INPLASY PROTOCOL

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Review Stage at time of this submission: Data extraction.

Conflicts of interest: None declared.

Comparative Efficacy of Five Most Common Traditional Chinese Medicine Monomers for promoting recovery of motor function in Rats with Blunt Spinal Cord Injury: A Network Meta-Analysis

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Review question / Objective: In this study, a network meta-analysis (NMA) was used to compare the efficacy of five traditional Chinese medicine (TCM) monomers for promoting motor function recovery in rats with blunt spinal cord injury (SCI).

Condition being studied: Neuroprotective Effects of Traditional Chinese Medicine Monomers for Spinal Cord Injury in Animal Model. Two trained researchers selected the papers and stringently extracted the data based on the inclusion/exclusion criteria, and the selections were cross-checked. In the case of disagreement, a third researcher settled the conflict with a common consensus.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 January 2023 and was last updated on 05 February 2023 (registration number INPLASY202310070).

INTRODUCTION

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third researcher settled the conflict with a common consensus.

METHODS

Search strategy: We searched scientific databases such as PubMed, Ovid-Embase, Web of Science, China National Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP), Wanfang Database, and China Biomedical Literature Database (SinoMed). The retrieval period was from inception to December 2022. Terms such as "curcumin," "turmeric yellow," "curcumin phytosome," "ginsenoside," "panaxosides," "resveratrol," "trans-resveratrol," "cis-resveratrol," "tanshinone," "tanshinone IIA," "tetramethylpyrazine," "ligustrazine," "chuanxiongzine," "spinal cord injuries," "spinal cord injury," "spinal injury," "spinal cord trauma," "spinal cord contusion," were used as subject words, keywords, free-text terms, or MeSH (Medical Subject Heading) terms to identify potentially eligible studies. The search strategy was adjusted for each database. There were no restrictions on blinding methods, language, and year of publication. Supplementary Table S1 describes the detailed search strategies of each database.

Participant or population: Rat model of spinal cord injury.

Intervention: TCM monomers (CUR, TMP, RSV, GS, TIIA).

Comparator: (1) Positive control: contrasts between different TCM monomers. (2) Negative control: normal saline, vehicle, blank, PBS, DMSO.

Study designs to be included: Control studies were included.

Eligibility criteria: Exclusion Criteria(1) SCI models induced by other causes, such as complete transverse SCI, hemisection SCI and spinal cord ischemia/reperfusion injury. (2) Studies that have not reported BBB scores. (3) Repeated publications. (4) Studies that do not provide complete raw data or data cannot be extracted.

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Main outcome(s): Weekly BBB score of four weeks after treatment with TCM monomer were included for final analysis, which could better reflect the dynamic changes of motor function recovery in rats.

Quality assessment / Risk of bias analysis: The independent reviewers assessed the quality of the included studies using SYRCLE's Risk of Bias tool for animal studies. The SYRCLE's Risk of Bias tool includes ten items: (1) sequence generation; (2) baseline characteristics; (3) allocation concealment; (4) random housing; (5) blinded intervention of animal; (6) random outcome assessment; (7) Blinded assessment of outcome; (8) Incomplete outcome data; (9) Selective outcome reporting; (10) Other types of bias. A difference in opinions was negotiated or decided by a third reviewer. Each study was graded as either "low," "high," or "unclear" risk.

Strategy of data synthesis: 1 Traditional Meta-Analysis - A traditional meta-analysis was conducted using STATA 16 software to compare BBB score results between TCM monomers and negative controls. Standardized mean difference (SMD) was regarded as the effect analysis statistic and provided its 95% CI. The heterogeneity among included studies was analyzed by χ^2 test (test level was α= 0.1) and was quantitatively judged by I^2. If there was no statistical heterogeneity, Fixed-effects models were used for the meta-analysis; otherwise, meta-analysis was performed using random-effects model. The a level was set at 0.05.
2 Network Meta-Analysis - We applied STATA 16 software to the extracted continuous variables for network meta-analysis (NMA) and generated the

standardized mean difference (SMD) with 95% confidence interval (CI). The evidence network diagram for SCI comparison of 5 TCM monomers was drawn to visually display the relationship between each TCM monomer and the size of the sample. The surface under the cumulative ranking area (SUCRA) was used to rank the probabilities for different interventions. The SUCRA values range from 0 to 100%, assigned to the worst and best treatments [27]. Publication bias and small-sample effects were assessed by funnel plots.

Subgroup analysis: No subgroup analysis was performed.

Sensitivity analysis: The sensitivity analysis of traditional meta-analysis was performed by stata software, and the sensitivity of the article was reflected by the effect size after the deletion of one of the articles.

Country(ies) involved: China.

Keywords: Traditional Chinese Medicine, monomer, spinal cord injury, motor function, animal studies, network meta-analysis.

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