INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Astragaloside IV for Heart Failure: Preclinical Evidence and Possible Mechanisms, a Systematic Review and Meta-Analysis

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Review question / Objective: **To explore the cardioprotective effects of astragaloside IV (AS-IV) in heart failure (HF). (1)P: Animal models of HF were prepared by abdominal aorta coarctation (AAC), transverse aortic constriction (TAC), ligation of the left anterior descending (LAD), injection of isoproterenol (ISO), injection of lipopolysaccharide (LPS) and injection of doxorubicin (Dox). (2)I: AS-IV was the only intervention. (3) C: The control treatments were positive or blank control. (4) O: Left ventricular ejection fraction (LVEF), left ventricular fractional shortening (LVFS), left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), left ventricular weight-to-body weight (LVW/BW) and B-type brain natriuretic peptide (BNP) were detected.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 March 2023 and was last updated on 04 March 2023 (registration number INPLASY202330012).

INTRODUCTION

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Condition being studied: Cardiovascular disease is a prominent cause of death worldwide. (1) Heart failure (HF) is not only the final outcome of all kinds of cardiovascular diseases, but also the focus and cause of difficulty in its prevention and treatment. Due to strict contraindications and adverse reactions, although new drug treatment strategies for HF are constantly emerging, the treatment efficacy is inadequate. (2) Thus, finding new therapeutic drugs is urgent.
Astragalus is an herbal medicine with good efficacy and safety, and has been widely used in Eastern countries for thousands of years. Astragaloside IV (AS-IV) is an active ingredient of Astragalus with cardioprotective effects.(3) The molecular structure of this chemical extract is C41H68O14, and its molecular weight is 784.97 g/mol. Modern pharmacological studies have shown that AS-IV improves HF by regulating energy metabolism,(4) reducing oxidative stress,(5) promoting angiogenesis,(6) reducing myocardial fibrosis,(7) and reducing ventricular remodeling.(8) In short, AS-IV seems to be a potential candidate for assisting in the prevention and treatment of HF.
However, the efficacy of AS- IV in an experimental HF model has not been systematically evaluated, and the potential mechanisms have not been summarized in detail. Moreover, the retrospective analysis of animal experimental data can evaluate the potential value of AS-IV in the treatment of HF from the laboratory to the clinic.(9) Therefore, this study evaluated the efficacy and mechanism of AS-IV in the treatment of HF, and to provided preclinical evidence for AS-IV in the treatment of HF.

METHODS

Participant or population: Animal models of HF were prepared by abdominal aorta coarctation (AAC), transverse aortic constriction (TAC), ligation of the left anterior descending (LAD), injection of isoproterenol (ISO), injection of lipopolysaccharide (LPS) and injection of doxorubicin (Dox).

Intervention: AS-IV was the only intervention.

Comparator: The control treatments were positive or blank control.

Study designs to be included: Animal experiment.

Eligibility criteria: The inclusion criteria were prespecified as follows: (1) Animal models of HF were prepared by abdominal aorta coarctation (AAC), transverse aortic constriction (TAC), ligation of the left anterior descending (LAD), injection of isoproterenol (ISO), injection of lipopolysaccharide (LPS) and injection of doxorubicin (Dox). (2) AS-IV was the only intervention. (3) The control treatments were positive or blank control. (4) Left ventricular ejection fraction (LVEF), left ventricular fractional shortening (LVFS), left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), left ventricular weight-to-body weight (LVW/BW) and B-type brain natriuretic peptide (BNP) were detected.

Information sources: PubMed, Excerpta Medica Database (EMBASE), Cochrane Library, Web of Science, Wanfang database, SINOMED, VIP database and China National Knowledge Infrastructure (CNKI).

Main outcome(s): Left ventricular ejection fraction (LVEF), left ventricular fractional shortening (LVFS), left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), left ventricular weight-to-body weight (LVW/BW) and B-type brain natriuretic peptide (BNP).

Quality assessment / Risk of bias analysis: The methodological quality of the included studies was assessed independently by two authors via the Cochrane Collaboration tool. And the differences were resolved by the third author. The review items included random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other biases.

Strategy of data synthesis: The data were analyzed with Stata (version 13.0) or Cochrane Collaboration software (Rev Man 5.3).(10) Discontinuous variables were expressed as the risk ratio (RR) with a 95% confidence interval (CI). For continuous data, if the unit or the measurement instrument was consistent, the mean difference (MD) with 95% CI was used, otherwise, the standard mean difference (SMD) with a 95% CI was used. The $\chi 2$ test and I2 test were used to assess heterogeneity among the included studies. (11) A fixed-effect model was used when heterogeneity was low ($P \geq 0.05$, $I2 \leq 50\%$), otherwise, a random-effect model was applied to decrease heterogeneity.

Subgroup analysis: A subgroup analysis was performed based on factors such as sex, weight, anesthesia method and duration to explore the source of heterogeneity.

Sensitivity analysis: The sensitivity analyses were performed to evaluate the reliability of results.

Country(ies) involved: China.

Keywords: Astragaloside IV; Heart failure; Pre-clinical evidence; Systematic review.

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