INPLASY

Intestinal Protective Effects and Mechanisms of Acupuncture in Animal Models of Ulcerative Colitis: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202590036

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 September 2025 and was last updated on 11 September 2025.

INTRODUCTION

Review question / Objective P (participants:) : ulcerative colitis animal model; I (intervention:) : acupuncture or electroacupuncture; C (comparison) : the control group comprised untreated control; O (outcomes) : the main outcome indicators are the disease activity index (DAI) score,tumor necrosis factor-α(TNF-α),interleukin-1 beta(IL-1β)and interleukin-6(IL-6);the secondary outcome indicators are zonula occludens-1 (ZO-1) and occludin; S (study design) : randomized controlled animal study.

Rationale Ulcerative colitis (UC) is a recurrent and refractory chronic inflammatory bowel disease that severely affects the quality of life of patients. Currently, the treatment for this disease still has limitations. Due to its safety and potential for multi-target therapy, acupuncture and moxibustion is expected to become an effective complementary and alternative treatment for UC.Animal models serve as crucial platforms for studying potential interventions and mechanisms of ulcerative colitis (UC), playing an irreplaceable role in exploring the pathogenesis and treatment strategies of UC. In recent years, a plethora of preclinical studies have focused on the effects of acupuncture or electroacupuncture interventions on animal models of UC. However, existing research results exhibit significant heterogeneity. Most individual studies are limited by small sample sizes and insufficient statistical power. In light of this, it is crucial to conduct a rigorous systematic evaluation and quantitative synthesis of existing evidence through systematic reviews and meta-analyses.

Condition being studied Ulcerative colitis is a chronic non-specific inflammatory bowel disease with unknown etiology, which is characterized by continuous and diffuse inflammatory changes in colorectal mucosa. At present, its incidence and prevalence are gradually increasing in the world. The treatment methods are mainly 5-aminosalicylic

acid drugs, thiopurine drugs, biological agents and small molecule drugs. Although the treatment options are expanding, there are still some patients with recurrent disease and adverse reactions after taking drugs, and even need to accept surgical treatment such as rectocolonic resection. It is necessary to carry out in-depth research to provide new treatment methods and means for the treatment of the disease.

Acupuncture is an important part of Chinese traditional medicine. As an effective treatment, it is widely used in clinic. A large number of studies have shown that acupuncture has obvious curative effect on UC. However, the mechanism of acupuncture intervention on ulcerative colitis animal model is still lacking. Therefore, this study aims to comprehensively analyze the relevant animal experiments, systematically and dynamically evaluate the therapeutic effect of acupuncture on ulcerative colitis, and explore its related mechanism, so as to further provide a scientific basis for the clinical practice of acupuncture in the treatment of ulcerative colitis.

METHODS

Search strategy We will search PubMed, Embase, Web of Science, the Cochrane Library, China National Knowledge Infrastructure, China Biology Medicine disc, Wanfang Database, and VIP Database, from the inception of each database until June 2025. A combination of MeSH and free-text terms will be used to identify relevant diseases and intervention measures.:“Colitis Gravis” “Idiopathic Proctocolitis”“Inflammatory Bowel Disease, Ulcerative Colitis Type”“Ulcerative Colitis” “Inflammatory Bowel Diseases”“proctocolitis” “proctosigmoiditis”“rectocolitis”“rectosigmoiditis” “proctitis”“colorectitis”“coloproctitis”“UC”“IBD” “Acupuncture”,“Acupuncture Therapy”, “Acupuncture Points”“Acupuncture Analgesia” “Acupuncture Treatment” “Acupuncture Treatments”“Treatment, Acupuncture” “Therapy, Acupuncture”“Acupuncture Point” “Point, Acupuncture”“Points, Acupuncture” “Acupoints”“Acupoint”“manual acupuncture” “Needling”“Electroacupuncture”“Electro-acupuncture”“meridians”“moxibustion”“Acupoint Therapy”“Needle Therapy”“needlepricking”“de qi” Searches will be performed using AND/OR operators. A comprehensive and systematic retrieval will be conducted according to the specific requirements of each database. The obtained literature will be imported into EndNote software.

Participant or population Ulcerative colitis animal model.

Intervention Acupuncture or electroacupuncture.

Comparator The control group comprised untreated control.

Study designs to be included Randomized controlled animal study.

Eligibility criteria Study type: randomized controlled animal study. Studies will be included if they are described as "randomized" or employ random allocation methods (e.g., random number table).

Study subjects: animal models of ulcerative colitis, with no restrictions on animal species or modeling methods.

Intervention: the treatment group will receive either acupuncture or electroacupuncture, while the control group will receive no intervention.

Outcome indicators:： the main outcome indicators are the disease activity index (DAI) score,tumor necrosis factor-α(TNF-α),interleukin-1 beta(IL-1β)and interleukin-6(IL-6);the secondary outcome indicators are zonula occludens-1 (ZO-1) and occludin.

Information sources We will search PubMed, Embase, Web of Science, the Cochrane Library, China National Knowledge Infrastructure, China Biology Medicine disc, Wanfang Database, and VIP Database, from the inception of each database until June 2025.

Main outcome(s) The main outcome indicators are the disease activity index (DAI) score,tumor necrosis factor-α(TNF-α),interleukin-1 beta(IL-1β)and interleukin-6(IL-6).

Additional outcome(s) The secondary outcome indicators are zonula occludens-1 (ZO-1) andoccludin.

Data management Two researchers will independently conduct literature screening and data extraction and will utilize EndNote X9 document management software for management and editing. After eliminating duplicate documents, they will review the titles and abstracts for preliminary screening. In accordance with the inclusion and ranking criteria, they will exclude documents that do not meet the criteria and will re-screen documents that may meet the criteria after reviewing the full text. Finally, they will determine the documents to be included in the analysis and will extract the relevant data. The following details will be extracted from the selected studies: (1) the name and year of publication of the

first author; (2) characteristics of laboratory animals used in each study (such as species, gender, weight, etc.); (3) the method of establishing the UC model (including the drug dose, route of administration, time required for establishing the model, and the criteria for determining successful model establishment); (4) the intervention scheme for the treatment group and the control group; (5) primary outcome measures and secondary outcome measures. If results are obtained at different time points, only the data from the last time point will be extracted for meta-analysis. If results are presented only in graphical form, we will attempt to contact the author to obtain the original experimental data. If the author does not respond, WebPlotDigitizer 4.8 software will be used to extract numerical data from the figures. Any disputes arising during data extraction will be resolved through discussion or by consultation with a third arbitrator.

Quality assessment / Risk of bias analysis Two researchers (Z.J and Z.X.H) will independently use the Systematic Review Center for Laboratory Animal Experimentation (SYRCLE) risk of bias tool (RoBT) 10-item scale to assess the risk of bias in each study. Each item will be as follows: (1) sequence generation, (2) baseline characteristics, (3) allocation concealment, (4) random housing, (5) blinding (for trial caregivers and researchers), (6) random outcome assessment, (7) blinding (for outcome assessors), (8) incomplete outcome data, (9) selective outcome reporting, and (10) other sources of bias. Each item will be assigned a value of 1 point, resulting in a total possible score of 10 points. Any disputes arising from the evaluation will be resolved through negotiation or third-party arbitration.

Strategy of data synthesis Predetermined outcomes will be considered as continuous variables. When outcomes are reported using different measurement methods or scales, the standardised mean difference (SMD) will be used instead of the mean difference (MD). A random-effects model will be employed to calculate the pooled effect. This model will take into account the accuracy of individual studies, the differences between studies, and the weight assigned to each study. Heterogeneity among the included studies will be expressed using the I^2 statistic. An I^2 value greater than 50% will suggest substantial heterogeneity. Heterogeneity will be further explored by conducting subgroup analyses. All statistical analyses will be performed using RevMan software (version 5.4). A P value of less than 0.05 will be considered statistically significant.

Subgroup analysis In order to explore the sources of heterogeneity and the influence of evaluation variables or study characteristics on the effect estimate, the following subgroup analyses will be pre-specified. If a sufficient number of studies are available per outcome (e.g., at least two studies per subgroup), these analyses will be performed based on: characteristics of animal models—species and strains (e.g., rats such as Sprague Dawley and Wistar, and mice such as C57BL/6 and BALB/c)—and methods of model establishment (including DSS, TNBS/ethanol solution, immunological methods, and local stimulation).

Sensitivity analysis A sensitivity analysis will be performed to assess the robustness of the results based on each study's contribution to the effect size. The effect estimate will be evaluated by systematically excluding each study, one at a time. The sensitivity analysis will be conducted using Stata 18.0 with the command db metaninf. A p-value of less than 0.05 will be considered statistically significan.

Language restriction we will not impose any language restrictions.

Country(ies) involved China.

Keywords Acupuncture; Electroacupuncture; Ulcerative colitis; Animal model; Mechanism of action; Systematic review; Meta analysis.

Dissemination plans Our primary objective is to publish the complete findings of this research in reputable peer-reviewed journals. In addition, we plan to present key outcomes at leading academic conferences to share insights and engage with the scholarly community.

Contributions of each author

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