The Protective Effect of Puerarin on Myocardial Infarction Reperfusion Injury (MIRI): A Meta-Analysis of Randomized Studies in Rat Models

Huang Wenjun*  
Wen Jing*  
Li Tao  
Mao Liang  
Yang Yan  
Zeng Xiaorong  
Zhou Rui

* Co-first author

Corresponding Author: Zhou Rui, e-mail: zhouhuaxizhu@126.com

Source of support: No. 2013JY0074 (Foundation of Applied Basic Research Program from Sichuan Provincial Department of Science and Technology); No. 13ZA0236 (Foundation of Key Program from Sichuan Provincial Department of Education); No. 2012QN-04 (Natural Science Foundation for Young Scientist from Luzhou Medical College)

Background: Although puerarin is generally considered as a protective agent for cardio-cerebrovascular diseases, the exact effect on reducing myocardial infarction reperfusion injury (MIRI) is not well understood. This study aimed to pool previous randomized controlled studies based on rat models to evaluate the effects of puerarin on MIRI.

Material/Methods: Relevant studies were searched among PubMed, Embase, Medline, and CNKI (China National Knowledge Infrastructure). To assess the therapeutic effects of protective effects of puerarin on myocardial infarction reperfusion injury, the outcome indicators which were reported in at least 3 original studies were extracted and pooled, including size of myocardial ischemia (MIS) and myocardial infarction (MIN), creatine kinase (CK), methylene dioxyamphetamine (MDA), and superoxide dismutase (SOD).

Results: Administration of puerarin could effectively reduce the size of MIN after MIR (mean difference: −29.20, 95%CI: −44.90 to −13.51, p=0.0003). Puerarin directly led to decreased CK (mean difference: −6.89, 95%CI: −9.40 to −4.38, p=0.00001) and MDA (mean difference: −2.41, 95%CI: −3.14 to −1.68, p<0.00001) and increased serum SOD (mean difference: 63.97, 95%CI: 38.19 to 89.75, p<0.00001).

Conclusions: Puerarin might have a protective effect in myocardial tissues during MIRI through increasing SOD and decreasing CK and MDA. However, more animal studies and randomized controlled clinical trials are required to confirm these results.

MeSH Keywords: Meta-Analysis as Topic • Myocardial Infarction • Myocardial Reperfusion Injury

Full-text PDF: http://www.medscimonit.com/abstract/index/idArt/894312
Background

Acute myocardial ischemia and myocardial infarction are the leading cause of morbidity and mortality of the world [1]. Early reperfusion to the ischemic area is necessary to rescue the ischemic myocardium. However, reperfusion is a ‘double edged sword’, since it may also accelerate and generate additional damage by introduction of oxidative stress and inflammation rather than restoration of normal function [2]. Oxygen radicals, calcium overloading, and neutrophils are the major mediators of reperfusion injury [1,3]. The oxygen radicals are released from injured endothelial cells and myocytes in the ischemic area and also from neutrophils moved to the area. The oxygen radicals become activated due to reperfusion and cause membrane damage, thereby leading to calcium overloading. The neutrophils entered the ischemic area also release inflammatory mediators, leading to microvascular obstruction and the no-reflow phenomenon [1]. The reversible dysfunction and irreversible necrosis associated with reperfusion are collectively called reperfusion injury and is one of the major problems for treatment of myocardial infarction [4–6].

Puerarin (7,4-dihydroxyisoflavone-8β-glucopyranoside) is a major natural compound extracted from the kudzu root (Pueraria lobata (Wild.) Howe), a famous traditional Chinese medicine [7]. This drug is widely prescribed for patients with cardio-cerebrovascular diseases in China. Previous studies also showed that puerarin has some therapeutic effects on diabetes mellitus [8], cerebral ischemia [9], myocardial ischemia [10], hypertension [11] and arteriosclerosis [12]. Studies showed the therapeutic effect of puerarin is closely related to its antioxidant role. Therefore, it acts as a scavenger of active oxygen radicals [13]. In addition, puerarin can also improve endothelial function through stimulating production of nitric oxide, phosphorylation of endothelial nitric oxide synthase and inhibiting cellular factors, such as C-reactive protein and adhesive molecules [7].

Although puerarin is generally considered as a protective agent for cardio-cerebrovascular diseases, the exact effect on reducing myocardial infarction reperfusion injury (MIRI) is not well understood. Previous animal based studies are usually small and thus had low statistical power. Therefore, this study aims to pool previous randomized controlled studies based on rat model to evaluate the effects of puerarin in MIRI.

Material and Methods

Literature search

Relevant studies were searched among PubMed, Embase, Medline and CNKI (China National Knowledge Infrastructure). The following the terms and strategy were applied to search relevant studies: (“puerarin”) AND (“myocardial infarction reperfusion injury”) AND (“rat”). To avoid missing qualified studies, references lists of included studies, relevant reviews and meta-analysis were manually searched. No language restrictions were set during searching.

Inclusion and exclusion criteria

Studies included for this meta-analysis have to meet the following criteria simultaneously: (1) randomized studies assessed the protective effects of puerarin supplementation on myocardial infarction reperfusion injury in rat model; (2) puerarin is either administrated before myocardial ischemia reperfusion or before myocardial ischemia; (3) the exact outcome data could be extract from original studies. Studies meeting any the following criteria were excluded: (1) studies based on other animal models; (2) case report, animal studies or review; (3) duplicate studies or detailed data could not be extracted.

Data extraction

The following basic information was extracted from original studies: surname of the first author; year of publication; animal model; methods of myocardial ischemia; number of rats in and experimental design of experimental and control group; timing of puerarin administration and the outcome indicators measured. To assess the therapeutic effects of protective effects of puerarin on myocardial infarction reperfusion injury, the outcome indicators which were reported in at least three original studies were extracted and pooled, including size of myocardial ischemia (MIS) and myocardial infarction (MIN), creatine kinase (CK), methylene dioxyamphetamine (MDA) and superoxide Dismutase (SOD). TTC staining was performed in the original studies to confirm the ischemia area. Size of MIN is defined as the weight of infarcted myocardium ×100% or the area of infarcted area/whole myocardium ×100%. Size of MIS is defined as the weight ischemic myocardium/weight of whole heart. If the studies reported outcome with different units, unit conversion (based on unit mentioned above) were performed before pooling the data. Two scholars independently performed data extraction. If the studies designed different dose groups of puerarin, each dose group was considered as an individual experimental arm. A third author was responsible for cross check of the data. Any disagreements were solved by discussion and consensus.

Data analysis

Data integration and analysis is based on Review Manager 5.3 (the Cochrane Collaboration). All outcome analyzed are continuous variables. Thus, the weighted mean different (WMD) and
the 95% confidence intervals (CI) were calculated. Chi-square based Q test and I$^2$ was used to assess between study heterogeneity. $p<0.1$ in Q test or I$^2>50\%$ indicates significantly heterogeneity. A random effect model (DerSimonian and Laird method) was used if significant between study heterogeneity detected. Otherwise, the fixed effect model based on Mantel-Haenszel method was applied. For the pooled results, $p<0.5$ in Z test was considered statistically significant.

**Results**

**Characteristics of Included Studies**

Through searching in relevant databases, a total of eight studies were included in this meta-analysis [14–21]. The general searching and screening process is summarized in Figure 1 and their basic characteristics are given in Table 1. The eight studies were published from 2006 to 2013. All of model of MIS was induced by ligation of left anterior descending coronary artery.

### Table 1. The key characteristics of studies included.

| Study   | Animal model | Method of MIS | No. animals | Experimental design | Timing of PUE administration | Outcome measured                                      |
|---------|--------------|---------------|-------------|---------------------|-----------------------------|-------------------------------------------------------|
| Gao 2006 | Rat          | Ligation of LAD | 11/11       | PUE (100 mg/kg) + IR | I/R Before MIS              | Size of MIS, size of MIN, CK, TnT, cell apoptosis      |
| Bao 2007 | Rat          | Ligation of LAD | 20/10       | PUE (100/200 mg/kg) + IR | I/R Before MIS              | CK, MDA, SOD, NO                                      |
| Gao 2007 | Rat          | Ligation of LAD | 11/11       | PUE (100 mg/kg) + IR | I/R Before MIS              | Size of MIS, size of MIN, CK, TnT, cell apoptosis      |
| Wang 2008 | Rat         | Ligation of LAD | 20/20       | IR+PUE (100 mg/kg)   | I/R Before MIR              | Size of MIS, LDH, CK, SOD, MDA                         |
| Lu 2009a | Rat          | Ligation of LAD | 6/6         | PUE (100 mg/kg) + IR | I/R Before MIS              | Size of MIS, size of MIN, CK, ET, NO                  |
| Lu 2009b | Rat          | Ligation of LAD | 6/6         | IR+PUE (100 mg/kg)   | I/R Before MIR              | Size of MIS, size of MIN, CK, ET, NO                  |
| Jia 2010 | Rat          | Ligation of LAD | 24/8        | IR+PUE (2/5/10 mg/kg)| I/R Before MIR              | SOD, MDA, GSH, GSH-Px                                 |
| Pan 2010 | Rat          | Ligation of LAD | 12/12       | IR+PUE (20 mg/kg)    | I/R Before MIR              | CK, MPO, MDA                                         |
| Li 2013  | Rat          | Ligation of LAD | 30/10       | IR+PUE (2/5/10 mg/kg)| I/R Before MIR              | Size of MIN, CK, LDH, NO, XO, SOD, MDA, GSH and GSH-Px|

MIR – myocardial ischemia reperfusion; MIS – myocardial ischemia; MIN – myocardial infarction; LAD – left anterior descending coronary artery; PUE – Puerarin; I/R – ischemia-reperfusion; CK – creatine kinase; MDA – methylene dioxyamphetamine; SOD – superoxide dismutase; GSH – glutathione; GSH-Px – glutathione peroxidase; MPO – myeloperoxidase; NO – nitrogen monoxide; TnT – cardiac troponin T; ET – endothelin; XO – xanthine oxidase; N.A. – not available; E – experimental; C – control.
MIS and five studies reported the outcome of MIN. Generally, three studies reported the effect of puerarin on the size of myocardial ischemia (MIS) and size of MIN, CK, MDA and SOD were the mostly reported outcome data.

### Puerarin significantly reduced size of MIN but not MIS

Three studies reported the effect of puerarin on the size of MIS and five studies reported the outcome of MIN. Generally, puerarin had no effect on size of MIS (mean difference: −1.40, 95% CI: −3.34 to 0.55, p=0.16), no matter administrated before MIS (mean difference: −0.91, 95% CI: −3.10 to 1.27, p=0.41) or before MIR (mean difference: −3.24, 95% CI: −7.51 to 1.03, p=0.14) (Figure 2). However, puerarin could effectively reduce the size of MIN (mean difference: −29.20, 95% CI: −44.90 to −13.51, p<0.0001) or before MIS (mean difference: −2.60, 95% CI: −6.91 to −13.51, p=0.0003) (Figure 3).

### Figure 2. The effect of puerarin on size of myocardial ischemia (MIS).

| Study or subgroup | Puerarin | Control | Mean difference | IV, fixed, 95% CI | Mean difference IV, fixed, 95% CI |
|------------------|----------|---------|-----------------|------------------|----------------------------------|
|                  | Mean     | SD      | Total           | Mean             | SD     | Total           | Weight | Mean difference | IV, fixed, 95% CI | Mean difference IV, fixed, 95% CI |
| 1.1.1 Before MIS |          |         |                 |                  |        |                 |        |                |                            |                              |
| Gao 2006         | 38.3     | 4.9     | 6               | 40.9             | 3.23   | 6               | 20.4%  | −2.60           | [−6.91, 1.71]          |                              |
| Gao 2007         | 40.6     | 2.59    | 6               | 40.39            | 1.82   | 6               | 58.9%  | −0.33           | [−2.86, 2.20]          |                              |
| Subtotal (95% CI)|          |         |                 |                  |        |                 |        | Heterogeneity: χ²=0.79, df=1 (P=0.37); I²=0% | Test for overall effect: Z=0.82 (P=0.41) |
|                  | 12       | 12      | 12              | 9.33            | 1.93   | 12              | 79.3%  | −0.91           | [−3.10, 1.27]          |                              |
| 1.1.2 Before MIR |          |         |                 |                  |        |                 |        |                |                            |                              |
| Lu 2009          | 37.66    | 4.85    | 6               | 40.9             | 2.23   | 6               | 20.7%  | −3.24           | [−7.51, 1.03]          |                              |
| Subtotal (95% CI)|          |         |                 |                  |        |                 |        | Heterogeneity: Not applicable | Test for overall effect: Z=1.49 (P=0.14) |
|                  | 6        | 6       | 12              | 20.7%           | −3.24  | [−7.51, 1.03]   | 1.83%  |                              |                              |
| Total (95% CI)   |          |         |                 |                  |        |                 |        | Heterogeneity: χ²=1.70, df=2 (P=0.43); I²=0% | Test for overall effect: Z=1.41 (P=0.16) |
|                  | 18       | 18      | 18              | 100.0%          | −1.40  | [−3.34, 0.55]   | 0%     |                              |                              |

### Figure 3. The effect of puerarin on size of myocardial infarction (MIN).

| Study or subgroup | Puerarin | Control | Mean difference | IV, random, 95% CI | Mean difference IV, random, 95% CI |
|------------------|----------|---------|-----------------|-------------------|-----------------------------------|
|                  | Mean     | SD      | Total           | Mean             | SD     | Total           | Weight | Mean difference | IV, random, 95% CI | Mean difference IV, random, 95% CI |
| 1.2.1 Before MIS |          |         |                 |                  |        |                 |        |                |                            |                              |
| Gao 2006         | 7.5      | 1.67    | 6               | 24.25            | 3.55   | 6               | 14.3%  | −16.75          | [−19.89, −13.61]       |                              |
| Gao 2007         | 8.51     | 1.24    | 6               | 25.08            | 3.42   | 6               | 14.3%  | −16.57          | [−19.48, −13.66]       |                              |
| Subtotal (95% CI)|          |         |                 |                  |        |                 |        | Heterogeneity: χ²=0.00, df=1 (P=0.93); I²=0% | Test for overall effect: Z=15.29 (P<0.00001) |
|                  | 12       | 12      | 24              | 28.7%           | −16.65 | [−18.79, −14.52] | 5.52%  |                              |                              |
| 1.2.2 Before MIR |          |         |                 |                  |        |                 |        |                |                            |                              |
| Li 2013a         | 51.26    | 2.18    | 10              | 78.35            | 3.12   | 3               | 14.3%  | −27.09          | [−30.87, −23.31]       |                              |
| Li 2013b         | 21.63    | 2.51    | 10              | 78.35            | 3.12   | 3               | 14.3%  | −56.72          | [−60.56, −52.86]       |                              |
| Li 2013c         | 18.27    | 1.03    | 10              | 78.35            | 3.12   | 5               | 14.3%  | −60.08          | [−63.20, −56.96]       |                              |
| Lu 2009          | 9.45     | 5.4     | 6               | 24.25            | 3.55   | 6               | 14.2%  | −14.80          | [−19.87, −9.63]        |                              |
| Wang 2008        | 11.96    | 6.81    | 10              | 24.18            | 4.25   | 10              | 14.2%  | −12.22          | [−17.20, −7.24]        |                              |
| Subtotal (95% CI)|          |         |                 |                  |        |                 |        | Heterogeneity: χ²=511.95, df=6 (P=0.00001); I²=99% | Test for overall effect: Z=3.37 (P=0.0008) |
|                  | 26       | 26      | 52              | 71.3%           | −34.24 | [−54.16, −14.32] | 100.0% |                              |                              |
| Total (95% CI)   |          |         |                 |                  |        |                 |        | Heterogeneity: χ²=445.02, df=6 (P=0.00001); I²=99% | Test for overall effect: Z=3.65 (P=0.0003) |
|                  | 58       | 58      | 58              | 100.0%          | −29.90 | [−44.90, −13.51] | 71.3%  |                              |                              |

artery. A total of 234 rats were included, including 140 in experimental group and 94 in control group. Three studies administrated puerarin before myocardial ischemia [14–16] and four studies administrated puerarin before myocardial ischemia reperfusion [17,19–21]. One studies had separate experimental arms administrated puerarin before myocardial ischemia or before myocardial ischemia reperfusion [18]. Size of MIS and size of MIN, CK, MDA and SOD were the mostly reported outcome data.
Puerarin significantly reduced serum CK

Five studies reported the effect of puerarin on serum CK. Puerarin could significantly reduce the level of serum CK (mean difference: –6.89, 95%CI: –9.53 to –4.38, p=0.0001). Puerarin given before MIS (mean difference: –7.65, 95%CI: –12.32 to –2.93, p=0.002) or before MIR (mean difference: –9.53, 95%CI: –13.10 to –6.02, p<0.0001) both had significant effect (Figure 4).

Puerarin significantly reduced serum MDA

Five studies reported the effect of puerarin on serum MDA. Puerarin could significantly reduce the level of serum MDA (mean difference: –3.79, 95%CI: –6.65 to –1.03, p=0.0003) given before MIS (mean difference: –6.40, 95%CI: –10.13 to –2.67, p<0.0001) or before MIR (mean difference: –6.40, 95%CI: –9.53 to –3.27, p<0.0001) both had significant effect (Figure 5).

### Table: Effect of Puerarin on Serum CK

| Study or subgroup | Puerarin | Control | Mean difference | IV, random, 95% CI |
|------------------|----------|---------|-----------------|-------------------|
| **Before MIS**   |          |         |                 |                   |
| Bao 2007a        | 11.8     | 3       | 10              | 9.1%              |
| Bao 2007b        | 7.8      | 3       | 10              | 10.1%             |
| Gao 2006         | 12.71    | 1.65    | 6               | 9.9%              |
| Gao 2007         | 12.26    | 1.4     | 6               | 10.0%             |
| **Subtotal (95% CI)** | 32      | 22      | 39.1%           |                   |
| **58**           |          |         | –7.65           | [–12.38, –2.93]   |

### Table: Effect of Puerarin on Serum MDA

| Study or subgroup | Puerarin | Control | Mean difference | IV, random, 95% CI |
|------------------|----------|---------|-----------------|-------------------|
| **Before MIS**   |          |         |                 |                   |
| Bao 2007a        | 3.72     | 0.26    | 10              | 12.8%             |
| Bao 2007b        | 1.84     | 0.19    | 10              | 12.8%             |
| **Subtotal (95% CI)** | 2.0      | 10      | 25.6%           |                   |
| **90**           |          |         | –2.17           | [–4.01, –0.33]    |

Figure 4. The effect of puerarin on serum CK.

Figure 5. The effect of puerarin on serum MDA.
The protective effect of puerarin on myocardial infarction reperfusion injury (MIRI)…

© Med Sci Monit, 2015; 21: 1700-1706

The protective effect of puerarin on myocardial infarction reperfusion injury (MIRI)…

Wenjun H. et al.:

2.3.1 Before MIS

| Study or subgroup | Control | Puerarin | Mean difference |
|------------------|---------|----------|----------------|
|                  | Mean    | SD       | Total          | Mean     | SD       | Total          | Weight | IV, random, 95% CI |
| Bao 2007a        | 641.66  | 19.27    | 511.67         | 6.72     | 2.12     | 511.67         | 7.2%    | 130.00 [58.43, 201.57] |
| Bao 2007b        | 766.81  | 24.12    | 511.67         | 6.62     | 2.01     | 511.67         | 6.6%    | 255.00 [177.74, 332.26] |
| Subtotal (95% CI)| 20      | 10       | 10             |          |          | 10             | 13.8%   | 191.62 [69.13, 314.10] |

Heterogeneity: Tau²=6368.85, Ch²=5.41, df=1 (P=0.02); I²=82%

Test for overall effect: Z=3.07 (P=0.002)

2.3.2 Before MIR

| Study or subgroup | Control | Puerarin | Mean difference |
|------------------|---------|----------|----------------|
|                  | Mean    | SD       | Total          | Mean     | SD       | Total          | Weight | IV, random, 95% CI |
| Jia 2010a        | 222.56  | 30.59    | 192.74         | 20.23    | 3.13     | 192.74         | 3.1%    | 29.82 [-1.38, 61.02] |
| Jia 2010b        | 231.24  | 25.99    | 192.74         | 20.23    | 3.14     | 192.74         | 3.1%    | 38.50 [9.40, 67.60] |
| Jia 2010c        | 234.42  | 21.48    | 192.74         | 20.23    | 3.13     | 192.74         | 3.1%    | 41.68 [9.94, 73.42] |
| Li 2013a         | 200.11  | 10.14    | 183.23         | 9.74     | 1.55     | 183.23         | 1.5%    | 16.88 [4.19, 29.57] |
| Li 2013b         | 241.25  | 11.04    | 183.23         | 9.74     | 1.55     | 183.23         | 1.5%    | 58.02 [45.05, 70.99] |
| Li 2013c         | 257.81  | 8.73     | 183.23         | 9.74     | 1.57     | 183.23         | 1.5%    | 74.50 [63.61, 85.55] |
| Subtotal (95% CI)| 54      | 18       | 18             |          |          | 18             | 86.2%   | 44.16 [21.37, 66.65] |

Heterogeneity: Tau²=661.24, Ch²=49.39, df=5 (P<0.00001); I²=90%

Test for overall effect: Z=3.85 (P=0.0001)

Test for subgroup differences: Ch²=5.39, df=1 (P=0.02); I²=81%

Subtotal (95% CI)

| Control | Puerarin | Mean difference |
|---------|----------|----------------|
| Mean    | SD       | Total          | Mean     | SD       | Total          | Weight | IV, random, 95% CI |
| 81      | 66       | 10             | 255.00   | 177.74   | 332.26         | 6.6%    | 255.00 [177.74, 332.26] |
| 74      | 28       | 100.0%         | 63.97    | 38.19    | 89.75          | 130.00  | 130.00 [58.43, 201.57] |

Heterogeneity: Tau²=1071.20, Ch²=80.78, df=7 (P<0.00001); I²=91%

Test for overall effect: Z=4.86 (P<0.00001)

Test for subgroup differences: Ch²=5.39, df=1 (P=0.02); I²=81.4%

Figure 6. The effect of puerarin on serum SOD activity.

(mean difference: −2.41, 95%CI: −3.14 to −1.68, p<0.00001). Puerarin given before MIS (mean difference: −2.17, 95%CI: −4.01 to −0.33, p=0.02) or before MIR (mean difference: −2.51, 95%CI: −3.30 to −1.72, p<0.00001) both had significant effect (Figure 5).

Puerarin significantly increased serum SOD activity

Five studies reported the effect of puerarin on serum SOD. Puerarin could significantly increase the level of serum SOD activity (mean difference: 63.97, 95%CI: 38.19 to 89.75, p<0.00001). Puerarin given before MIS (mean difference: 191.62, 95%CI: 69.13 to 314.10, p=0.002) or before MIR (mean difference: 44.16, 95%CI: 21.67 to 66.65, p=0.0001) both had significant effect (Figure 6).

Discussion

In China, puerarin has been used to treat patients with coronary artery diseases. A series of studies explored its effect in clinical use and found this agent could improve signs and symptoms of unstable angina and also attenuate ischemia-reperfusion injury [10,22]. In this study, we pooled previous studies that evaluated the effects of puerarin in MIRI based on rat models. Generally, we found administration of puerarin before MIS or before MIR could both effectively reduce the size of MIN after MIR, suggesting puerarin does have a protective effect for myocardial tissues.

Previous mechanism studies showed that the therapeutic effects of puerarin might be achieved through increasing SOD activity, upregulating Bcl-2, improving the myocardial ultramicrostructure, activating the mitochondrial ATP-sensitive potassium channel, inhibiting myocardial apoptosis, reducing Bax expression, inhibiting the production of proinflammatory cytokines, refraining the calcium overload, and inhibiting mitochondrial permeability transition pore opening [23]. However, the mechanism studies are largely based on measurement of typical serum or tissue indicators in animal models. Due to the small number of animals in individual studies, their statistically power is relatively weak. In fact, the molecular mechanism of myocardial infarction reperfusion injury is complex. It is necessary to assess the outcome indicators with a large sample base. Generally, this injury is largely related to free radicals and other reactive oxygen species. During the MIR, a large amount the radicals and reactive oxygen species are generated, leading to peroxidation of the lipids of cell membranes. MDA formed by the breakdown of lipid peroxides can result in protein conjugation and further damage membrane structure and functions [24]. Thus, the level of MDA can indicate the level of lipid peroxidation and thus indirectly reflect the degree of cell damage. CK is released from damaged myocardial cells and is considered a cardiac-specific marker of acute myocardial infarction [25]. SOD can catalyze the dismutation of the superoxide (O₂⁻) radical into either ordinary molecular oxygen (O₂) or hydrogen peroxide (H₂O₂). If the activity of this enzyme decreased, oxygen-free radicals are accumulated and thereby resulting in higher level of damage. Therefore, SOD activity can reflect antioxidant function in vivo and is an important antioxidant protecting cells from damage due to superoxide. In this study, we observed that compared with I/R group, puerarin+IR group had significantly lower serum CK and MDA, but had higher SOD, suggesting puerarin can induce
higher level of serum of SOD and thus partly offset the negative effects of MIRI.

This study also has several limitations. Firstly, the outcome indicators were not consistent in original studies. Therefore, some important myocardial functional indicators, such as LDH, NO, and GSH were only reported in 1 or 2 original studies; therefore, it would be meaningless to pool these data. Secondly, since the agent is extracted from a traditional Chinese medicine, the original studies were all published in Chinese. The methodological quality of the included studies was generally poor. Most of the original studies had higher risk of bias in binding assessment of outcome, which means the effect of puerarin was likely to be overestimated. This also might be a reason for the high heterogeneity of the results. Therefore, to further confirm the therapeutic effects of puerarin in MIRI, more animal studies and randomized controlled clinical trials are required.

Conclusions

Puerarin might have a protective effect for myocardial tissues during MIRI through increasing SOD and decreasing MDA and CK. However, more animal studies and randomized controlled clinical trials are needed to confirm these results.

References:

1. Sanada S, Komuro I, Kitakaze M: Pathophysiology of myocardial reperfusion injury: preconditioning, postconditioning, and translational aspects of protective measures. Am J Physiol Heart Circ Physiol, 2011; 301(5): H1723–41
2. Sirotkovic-Skerlev M, Plestina S, Bilic I, Kovac Z: [Pathophysiology of ischemia-reperfusion injury]. LJijenicki vjesnik, 2006;128(3–4): 87–95 [in Croatian]
3. Luo CF, Hou N, Tian J et al: Metabolic profile of puerarin in rats after intragastric administration. Med Sci Monit, 2011; 17(9): CR474–79
4. Yellon DM, Baxter GF: Protecting the ischaemic and reperfused myocardium in acute myocardial infarction: distant dream or near reality? Heart, 2000; 83(4): 381–87
5. Szczesny B, Modis K, Yanagi K et al: AP39, a novel mitochondria-targeted hydrogen sulfide donor, stimulates cellular bioenergetics, exerts cytoprotective effects and protects against the loss of mitochondrial DNA integrity in oxidatively stressed endothelial cells in vitro. Nitric Oxide, 2014; 41: 120–30
6. Wang L, Li G, Wang Z et al: Elevated expression of CSG protein in the peri-infarct myocardium of rats. Med Sci Monit Basic Res, 2013; 19: 1–5
7. Luo CF, Hou N, Tian J et al: Metabolic profile of puerarin in rats after intragastric administration of puerarin in solid lipid nanoparticles. Int J Nanomedicine, 2013; 8: 933–40
8. Hsu FL, Liu IM, Kuo DH et al: Antihyperglycemic effect of puerarin in streptozotocin-induced diabetic rats. J Nat Prod, 2003; 66(6): 788–92
9. Gao L, Ji X, Song J et al: Puerarin protects against ischemic brain injury in a rat model of transient focal ischemia. Neurol Res, 2009; 31(4): 402–6
10. Zhang S, Chen S, Shen Y et al: Puerarin induces angiogenesis in myocardium of rat with myocardial infarction. Biol Pharm Bull, 2006; 29(5): 945–50
11. Xu ME, Xiao SZ, Sun YH et al: The study of anti-metabolic syndrome effect of puerarin in vitro. Life Sci, 2005; 77(25): 3183–96
12. Yan LP, Chan SW, Chan AS et al: Puerarin decreases serum total cholesterol and enhances thoracic aorta endothelial nitric oxide synthase expression in diet-induced hypercholesterolemics rats. Life Sci, 2006; 79(4): 324–30
13. Han RM, Tian YX, Becker EM et al: Puerarin and conjugate bases as radical scavengers and antioxidants: molecular mechanism and synergism with beta-carotene. J Agric Food Chem, 2007; 55(6): 2384–91
14. Boa X, Li Z, Qin XT: [Protective effect of puerarin preconditioning on myocardial ischemia-reperfusion injury in isolated rat hearts.] Journal of Clinical Medicine in Practice, 2007; 6(11): 15–18 [in Chinese]
15. Gao X, Li T, Gao Q et al: [The protective effect of puerarin preconditioning against myocardial ischemia-reperfusion injury in rats.] Journal Of Guiyang Medical College, 2006; 31(6): 523–26 [in Chinese]
16. Gao X, Gao Q, Li T, Lu DQ: [The mechanism of protective effect of puerarin on myocardial ischemic reperfusion injury in rats.] Journal of Guiyang Medical College, 2007; 32(1): 37–41 [in Chinese]
17. Wang J, Shang L, Cui M, Li M: [Experimental study of protective effects and mechanism of puerarin on myocardial ischemia reperfusion injury in rats.] Journal of Henan University of Chinesemedicine, 2008; 23(134): 32–34 [in Chinese]
18. Lu DQ, Gao X, Li BL: [Protective effect of puerarin preconditioning on myocardial ischemia-reperfusion injury in Rat.] Journal of Guiyang Medical College, 2009; 34(5): 301–7
19. Jia C, Qin Y, Ren B: [Puerarin protects heart against oxidative stress induced by acute myocardial ischemia-reperfusion injury in rats.] Journal of Liaoning University Of TCM, 2010; 12: 230–32 [in Chinese]
20. Pan S, Chen W: The protective effect of puerarin over myocardial ischemia reperfusion injury in rat model. Chinese Journal of Gerontology, 2010; 30: 332–34 [in Chinese]
21. Liu J, Huang K, Wang Y, Shi B: Effect of puerarin on myocardial ischemia-reperfusion injury in rat cardiac enzymes. Chinese Journal of Lab Diagnosis, 2013; 17: 244–46 [in Chinese]
22. Xie RQ, Du J, Hao YM: [Myocardial protection and mechanism of Puerarin Injection on patients of coronary heart disease with ischemia/reperfusion]. Chinese journal of Integrated Traditional and Western Medicine, 2003; 23(12): 895–97 [in Chinese]
23. Feng QG, Wang Y, Guo ZR et al: The synthesis of puerarin derivatives and their protective effect on the myocardial ischemia and reperfusion injury. J Asian Nat Prod Res, 2010; 12(10): 843–50
24. Wu L, Qiao H, Li Y, Li L: Protective roles of puerarin and Danshenosu on acute ischemic myocardial injury in rats. Phytomedicine, 2007; 14(10): 652–58
25. Zhang Z, Lam TN, Zuo Z: Radix Puerariae: an overview of its chemistry, pharmacology, pharmacokinetics, and clinical use. J Clin Pharmacol, 2013; 53(8): 787–811