p-value of 0.05 as data significance. When the p-value is less than 0.05, it is considered that the heterogeneity between studies is statistically significant.

Subgroup analysis We consider conducting subgroup analyses of the data to be analyzed based on criteria such as the type of drug, dosage, and type of animal model.

Sensitivity analysis In the combined meta-analysis, if there is significant heterogeneity, a sensitivity analysis is conducted to identify outliers.For literatures with excessive heterogeneity, further analysis should be conducted based on the actual situation to determine the source of heterogeneity.

Country(ies) involved China.

Keywords quercetin/colorectal cancer.

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