

Anti-Inflammatory Effects of Herbal Medicine Ingredients in Rat Models of Liver Transplantation: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION**Support - No.****Review Stage at time of this submission - Preliminary searches.****Conflicts of interest - None declared.****INPLASY registration number: INPLASY202510050****Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 January 2025 and was last updated on 15 January 2025.**INTRODUCTION**

Review question / Objective Do Herbal Medicine Ingredients attenuate immune rejection after liver transplantation compared to control therapy alone?

Condition being studied The procedure was first performed on humans by Thomas Starzl in 1963 and has become a standard treatment for patients with life-threatening liver disease. Although the survival rate of liver transplant recipients is significantly improved, the postoperative complications are more, the readmission rate is higher, and the quality of life is still poor. Immunosuppressants (IS) are often used after surgery to control rejection and reduce irreversible immune-mediated graft damage. The most common protocol is to use calcineurin inhibitor (CNI), but the use of IS can also cause tumor recurrence, liver and kidney damage, metabolic syndrome and other related infectious complications, which brings a huge financial burden to organ transplant patients. This

has prompted efforts to explore alternative or adjunctive immunosuppressive therapies. In recent years, relevant studies have found that herbal medicine ingredients can alleviate the immune response after liver transplantation in animal models, so we conducted this meta-analysis.

METHODS

Search strategy Relevant Chinese and English studies published from inception to December 1, 2024 were searched in nine databases: PubMed, EMBASE, Cochrane Library, Web of Science, Wang Fang, China Science and Technology Journal Database, SinoMed and China National Knowledge Infrastructure (CNKI). Other potentially relevant studies were identified by manually searching the reference lists of the obtained studies. The keywords in the English database were “Herbal Medicine Ingredients”, “Liver Transplantation”, “animals”.

Participant or population Animal Rats model of liver transplantation.

Intervention The intervention used were herbal medicine ingredients.

Comparator Vehicle-treated control animals/all other control conditions.

Study designs to be included Experimental study of all herbal medicine ingredients in animal experimental model of liver transplantation.

Eligibility criteria Inclusion criteria: (1) Rat animal models of liver transplantation in randomized controlled trials; (2) animal models of liver transplantation without strain, sex and age restrictions that were successfully established in different ways; (3) the intervention used were herbal medicine ingredients; (4) the restricted transplantation method was allogeneic liver transplantation.

Exclusion criteria:(1) studies that did not establish a suitable animal model, such as other organ transplants, xenotransplants or artificial transplants; (2) studies in which the interventions used in the treatment group are a combination of traditional Chinese medicine, capsules or individual drugs or other therapies. (3) studies that did not meet the inclusion criteria after manual screening were also excluded.

Information sources PubMed, EMBASE, Cochrane Library, Web of Science, Wang Fang, China Science and Technology Journal Database, SinoMed and China National Knowledge Infrastructure (CNKI).

Main outcome(s) liver function indicators such as ALT, AST, TBIL.

Additional outcome(s) Inflammatory cytokines such as tumor necrosis factor- α and Interleukin-1 β ; apoptosis factor B-cell lymphoma 2(Bcl-2); Banff schema and median survival time (MST).

Quality assessment / Risk of bias analysis Use the Systematic Review Center for Laboratory Animal Experimentation (SYRCLE) risk of bias tool (RoBT) . This RoB tool can assess deviations in the following 10 areas: (1) sequence generation, (2) baseline characteristics, (3) allocation concealment, (4) random housing, (5) blinding of caregivers and investigators, (6) random outcome assessment, (7) blinding of outcome assessment, (8) incomplete outcome data, (9) selective outcome reporting, and (10) other sources of bias.

Strategy of data synthesis Data analysis was performed using R 4.3 software. All outcomes were treated as continuous variables. When studies

reported outcomes using different measures or units, the standardized mean difference (SMD) was used as the effect size index. Confidence intervals (CIs) were set at 95%, and a p-value < 0.05 was considered statistically significant. Heterogeneity was assessed using the Q-test and the I² statistic. If I² < 50%, a fixed effects model was used, otherwise a random effects model was used. Sensitivity analyses were performed to assess the stability and reliability of the results.

Subgroup analysis None planned.

Sensitivity analysis To test the robustness of our findings when selecting the time point of greatest efficacy we will re-run the analysis with data from the latest possible time point.

Country(ies) involved China.

Keywords Herbal Medicine Ingredients, Liver Transplantation, Anti-Inflammatory , Meta-Analysis.

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