INPLASY

The Role and Mechanisms of Naringenin in Myocardial Ischemia-Reperfusion Injury: A Systematic Review and Preclinical Meta-Analysis

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ADMINISTRATIVE INFORMATION

INTRODUCTION

*R*eview question / Objective To systematically evaluate the protective effects and mechanisms of naringenin on myocardial ischemia-reperfusion injury models in preclinical animal studies, and to provide evidence for clinical translation.

Condition being studied Myocardial ischemia-reperfusion injury (MI/RI) refers to a pathophysiological process where myocardial damage worsens after blood flow restoration to the ischemic myocardium, commonly observed following reperfusion therapy for acute myocardial infarction. Its mechanisms involve ATP depletion and calcium overload during the ischemic phase, as well as oxidative stress, inflammation, and mitochondrial dysfunction upon reperfusion. This can induce cardiomyocyte death, arrhythmias, cardiac function deterioration, and expanded infarct size. As a key bottleneck limiting the benefits of reperfusion therapy, it lacks specific and effective interventions, making it a core research direction in cardiovascular medicine.

METHODS

Participant or population Participants in this study are experimental mice and rats with induced myocardial ischemia-reperfusion injury (MI/RI) models, including common laboratory strains such as Sprague Dawley (SD) rats and Wistar rats. This preclinical systematic review and meta-analysis does not involve human participants.

Intervention Naringenin (a natural flavonoid) administered via various routes (e.g., intragastric gavage, intraperitoneal injection) at doses ranging from 25 to 400 mg/kg, with treatment durations from 1 hour to 8 weeks, for the intervention of myocardial ischemia-reperfusion injury (MI/RI) in preclinical animal models.

Comparator Vehicle control (e.g., normal saline, DMSO) or no additional treatment, administered to MI/RI model animals in the same volume and schedule as the naringenin intervention group, to isolate the specific effects of naringenin.

Study designs to be included This review will only include preclinical randomized controlled in vivo animal studies focusing on naringenin intervention for myocardial ischemia-reperfusion injury (MI/RI) models, excluding in vitro cell experiments, clinical studies, reviews, conference abstracts, and non-experimental studies.

Eligibility criteria Additional inclusion criteria: ①
Studies are limited to Chinese and English languages; ② Extractable data of at least one core outcome (myocardial infarct size, myocardial enzymes, cardiac function) is provided.Additional exclusion criteria: ① Duplicate publications; ②
Studies with missing or unextractable key data.

Information sources PubMed, Embase, Cochrane Library ,Web of science, China National Knowledge Infrastructure, Wan Fang database, Chinese Scientific Journal Database.

Main outcome(s) Primary Outcomes: Myocardial infarct size, myocardial enzymes (LDH, CK, CK-MB), cardiac function parameters (LVDP, LVEDP, ±LVdP/dtmax).
Secondary Outcomes: Heart rate (HR); apoptosis-related indicators (apoptosis index, Bax, Bcl-2); inflammatory factors (IL-1β, TNF-α); oxidative stress indicators (SOD, MDA).

Quality assessment / Risk of bias analysis The methodological quality of the 32 included animal experiments investigating naringenin intervention in myocardial ischemia-reperfusion injury was independently assessed using the SYRCLE's Risk of Bias Tool for Animal Studies (Systematic Review Centre for Laboratory Animal Experimentation Risk of Bias Tool).Publication bias was evaluated via Egger's test.

Strategy of data synthesis Statistical analyses were conducted using Stata 15.1 and Review Manager 5.4.

Subgroup analysis A detailed subgroup analysis was performed.

Sensitivity analysis Sensitivity analysis was performed using the one-by-one exclusion method.

Country(ies) involved China.

Keywords Naringenin ; Myocardial Ischemia-Reperfusion Injury ; Systematic Review ; Preclinical Meta-Analysis.

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