INPLASY PROTOCOL

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

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Quercetin for Myocardial Ischemia/ Reperfusion Injury: A Preclinical Systematic Review and Meta-Analysis

Lu, LY[1]; Ma, XC[2]; Zheng, JH[3]; Li, LJ[4]; Yang, WN[5]; Xu, WH[6]; Kong, YX[7]; Wang, J[8]; Chen, X[9]; Xu, XM[10].

Review question / Objective: **P: rats in myocardial ischemia/ reperfusion injury; I: received quercetin treatment merely; C: received vehicle or no treatment; O: primary outcomes were myocardial infarction size, myocardial injury marker, secondary outcomes were serum indices or protein levels relative to the mechanisms of quercetin in myocardial I/R injury; S: randomized controlled studies.**
Condition being studied: **At present, many animal experiments have reported that quercetin has a positive effect on myocardial ischemia-reperfusion injury, and the adjuvant treatment of limiting myocardial ischemia-reperfusion injury is still the current research focus. Therefore, preclinical systematic review and meta-analysis of quercetin for myocardial ischemia-reperfusion injury is of great significance to transform basic research into clinical treatment.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 April 2020 and was last updated on 23 April 2020 (registration number INPLASY202040162).

INTRODUCTION

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METHODS

Participant or population: Rats in myocardial ischemia/reperfusion injury.

Intervention: Received quercetin treatment merely.

Comparator: Received vehicle or no treatment.

Study designs to be included: Randomized controlled studies.

Eligibility criteria: Studies were included for analysis when they meet:(1) animal studies assessing the administration of quercetin for myocardial I/R model; (2) analyzed intervention received quercetin treatment merely; comparator intervention received vehicle or no treatment;(3) primary outcomes were myocardial infarction size, myocardial injury marker, secondary outcomes were serum indices or protein levels relative to the mechanisms of quercetinin myocardial I/R injury.

Information sources: We searched for animal studies of quercetin for myocardial I/R injury in Chinese National Knowledge Infrastructure (CNKI), EMBASE, PubMed, VIP information database, Web of Science, China Biology Medicine disc(CBM) and Wanfang data Information. All the databases were searched from inception to March 2020. (2) Searching other resources: Grey literature compiles materials and researches that are not covered in the databases mentioned, as well as the sites of animal research organizations, Google Scholar and Baidu Scholar.

Main outcome(s): Main outcomes were myocardial infarction size and markers of myocardial injury.

Additional outcome(s): Additional outcomes were serum indices or protein levels relative to the mechanisms of quercetin in myocardial I/R injury.

Quality assessment / Risk of bias analysis: The study quality assessment was independently valued with the Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies (CAMARADES). Two authors independently evaluated the quality of study using the 10-point scoring scale: A, peer reviewed publication; B, control of temperature; C, random allocation to treatment or control; D, blinded induction of model; E, blinded assessment of outcome; F, use of anesthetic without significant intrinsic cardioprotective activity; G, animal model(aged, diabetic, or hypertensive); H, sample size calculation; I, compliance with animal welfare regulations; J, statement of potential conflict of interests. Risk of bias analysis: SYRCLE's risk of bias tool for animal studies.

Strategy of data synthesis: Manager 5.2 version software. The estimate of the combined effect sizes was calculated by the standardized mean difference (SMD). The heterogeneity assumption was checked by I2 statistics, when I2 was less than 50%, fixed effects model was used for meta-analysis, otherwise, random effects model was carried out. 95% confidence intervals of all results were calculated, the significance was determined by Z-test, with a P value<0.05 as significant level.

Subgroup analysis: If the included studies have high heterogeneity, we will conduct a subgroup analysis. The subgroup analysis will be implemented according to animal species, the duration and dosage of treatment and the method of animal model induced.

Sensibility analysis: The sensibility analysis of the overall comprehensive effect of all outcome indicators was carried out by exclusion method, each study will be excluded, and the remaining studies were reanalyzed to assess the stability of the

results. If the results show that there is no qualitative change in the comprehensive effect, the results are stable and credible.

Country(ies) involved: China.

Keywords: Quercetin, Myocardial ischemia reperfusion injury, Preclinical analysis, Meta-Analysis.

Contributions of each author:
Author 1 - Author 1 drafted the manuscript.
Author 2 - The author provided statistical expertise.
Author 3 - The author read, provided feedback and approved the final manuscript.
Author 4 - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.