# INPLASY PROTOCOL

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

**Conflicts of interest:** None declared.

## Effect of Sodium Tanshinone IIA Sulfonate Injection on Vascular endothelial function and inflammatory factors in Patients With Coronary Heart Disease: A Systematic Review and Meta-Analysis

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**Review question / Objective:** Vascular endothelial dysfunction and inflammatory response are very important in the occurrence and development of coronary heart disease (CHD). A large number of studies have proved that Tanshinone IIA Sulfonate Injection (STS) has a certain curative effect on coronary heart disease, and also has the effect of improving vascular endothelial function and inflammatory factors. However, there is no meta-analysis on the effect of STS on endothelial function and inflammatory factors. Therefore, We systematically evaluated the effect of STS on vascular endothelial function and inflammatory factors in patients with coronary heart disease using meta-analysis method.

**Information sources:** A computerized search of published relevant studies on STS in the treatment of CHD was performed. PubMed, Cochrane Library, Web of Science, Embase, China National Knowledge Infrastructure(CNKI), Chinese Biomedical Literature Database(CBM), Chinese Scientific Journals Database(VIP) and Wanfang database were searched.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 July 2022 and was last updated on 07 July 2022 (registration number INPLASY202270037).

## INTRODUCTION

**Review question / Objective:** Vascular endothelial dysfunction and inflammatory response are very important in the occurrence and development of coronary heart disease (CHD). A large number of studies have proved that Tanshinone IIA Sulfonate Injection (STS) has a certain curative effect on coronary heart disease, and also has the effect of improving vascular endothelial function and inflammatory factors. However, there is no meta-analysis on the effect of STS on endothelial function and inflammatory

factors. Therefore, We systematically evaluated the effect of STS on vascular endothelial function and inflammatory factors in patients with coronary heart disease using meta-analysis method.

**Condition being studied:** Coronary heart disease (CHD) is a disease caused by myocardial ischemia, hypoxia or necrosis caused by coronary atherosclerosis resulting in stenosis, spasm or obstruction of the lumen, and is one of the most common clinical cardiovascular diseases. Studies have shown that the damage of vascular endothelial function and inflammatory response act on the early stage of atherosclerosis, which is the initial link of atherosclerosis. Early attention to vascular endothelial function and inflammatory response can effectively reduce the occurrence and development of coronary heart disease.

## METHODS

**Participant or population:** Patients with CHD, including patients with angina pectoris(AP) and heart failure(HF).

**Intervention:** Sodium Tanshinone IIASulfonate+conventional chemical medicine (CCM).

**Comparator:** CCM;intervention and control groups that used routine therapy (RT) simultaneously

**Study designs to be included:** Published randomized controlled trial (RCT), the language is limited to Chinese and English.

**Eligibility criteria:** Inclusion criteria: (1) Types of studies:Published randomized controlled trial (RCT), the language is limited to Chinese and English; (2) Types of participants:Patients with CHD,including patients with angina pectoris(AP) and heart failure(HF); (3) Types of interventions: STS+conventional chemical medicine (CCM); (4) Types of comparators: CCM;intervention and control groups that used routine therapy (RT) simultaneously; (5) Types of outcome measures:Vascular

endothelial function indicator(including ET-1,NO,TXB2,VEGF) and inflammatory factor(including CRP,TNF-α,APN). Exclusion Criteria: (1) Study types as following: reviews, meta-analysis,cluster RCTs, animal experiments, expert experience, or case-control studies; (2) Diagnostic assessment criteria was not mentioned; (3) Duplicate publications; (4) Literature with obvious statistical errors.

**Information sources:** A computerized search of published relevant studies on STS in the treatment of CHD was performed. PubMed, Cochrane Library, Web of Science, Embase, China National Knowledge Infrastructure(CNKI), Chinese Biomedical Literature Database(CBM), Chinese Scientific Journals Database(VIP) and Wanfang database were searched.

**Main outcome(s):** Vascular endothelial function indicator(including ET-1,NO,TXB2,VEGF, etc) and inflammatory factor(including CRP,TNF-α,APN, etc).

**Quality assessment / Risk of bias analysis:** The assessment of risk of bias literatures was evaluated by 2 investigators (Xujie Li and Ziyang Zhou) according to the risk of bias assessment tool in Cochrane Reviewers Handbook 6.1.0 [26] , mainly including the following 7 aspects: random sequence generation; allocation concealment; implementation of blind method for patients and trial personnel; implementation of blind method for outcome assessors; incomplete result data; selective reporting; and other biases (such as potential bias related to special study design in studies, false statement, etc.). Eventually, it is necessary to make a judgment on "low risk", "high risk" and "unclear risk" in the literatures. Disagreement will be settled by team discussion. Review manager V.5.4 will be used to make the risk of bias diagram.In addition, we used the grading of recommendations assessment, development, and evaluation (GRADE) approach to evaluate the quality of included evidences.

**Strategy of data synthesis:** We used Review manager V.5.4 and Stata V.16.0 for statistical analysis.Because the indicators to be analyzed are all continuous variables, we chose the mean difference (MD) as the effect scale. All results were presented with 95% confidence intervals (CI). Heterogeneity among trials was assessed by Cochrane's Q test and I-squared statistic. When I2<50%, it means that the heterogeneity among studies is small, and the fixed effect model is used for analysis; If I2≥50%, the random effect model is used.Furthermore,The sensitivity analysis was also performed by removing each study one at a time to evaluate the stability of the results.Subgroup analysis was performed according to different duration of intervention and doses of STS. The publication bias was evaluated by the funnel plot, the Begger's test and the Egger's test.If publication bias was present, results were adjusted using the trim and fill method.

**Subgroup analysis:** To explore the sources of heterogeneity and improve the persuasiveness of the evidence, we conducted a subgroup analysis based on the study characteristics(duration of treatment, dose of STS and types of CCM).

**Sensitivity analysis:** To further confirm the stability of the results of the meta-analysis,sensitivity analysis was conducted by excluding the studies from the analysis one by one.

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

**Keywords:** Sodium Tanshinone IIA Sulfonate, coronary heart disease, vascular endothelial function, inflammatory factor, meta analysis, systematic review.

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