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Efficacy of emodin in animal models of non-alcoholic fatty liver disease: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - This work is being supported by the National Natural Science Foundation Project of China (No. 81973743). NSFC (No. 81973743).

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202380069

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 August 2023 and was last updated on 16 August 2023.

INTRODUCTION

Review question / Objective What is the effect of emodin on animal models of nonalcoholic fatty liver disease and its mechanism?

Condition being studied Non-alcoholic fatty liver disease (NAFLD) is prevalent worldwide and leads to an increased risk of cardiovascular disease, cirrhosis, and liver cancer. Unfortunately, there are currently no approved drugs to treat the disease. At present, emodin has significantly benefited animal models of NAFLD. However, there is currently insufficient evidence to reveal the efficacy of emodin treatment. The purpose of this study is to conduct a systematic review and meta-analysis of the literature to evaluate the efficacy and mechanism of emodin in the treatment of NAFLD.

METHODS

Search strategy #1 “Fatty Liver”[MeSH]
#2 (fatty AND (liver* OR hepat*)) [Title/Abstract] OR (liver AND steato*) [Title/Abstract] OR steatohepat* [Title/Abstract] OR NAFL* [Title/Abstract] OR NASH* [Title/Abstract]
#3 “Emodin”[MeSH]
#4 Emodin [Title/Abstract] OR Rheum [Title/Abstract] OR Rhubarb [Title/Abstract] OR “Dahuang” [Title/Abstract]
#5 #1OR#2
#6 #3OR#4
#7 #5OR#6.

Participant or population NAFLD model animals.

Intervention Emodin with all dosages and duration.

Comparator Same solvent (e.g., water and saline), no intervention, et.

Study designs to be included Randomized controlled experiment.

Eligibility criteria Studies were included if they met the following criteria: (1) Subjects: animal models with NAFLD; (2) Intervention: emodin with all dosage and duration; (3) Comparator: same solvent (e.g., water and saline), no intervention, etc.; (4) Outcomes: ALT, AST, TC, TG, LDL-C, HDL-C, FBG, FINS, HOMA-IR, body weight, liver wet weight, liver index, FFA, IL-1β, IL-6, and TNF-α. Studies were excluded if: (1) studies for which the data could not be extracted; (2) in vitro studies or clinical trials; (3) repeated publication or duplicate data; (4) outcome measures were poorly described.

Information sources Cochrane Library, PubMed, EMBASE, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), VIP Chinese Science and Technology Periodical Database (VIP), and Wanfang Data will be searched for relevant information, updated to Jun 2023.
No language or date restrictions will be applied.

Main outcome(s) 1. Liver function including alanine aminotransferase (ALT) and aspartate transaminase (AST).
2. Blood lipids including total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL-C), and high-density lipoprotein (HDL-C).
3. Glucose metabolism including fasting blood glucose (FBG), fasting insulin (FINS), and homeostatic model assessment of insulin resistance (HOMA-IR).

Data management Two reviewers will independently review the titles and abstracts of the studies retrieved in the searches to identify relevant studies for inclusion. We will record the selection process in sufficient detail to complete a PRISMA flow diagram. Two reviewers will then independently extract the following information from the studies selected for inclusion: authors, year of publication, country, species, sample size, NAFLD animal models, interventions, comparisons, and outcomes. If there are disagreements between the two reviewers, a third reviewer will be consulted to determine the final result.

Quality assessment / Risk of bias analysis Two reviewers will independently evaluate the quality of the selected studies according to the SYstematic Review Center for Laboratory Animal Experimentation Risk of Bias (SYRCLE's RoB) tool. The SYRCLE's RoB tool for animal experiments contains ten entries based on six types of bias: 1) Sequence generation (selection bias); 2) Baseline characteristics (selection bias); 3) Allocation concealment (selection bias); 4) Random housing (performance bias); 5) Blinding (performance bias); 6) Random outcome assessment (detection bias); 7) Blinding (detection bias); 8) Incomplete outcome data (attrition bias); 9) Selective outcome reporting (reporting bias); 10) Other sources of bias (other). The results of the assessment are "yes," "no," and "unclear," representing "low risk of bias," "high risk of bias," and "insufficient details have been reported to assess the risk of bias properly". Results from these questions will be graphed and assessed using Review Manager 5.4.

Strategy of data synthesis The meta-analyses will be performed by the Review Manager 5.4 and Stata V17.0 software. The continuous variables will be analyzed with a standard mean difference (SMD) with 95% CIs. Between-study heterogeneity will be assessed using the I^2 statistic, and substantial heterogeneity is considered when I2 is >50%. The random effects model will be applied to estimate the summary SMD and 95% CIs. Outcomes will be calculated using P values and $P < 0.05$ is considered statistically significant. Funnel plots, Egger's tests, and Bgger's tests will be conducted to check for potential publication bias when the number of studies was ≥ 10.

Subgroup analysis Subgroup analysis will be performed to investigate the possible sources of heterogeneity based on emodin dose, duration of intervention, NAFLD model, and species.

Sensitivity analysis Sensitivity analysis will be performed to ascertain the results of the meta-analysis by excluding each of the individual studies.

Language restriction No language restrictions.

Country(ies) involved China.

Keywords Emodin; non-alcoholic fatty liver disease; animal models; systematic review; meta-analysis.

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