# INPLASY PROTOCOL

To cite: Li et al. Efficacy and safety of Chinese herbal for Carotid Atherosclerosis：A protocol for systematic review and network meta-analysis. Inplasy protocol 2021100112. doi: 10.37766/inplasy2021.10.0112

Received: 28 October 2021

Published: 29 October 2021

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**Support:** **2019-0096.**

**Review Stage at time of this submission:** **Preliminary searches.**

**Conflicts of interest:**
**None declared.**

# Efficacy and safety of Chinese herbal for Carotid Atherosclerosis: A protocol for systematic review and network meta-analysis

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**Review question / Objective:** **1.Participants： Patients diagnosed as CAS by vascular ultrasound. Age, race, disease severity, and disease duration were not limited. 2.Interventions： The treatment group received Chinese herbal therapies, including decoctions, Chinese patent medicines, powders, pills, with no restrictions on dosage form, dosage and usage. The control group received regular western medicine, other conventional treatment, no treatment or placebo. Both two groups can be treated with conventional drugs. 3.Outcomes： (1) Primary outcomes: total carotid plaque area, IMT, crouse plaque score; (2) Secondary outcomes: total cholesterol, triacylglycerol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, the incidence of adverse reactions. 4.Type of studies： The study will include a randomized controlled trial using Chinese herbal medicine to treat CAS in Chinese or English.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 October 2021 and was last updated on 29 October 2021 (registration number INPLASY2021100112).

## INTRODUCTION

**Review question / Objective:** **1.Participants： Patients diagnosed as CAS by vascular ultrasound. Age, race, disease severity, and disease duration were not limited. 2.Interventions： The treatment group received Chinese herbal therapies, including decoctions, Chinese patent medicines, powders, pills, with no restrictions on dosage form, dosage and usage. The control group received regular western medicine, other conventional treatment, no treatment or placebo. Both two groups can be treated with conventional drugs. 3.Outcomes： (1)**

Primary outcomes: total carotid plaque area, IMT, crouse plaque score; (2) Secondary outcomes: total cholesterol, triacylglycerol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, the incidence of adverse reactions. 4.Type of studies: The study will include a randomized controlled trial using Chinese herbal medicine to treat CAS in Chinese or English.

**Condition being studied:** Carotid atherosclerosis (CAS) can cause acute events such as myocardial infarction and stroke, seriously injuring human health. There are some shortcomings for statins and surgical in the treatment of CAS. Research has proved that Chinese herbal shows its unique advantages with the multi-channel and multi-target treatment strategy. As a result, we propose this study to evaluate the efficacy and safety of Chinese herbal in the treatment of CAS.

## METHODS

**Search strategy:** The study will search PubMed, web of science, Cochrane Central Register of controlled trials, EMBASE, Cochrane Library, China biomedical literature database (SinoMed), China National Knowledge Infrastructure (CNKI), Wanfang database, and VIP database from the beginning to July 2021. In addition, we will search the research registered on the World Health Organization International Clinical Trial Registry Platform (WHO ICTRP) and track the references in the meta-analysis. We will combine medical subject headings (MeSH) and free-text terms to formulate the search strategy. The search string will be built as follows: (""Carotid atherosclerosis" [MeSH Terms] OR Arter* Disease*, Carotid[Title/Abstract] OR Carotid Arter* Disease*[Title/Abstract] OR Artery Disorder*, Carotid[Title/Abstract] OR Carotid Artery Disorder[Title/Abstract] OR Disorders, Carotid Artery[Title/Abstract] OR Carotid Atherosclero*[Title/Abstract] OR Atherosclerotic Disease*, Carotid[Title/Abstract] )AND ("Medicine, Chinese Traditional"[MeSH Terms]OR Medicine, Chinese Traditional[Title/Abstract] OR Traditional Chinese Medicine[Title/Abstract] OR Traditional Medicine, Chinese[Title/Abstract] OR Zhong Yi Xue[Title/Abstract] OR Chinese Traditional Medicine[Title/Abstract] OR Chinese Medicine, Traditional[Title/Abstract] OR "Drugs, Chinese Herbal"[MeSH Terms] OR Drugs, Chinese Herbal[Title/Abstract] OR Chinese Drugs, Plant[Title/Abstract] OR Chinese Herbal Drugs[Title/Abstract] OR Herbal Drugs, Chinese[Title/Abstract] OR Plant Extracts, Chinese[Title/Abstract] OR Chinese Plant Extracts[Title/Abstract] OR Extracts, Chinese Plant[Title/Abstract]) AND ("Randomized Controlled Trials as Topic"[MeSH Terms] OR "Randomized Controlled Trial"[Publication Type] OR Clinical Trials,Randomized[Title/Abstract] OR Trials,Randomized Clinical[Title/Abstract] OR Controlled Clinical Trials,Randomized[Title/Abstract] ).

**Participant or population:** Patients diagnosed as CAS by vascular ultrasound. Age, race, disease severity, and disease duration were not limited.

**Intervention:** The treatment group received Chinese herbal therapies, including decoctions, Chinese patent medicines, powders, pills, with no restrictions on dosage form, dosage and usage.

**Comparator:** The control group received regular western medicine, other conventional treatment, no treatment or placebo.

**Study designs to be included:** The study will include a randomized controlled trial using Chinese herbal medicine to treat CAS in Chinese or English.

**Eligibility criteria:** The study will include a randomized controlled trial using Chinese herbal medicine to treat CAS in Chinese or English. Does not include non-randomized controlled trials, observational studies, animal experiments and case reports.

**Information sources:** The study will search PubMed, web of science, Cochrane Central Register of controlled trials, EMBASE,

Cochrane Library, China biomedical literature database (SinoMed), China National Knowledge Infrastructure (CNKI), Wanfang database, and VIP database from the beginning to July 2021. In addition, we will search the research registered on the World Health Organization International Clinical Trial Registry Platform (WHO ICTRP) and track the references in the meta-analysis. If the required information is incomplete, we will try to contact the corresponding author. If there is no reply, we will record this and extract the data available for analysis.

**Main outcome(s):** Primary outcomes: total carotid plaque area, IMT, crouse plaque score.

**Additional outcome(s):** Total cholesterol, triacylglycerol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, the incidence of adverse reactions.

**Data management:** Two researchers imported the retrieved literature into Endnote x9 for inspection, screening and excluded irrelevant literature. If there are differences, they will be resolved through discussion or seeking a third independent researcher. The two researchers independently extracted the required data into Microsoft Excel 2019. If the required data is incomplete, we will contact the author for it. If there is no response, the literature will decide whether to exclude it after group discussion.

**Quality assessment / Risk of bias analysis:** Two researchers will use Cochrane Collaboration's bias risk assessment tool for quality assessment.54. Each aspect will be classified as "low", "high", or "unclear". In case of disagreement, they will be resolved through discussion or by seeking a third-party researcher.

**Strategy of data synthesis:** 1.Pairwise meta-analysis: We will use STATA16.0 software for paired meta-analysis. Binary variable data will use odds ratio (OR) as the adequate analysis statistics, and continuous variable data will use weighted mean square deviation (WMD). Besides, each effect quantity is expressed by a 95% confidence interval (CI). 2.network meta-analysis: NMA was performed using WinBUGS 1.4.3 and STATA16.0. We use three Markov chain Monte Carlo (MCMC) chains for simulation, and set the number of iterations to 50000, of which the first 20000 annealing to eliminate the influence of the initial value.We will use trace graph and Brooks-Gelman-Rubin graph to ensure convergence. If the potential scale reduction factor (PSRF) tends to 1, the convergence is better, and the results are more reliable. In addition, we will calculate the surface under the Cumulative Ranking Curve value to rank the interventions, with a value range of 0-1. The closer the value is to 1, the better the treatment effect. If there is a closed-loop, a consistency assessment is required. The node splitting method will be used to evaluate the consistency between direct comparison evidence and indirect comparison evidence.

**Subgroup analysis:** We will analyze the subgroup of patients according to the course of disease, age and blood lipid level to explore the impact of these factors on the results.

**Sensitivity analysis:** We will exclude the literature one by one to determine whether the literature has an impact on heterogeneity. If there is no significant change in heterogeneity before and after elimination, the results are stable and reliable. Otherwise, the literature may be a source of heterogeneity, and we will discuss whether to delete the literature.

**Language:** The language will be restricted to Chinese or English.

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

**Keywords:** Carotid atherosclerosis, Chinese herbal, network meta-analysis, protocol.

**Contributions of each author:**
Author 1 - Haitao Li.
Author 2 - Hongwei Zhi.
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**Author 4 - Yahan Wang.**
**Author 5 - Shuai Zhang.**
**Author 6 - Sishuo Zhang.**