

# INPLASY PROTOCOL

To cite: Wu et al. Quality of Evidence Supporting the Effects of Ginkgo Terpene Lactone Preparations in Ischemic Stroke :An Overview of Systematic Reviews and Meta-Analyses. Inplasy protocol 202290124. doi: 10.37766/inplasy2022.9.0124

Received: 29 September 2022

Published: 29 September 2022

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

**Conflicts of interest:**  
None declared.

## Quality of Evidence Supporting the Effects of Ginkgo Terpene Lactone Preparations in Ischemic Stroke: An Overview of Systematic Reviews and Meta-Analyses

Wu, XQ<sup>1</sup>; Fan, MX<sup>2</sup>; Pan, YB<sup>3</sup>; Guo, D<sup>4</sup>.

**Review question / Objective:** 2.2.1 Type of studies SRs/MAs of Randomized Controlled Trials (RCTs) of GTLP for IS in any language. 2.2.2 Type of Participants Included patients were diagnosed with IS according to international or national standards, regardless of race, age, gender, time of onset, and source of cases. 2.2.3 Type of Intervention The intervention method in the control group was routine treatment, and the intervention method in the intervention group was GTLP treatment or GTLP combined with the treatment of the control group. 2.2.4 Types of outcomes Conclusions at least need to include clinical efficacy analysis and National Institute of Health Stroke Scale (NIHSS).

**Condition being studied:** Stroke is the second leading cause of death and third leading cause of disability globally. Among them, ischemic stroke (IS) accounts for 70% of all stroke types. It is a central nervous system disease caused by cerebral blood circulation disorder, ischemia and hypoxia. The incidence rate is high and increasing year by year, the age of onset is younger, the disability rate is high, and most patients have different degrees of limb motor dysfunction. In order to reduce the burden of stroke on the society and the patient's family, many articles proposed to strengthen the primary stroke prevention - behavior change and drug intervention.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 September 2022 and was last updated on 29 September 2022 (registration number INPLASY202290124).

### INTRODUCTION

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treatment, and the intervention method in the intervention group was GTLP treatment or GTLP combined with the treatment of the control group. 2.2.4 Types of outcomes  
**Conclusions** at least need to include clinical efficacy analysis and National Institute of Health Stroke Scale (NIHSS).

**Rationale:** Ginkgolides belong to diterpene lactones, which mainly include ginkgolides A, B, C, K, J, L, M, N, P, and Q. Ginkgolides are the unique active ingredients in *Ginkgo biloba*. Numerous studies have shown that they have neuroprotective and repairing effects, including maintaining blood-brain barrier function, reducing cerebral edema, improving energy metabolism, anti-oxidation, anti-inflammatory, anti-apoptotic, It can reduce amino acid toxicity, promote angiogenesis and nerve excitability, and can play a therapeutic role in different pathological links of ischemic stroke (IS). It is often used to treat diseases related to the central nervous system, such as Alzheimer's disease, stroke, etc. Ginkgo Terpene Lactone Preparations (GTLP) include Ginkgo Diterpene Lactone Meglumine Injection (DGMI) and Ginkgolide Injection (GI). It is widely used in China for the prevention and treatment of various cardiovascular and cerebrovascular diseases due to its good safety and clinical efficacy.

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## METHODS

**Search strategy:** Four English databases (PubMed, Web of Science, EMBASE, Cochrane Library) and four Chinese databases (Wan-fang database, CNKI, Chinese Biomedical Literature Database, VIP Database) will be searched. Simultaneously, manual retrieval was carried out for references in the included literatures to maximize the obtainment of relevant literatures. In addition, the Chinese Clinical Trial Registry Centers and Grey Literature will also be searched. The time is limited from inception until August 2022. The authors will be contacted if essential data is missing. The following keywords were applied during the literature retrieval: "Ischaemic Stroke", "Ginkgo terpene lactone injection", "Ginkgolides", "Meta-Analysis". The search strategy of the PubMed database is presented in Table 1.

**Participant or population:** Included patients were diagnosed with IS according to international or national standards, regardless of race, age, gender, time of onset, and source of cases.

**Intervention:** The intervention method in the intervention group was GTLP treatment or GTLP combined with the treatment of the control group.

**Comparator:** The intervention method in the control group was routine treatment.

**Study designs to be included:** SRs/MAs of Randomized Controlled Trials (RCTs) of GTLP for IS in any language.

**Eligibility criteria:** Animal studies; network meta-analyses; research protocols, repeated publications, reviews, conference abstracts, editorials, and guidelines were excluded.

**Information sources:** Four English databases (PubMed, Web of Science, EMBASE, Cochrane Library) and four Chinese databases (Wan-fang database, CNKI, Chinese Biomedical Literature Database, VIP Database) will be searched. Simultaneously, manual retrieval was carried out for references in the included literatures to maximize the

obtainment of relevant literatures. In addition, the Chinese Clinical Trial Registry Centers and Grey Literature will also be searched. The time is limited from inception until August 2022. The authors will be contacted if essential data is missing.

**Main outcome(s):** Conclusions at least need to include clinical efficacy analysis and National Institute of Health Stroke Scale (NIHSS).

**Additional outcome(s):** None.

**Data management:** Four English databases (PubMed, Web of Science, EMBASE, Cochrane Library) and four Chinese databases (Wan-fang database, CNKI, Chinese Biomedical Literature Database, VIP Database) will be searched. Simultaneously, manual retrieval was carried out for references in the included literatures to maximize the obtainment of relevant literatures. In addition, the Chinese Clinical Trial Registry Centers and Grey Literature will also be searched. The time is limited from inception until August 2022. The authors will be contacted if essential data is missing. Literature screening and information extraction were performed independently by two researchers (XQW and YBP). The studies retrieved from the database with the search strategy described above will be imported into Endnote X9, and duplicates will be removed. Filter titles and abstracts of all articles, retrieve potentially eligible articles for easy browsing, filter irrelevant articles and remove duplicates. Then read the full text to determine the final inclusion. Two researchers (XQW and YBP) used standardized forms to extract the following from each eligible studies: first author, country, year of publication, number of participants, quality assessment tools included in the RCTs, treatment and control measures, and main conclusion. Finally, these results are discussed together. Any differences were discussed and resolved with the third researcher (MXF).

**Quality assessment / Risk of bias analysis:** Two review authors will independently

assess the risk of bias in included studies using ROBIS (Risk of Bias in Systematic reviews). Disagreements between 2 researchers will be resolved by the discussion and contacting third researcher when necessary.

**Strategy of data synthesis:** As a result, we will not conduct a meta-analysis of results; rather, we will present a narrative synthesis of the findings from the included meta-analysis reviewed. AMATAR-2 will be applied to assess report quality, and GRADE for the quality of evidence and ROBIS for the bias, which will be conducted in tabular form for each review.

**Subgroup analysis:** This is a qualitative synthesis and while subgroup analyses may be undertaken it is not possible to specify the groups in advance.

**Sensitivity analysis:** None.

**Language restriction:** None.

**Country(ies) involved:** China.

**Keywords:** ischemic stroke, ginkgo terpene lactone injections, meta-analysis, overview, systematic reviews.

**Contributions of each author:**

Author 1 - Xiaoqi Wu designed this study and searched, screened, extracted the information of the included studies.

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Author 2 - Maoxia Fan assessed the methodology and reporting quality of the included articles.

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Author 3 - Yaobo Pan searched, screened, extracted the information of the included studies.

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Author 4 - Dong Guo revised the manuscript.

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