**INTRODUCTION**

Review question / Objective: We wondered the trends and mechanisms of the dual effects of geniposide on rat liver. Question: What circumstance will geniposide present the efficacy or toxicity? And what the mechanism of its medicinal value and toxicity?

Rationale: Liver injury includes various diseases of the liver in various internal medicine systems, that is, inflammatory diseases of various livers, and liver injury is a common disease associated with various liver diseases that often progresses to fibrosis, cirrhosis, and even hepatocellular carcinoma. Geniposide, a class of iridoid terpenoids extracted from Gardenia, is often used in the treatment of liver diseases due to its therapeutic potential.

**INPLASY PROTOCOL**


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**Bidirectional effect of geniposide on liver injury: A preclinical evidence construction based on meta-analysis**

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Condition being studied: Liver injury includes various diseases of the liver in various internal medicine systems, that is, inflammatory diseases of various livers, and liver injury is a common disease associated with various liver diseases that often progresses to fibrosis, cirrhosis, and even hepatocellular carcinoma. The common ones mainly include viral hepatitis, drug-induced hepatitis, alcoholic hepatitis, nonalcoholic fatty liver disease, inherited metabolic liver disease and autoimmune liver disease, among others, and their clinical manifestations are mostly abnormal liver function.
jasminoides, a plant of the Rubiaceae family, is one of the most active substances in Gardenia jasminoides. A large number of studies have shown that geniposide protects the liver from injury, and its protective effect may be achieved through different mechanisms, such as inhibiting the expression of related signaling pathways and thereby reducing the release of inflammatory factors, etc. Besides that, geniposide has certain hepatotoxicity, which has been reported to be associated with the generation of oxidative stress, inflammatory response and thereby inducing necrosis and apoptosis of hepatocytes, But the exact mechanism regarding the hepatotoxicity of Gardenia remains obscure. In order to obtain clinical evidence of geniposide on liver protection as well as hepatotoxicity, we conducted analyses of animal studies to obtain a large amount of preclinical evidence, which provided systematic and scientific support for further clinical studies.

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**METHODS**

**Search strategy:** To investigate the subject on PubMed/Weipu/Wanfang/CNKI/Web of Science, we search the published papers at some stage in 2005-2023 and accumulate the essential indicator of the liver injury within the mice and rat. We used "geniposide " and "hepatotoxicity " or "hepatoprotection ", and other main words to search in the databases. As in PubMed database, the search methods were "geniposide " and "hepatotoxicity " or "hepatoprotection ".

**Participant or population:** Subjects: Liver injury and liver protection affects rats and mice in a variety of ways.

**Intervention:** Incusion criteria: We encompass research in serous situation: 1. period: one to ninety days 2. course of administration: eating regimen or injection 3. dose: 5mg to 1680mg/kg. Exulsion criteria: We exclude the references that isn't pleased the inclusion condition.

**Comparator:** Inclusion criteria: On this study, we only use controlled studies with separate treatment corporations because it would be less complicated and clearer. Exclusion criteria: We exclude the case studies and cross-over research because all references we gathered display controlled studies with separate treatment organizations in those experiments.

**Study designs to be included:** We use the following factors to guide the selection of the articles: (1) Subjects: Liver injury and liver protection affects rats and mice in a variety of ways. (2) Intervention (I) and control (C): The model group received no treatment or non-functional medications, while the experimental group received any dosage of geniposide unit medicinal herbs. (3) The Results: In this study, the expression of AST, ALT showed the degree of liver injury. As additional secondary markers of liver injury, we chose TBIL, ALP and liver index. For the hepatoprotective effect, we took ALT, AST to exhibit its prote

**Eligibility criteria:** 1. We first exclude keywords inside the identify, summary or complete text that don't seem liver injury or liver protection. 2. Within the experimental consequences, there isn't mice or rat animal version. 3. Excluding the references that did not amount bio-markers the use of molecular biology or histological strategies. 4. Furthermore, except the records that isn't always extensive.
Information sources: We use universal desktop ruler to measure the data and always contact with the authors of eligible studies in Chinese medicine. The number of reviewers are unconfirmed so we do not know. We always check the data for three times that is collected by different people and calculate the means and SD.

Main outcome(s): Primary outcome is the quantity of ALT, AST, and the unit of ALT, AST is U/L. The primary outcomes are continuous.

Additional outcome(s): Secondary final results are to statistic whether the indicator is significant by STATA, and the secondary outcomes include: Liver index, ALP, TBIL, TG, MDA, SOD, the levels of TNF-α, IL-6, IL-1β. The secondary outcomes are continuous.

Data management: All data and records are to statistic whether the indicator is significant by STATA. The SYRCLE list (10 items) was used to evaluate the quality of the included literature.

Quality assessment / Risk of bias analysis: By use of SYRCLE's risk of bias tool. We are demonstrating the risk of bias and quality of evidence. Methodological quality and risk of bias assessments were evaluated independently by two investigators (Xinyu Zeng and Simiao Liu) using the Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies (SYRCLE) 10-point scoring scale, wwhich is performed by Hooijmans et al.

Strategy of data synthesis: We can evaluate the extent of ALT, AST, ALP etc to investigate the geniposide tendency in liver injury or liver protection. We are able to desire the forest plot to conclude the end result and show threshold for heterogeneity.

Subgroup analysis: We take a better examine whether geniposide is the same effect to liver damage, that are brought on via different factors, including chemical, physical and biological.

Sensitivity analysis: We used STATA to perform a sensitivity analysis of the included literature.

Language restriction: Chinese-Simplified and English.

Country(ies) involved: China.

Keywords: Geniposide, Liver injury, Liver protection, Hepatotoxicity, Hepatoprotective, Meta-analysis

Contributions of each author: Author 1 - Xinyu Zeng - Author 1 searched the literature, drafted the manuscript, completed the visualization. Email: 2486181376@qq.com Author 2 - Jiajie Jiang - Author 2 searched the literature, drafted the manuscript. Author 3 - Simiao Liu - Author 3 completed the visualization.

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