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## A role for curcumin in preventing liver fibrosis in animal: A systematic review and meta-analysis

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#### ADMINISTRATIVE INFORMATION

**Support -** This project is supported by the National Key R&D Program of China (No. 2018YFC1705700).

Review Stage at time of this submission - Data extraction.

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 11 January 2024 and was last updated on 11 January 2024.

#### **INTRODUCTION**

 ${\cal R}^{\rm eview \, question \, / \, Objective}_{\rm potential \, mechanisms \, of \, curcumin \, in}$  animal models of liver fibrosis.

**Condition being studied** Liver fibrosis is a type of liver disease caused by the excessive accumulation of extracellular matrix proteins with specific collagen peptides (Kisseleva & Brenner, 2021). This disease is considered a common pathological stage of chronic liver injury, such as cirrhosis, portal hypertension, and liver cancercurcumin appears to have high clinical value for the treatment of liver fibrosis, and the integration of existing relevant research data through a systematic review can improve the credibility of the evidence and strengthen this conclusion.

#### **METHODS**

Search strategy Four databases, including PubMed, Web of Science, Embase, Cochrane Library were searched systematically between January 2000 and November 2023 without language restrictions. The keywords primarily used were "liver cirrhosis", "Hepatic Cirrhosis", "Cirrhosis, Hepatic", and "Curcumin", "Turmeric Yellow", "Yellow, Turmeric", "Curcumin Phytosome".

Participant or population Animal.

**Intervention** There is an accurate description of curcumin and its administration mode, time, dosage and duration.

Comparator Vehicle-treated control animals.

**Study designs to be included** Papers describing the number of animals used, published in Englishlanguage journals, using liver fibrosis animal models, with Curcumin as the sole intervention.

**Eligibility criteria** Excluded documents encompassed clinical studies, reviews, in vitro studies, conference reports, and comments. Additionally, documents without an animal model, lacking a control group, featuring interventions other than Curcumin, and unpublished or duplicate literature were not considered.

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

Main outcome(s) Alanine aminotransferase (ALT), aminotransferase (AST), hydroxyproline (HYP).

Quality assessment / Risk of bias analysis We assessed the methodological quality according to SYRCLE's risk of bias tool for animal studies It mainly comprises ten aspects, including random sequence generation (selection bias), baseline characteristics (selection bias), allocation concealment (selection bias), random housing (performance bias), blinding of participants and personnel (performance bias), random selection of animals in the evaluation results (detection bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other bias, the risk of bias assessment will be performed independently by two researchers, and if the results are inconsistent, they will be submitted to a third researcher for arbitration.

Strategy of data synthesis Summary statistics were assessed using the standard mean difference (SMD) and 95% confidence interval (CI). Heterogeneity of the studies was evaluated using the I2 statistics. Based on the level of heterogeneity, different effect models were employed. The random effect model was utilized when I2 > 50%, while the fixed effect model was employed otherwise. Stata 16.0 was used for all statistical analyses. When the number of included studies exceeded 10, publication bias was assessed using a funnel plot. A significance level of P<0.05 indicated a statistically significant difference.

**Subgroup analysis** The following study characteristics will be examined as potential source of heterogeneity:animal species, Molding method,. For stratified analyses, a minimum number of 6 studies per subgroup is required.

**Sensitivity analysis** The source of heterogeneity was identified through subgroup analysis and sensitivity analysis.

Language restriction Only English.

#### Country(ies) involved China.

Keywords curcumin, preclinical study, liver fibrosis, meta-analysis.

#### **Contributions of each author**

Author 1 - Bohao Huang is the main contributor to this manuscript. Email: 982467965@gg.com Author 2 - Bohan Lv screened the literature and extracted the data and revised the manuscript. Email: lvbohan222@hotmail.com Author 3 - Ziwei Guo. The author was responsible for data analysis Email: guoziweigzw0612@163.com Author 4 - Ziwen Zhuo. The author was responsible for data analysis Email: 2533398868@gg.com Author 5 - Yanbo Li. The author screened the literature and extracted the data. Email: 1418664324@gg.com Author 6 - Wenliang Lv. Corresponding author Email: lvwenliang@sohu.com