INPLASY

Comparative Efficacy of Antrodia cinnamomea on Liver Function Biomarkers in Mouse Models: A Network Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Completed but not published.

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 13 April 2025 and was last updated on 13 April 2025.

INTRODUCTION

Review question / Objective P: Mouse and rat models with experimentally induced liver injury. I : Antrodia cinnamomea extracts, including triterpenoids, polysaccharides, and antroquinonol, at various dose levels (low, medium, high). C: Vehicle-treated model controls, negative controls, and positive hepatoprotective agents (e.g., silymarin) O: Primary: serum ALT and AST levels; Secondary: MDA and TNF-α levels. S : In vivo animal studies.

Objective:
To systematically compare the hepatoprotective efficacy of different types and doses of Antrodia cinnamomea extracts using a network meta-analysis of animal studies evaluating liver function biomarkers.

Rationale Liver diseases are common and serious, and Antrodia cinnamomea has shown potential hepatoprotective effects in animal studies. However, the relative efficacy of its different extract types and doses remains unclear. Traditional meta-analyses cannot compare multiple interventions at once. This study uses a NMA to systematically evaluate and rank the effectiveness of various A. cinnamomea extracts on liver biomarkers, aiming to guide future research and clinical use.

Condition being studied Liver injury and dysfunction, particularly from non-alcoholic fatty liver disease (NAFLD), oxidative stress, and inflammation, are major global health concerns. These conditions are often modeled in animals using agents such as alcohol, high-fat diets, or chemical toxins. Biomarkers such as ALT, AST, MDA, and TNF-α are commonly used to assess liver function and damage severity. Identifying effective hepatoprotective agents is critical for prevention and treatment of liver diseases.

METHODS

Search strategy A comprehensive search was conducted in PubMed, Embase, Cochrane CENTRAL, and Web of Science. Keywords and Boolean operators used included: “Antrodia cinnamomea” OR “Antrodia camphorata” AND

"liver injury" OR "hepatoprotection" OR "triterpenoid" OR "polysaccharide" OR "antroquinonol".

Participant or population This review includes in vivo animal studies using standardized mouse and rat models. All included studies involve experimental induction of liver injury and assess the effects of Antrodia cinnamomea or its bioactive extracts. No human or in vitro studies are included.

Intervention The interventions include various types and doses of Antrodia cinnamomea extracts administered to animal models. These include triterpenoids, polysaccharides, and antroquinonol. Extracts were administered via oral gavage. The effects of these interventions on liver biomarkers (ALT, AST, MDA, and TNF-α) were assessed to determine their hepatoprotective efficacy.

Comparator The comparators include model control groups and positive control groups treated with known hepatoprotective agents such as silymarin, N-acetylcysteine (NAC), metformin, or resveratrol. These groups serve as reference points to evaluate the relative efficacy of different Antrodia cinnamomea extract interventions.

Study designs to be included Only in vivo controlled animal studies using mouse or rat models will be included. Eligible studies must evaluate the effects of Antrodia cinnamomea extracts on liver injury and report quantitative data on relevant biomarkers (e.g., ALT, AST, MDA, TNF-α). In vitro, clinical, or review studies will be excluded.

Eligibility criteria Only original, peer-reviewed full-text articles published in English will be included. Studies must report sufficient quantitative outcome data. Studies co-administering Antrodia cinnamomea with other herbal compounds without isolating its effects will be excluded. Abstracts, reviews, editorials, conference papers, and in vitro or clinical studies will also be excluded.

Information sources We will search PubMed, Embase, Cochrane CENTRAL, and Web of Science to identify eligible studies. Additional studies will be identified by manually screening reference lists of relevant articles. If necessary, corresponding authors will be contacted for missing data. No trial registries or grey literature will be included.

Main outcome(s) The primary outcomes are alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, which are widely used biomarkers of liver injury and hepatocellular function. Outcome measures will include the ALT and AST levels between intervention and control groups. Measurements must be reported at the end of the treatment period in each included study.

Additional outcome(s) Secondary outcomes include serum malondialdehyde (MDA) levels, a marker of oxidative stress, and tumor necrosis factor-alpha (TNF-α), a pro-inflammatory cytokine. These biomarkers reflect oxidative and inflammatory responses related to liver injury.

Quality assessment / Risk of bias analysis The methodological quality of included animal studies will be assessed using SYRCLE's Risk of Bias (RoB) tool, specifically designed for preclinical studies. This tool evaluates domains such as sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting. Two reviewers will assess each study independently. Disagreements will be resolved through discussion or consultation with a third reviewer. Results will be presented in tabular and graphical formats.

Strategy of data synthesis A frequentist network meta-analysis will be conducted using MetaInsight (version 6.3.0), which implements the netmeta R package. A random-effects model will be used to account for between-study heterogeneity. Mean differences (MD) with 95% confidence intervals (CI) will be calculated for continuous outcomes. Ranking of interventions will be performed using P-scores. Inconsistency will be assessed using node-splitting methods. Sensitivity analyses will include leave-one-out procedures to test the robustness of findings.

Subgroup analysis No subgroup analysis is planned for this review.

Sensitivity analysis Sensitivity analyses will be performed using a leave-one-out approach, where each study is sequentially removed to assess its influence on the overall results and treatment rankings.

Country(ies) involved Taiwan.

Keywords Antrodia cinnamomea, network meta-analysis, liver function, animal models, biomarkers.

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