surgery without LAD ligation; b). Sham-H-PHC group. The rats were administrated with high dose of peneycycline hydrochloride (H-PHC; 1 mg/kg bodyweight) by i.v. 30 min before sham surgery; c). Ischemia reperfusion (I/R) group: The rats were subjected to a 30 min LAD coronary artery ligation followed by 3h reperfusion; d). I/R-H-PHC group: The rats were administrated with low dose of PHC (0.3 mg/kg bodyweight, i.v.) 30 min before I/R; e). ISOL- PHC group: The rats were administrated with moderate dose of PHC (M-PHC; 0.3 mg/kg bodyweight) 30 min before I/R; f). I/R-H-PHC group: The rats were injected with H-PHC (1 mg/kg bodyweight) 30 min before I/R. Cardiac function was measured by echocardiography after 3h reperfusion. Blood samples were collected. Then, the activities and levels of myocardial enzymes and antioxidant enzymes in serum were detected. Evans blue/TC double staining was performed to assess infarct size. Cardiomyocyte apoptosis was evaluated by TUNEL assay. The release of inflammatory cytokines and inflammatory mediators was detected by ELISA. Western blot was performed to analyze the expression of COX-2, p-IκB, IκB and NF-κB.

**RESULTS** We found that PHC improved cardiac function by elevating ejection fraction (EF), fractional shortening (FS) and left ventricular end systolic pressure (LVESP), and downregulating left ventricular end-diastolic pressure (LVEDP). PHC treatment remarkably decreased the activities of creatine kinase (CK), aspartate aminotransferase (AST), lactate dehydrogenase (LDH) and malondialdehyde (MDA) content, and superoxide dismutase (SOD) activity. Additionally, PHC reduced the infarct size and the apoptotic rate of cardiomyocytes in a dose dependent manner. Administration of PHC significantly decreased serum IL-1β, TNF-α, PEG-2 and IL-6 levels and myocardium COX-2 level. Meanwhile, the expression levels of p-IκB and phosphorylated IκB (p-IκB) was upregulated, the expression of COX-2 was downregulated. These results suggest that PHC exert dose-dependent effects on I/R-induced myocardial injury by inhibiting oxidative stress, apoptosis and inflammation, and reduce the levels of nuclear NF-κB and p-IκB.

**CONCLUSIONS** PHC presented significantly dose dependent effects on myocardial IRI by inhibiting inflammation, oxidative stress and apoptosis, and reducing the level of nuclear NF-κB and p-IκB.

**G2W–e1245**

Atractylenolide II and Atractylenolide III Inhibit Platelets Activities and Thrombus Formation

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**OBJECTIVES** Antiplatelet treatment has been proved to be an effective strategy for the prevention of cardiovascular disease (CVD). However, a major disadvantage of this strategy is the increasing risk of hemorrhages. Developing new platelet inhibitors with minimal adverse effects is important for clinical treatment of CVD. Atractylenolide (ATII) and IIIATII are the major active components in Atractylodes macrocephala. The effects of the components including anti-inflammatory and anti-cancer have been demonstrated. However, their effects on platelet activation are unknown. Therefore, we explored the effects of ATII and ATIII on platelet activities such as platelet aggregation, platelet spreading, thrombus formation and so on. We also investigated the effects of ATII and ATIII on essential signaling mediator in platelet activation.

**METHODS** Human platelets were adjusted to 3×10⁸platelets/ml for platelet aggregation. ATII, ATIII and Acetylsalicylic acid were incubated with the platelets for 3 min prior to stimulation, respectively. When the platelet aggregation was terminated, the target proteins were detected to detect the phosphorylation levels of signaling molecules by Western blotting. For platelet spreading on immobilized fibronogen, platelets were incubated with ATII and ATIII respectively for 3min and allowed to spread on immobilized fibronogen. The cell reaction was done as following, human platelet-depleted plasma was mixed with washed human platelets to a concentration of 4×10⁸/ml and was incubated with ATIII for 3min respectively. Plasma was induced to coagulate with 0.4U/ml thrombin. We examined thrombosis formation by FeCl₃-induced carotid artery injury murine thrombosis model. After mice were treated with ATII(10U/kg) at 60mg/kg dose by oral administration, carotid artery blood flow was monitored.

**RESULTS** Compared to Acetylsalicylic acid, ATIIIATII inhibited platelet aggregation with lower concentration(10U/M) in response to thrombin and collagen. Akt and other signaling molecules such as p-38, Erk have been proved to play critical roles in platelet activation. Akt Ser473phosphorylation levels were significantly diminished for ATIII treatment in response to thrombin, but no changes were found in the phosphorylation levels of p-38 and Erk. The average size of the platelets that spread on Fg were 1900.4±108.66 pixels for ATIII, 1895.1±167.07 pixels for ATII-M versus 950.8±2107.95 pixels for the platelets in the presence of DMSO. In the FeCl₃-induced carotid artery thrombosis model, the average time to first occlusion was 12.19 min for the ATII and 9.67 min for ATIII. In contrast to 6760.4 in control mice. The average ratio of clot retraction of ATII with platelets was 0.1659±0.0115, ATIII with platelets was 0.2892±0.0118 versus DMSO with platelets 0.7183±0.0359.

**CONCLUSIONS** The work demonstrates that ATII and AT III inhibit platelets aggregation, spreading, clot retraction and arterial thrombosis formation in vivo. The results suggest that ATII& III have the potential to be an efficient platelet inhibitors.

**GW26–e1464**

PHA665752, Hepatocyte Growth Factor/c-Met Inhibitor, Reduces the Ventricular Fibrillation Threshold in Myocardial Infarction Rats Treated with Cardiac Stem Cells Transplantation

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**OBJECTIVES** Our previous studies found that cardiac stem cells (CSCs) transplantation improved the ventricular fibrillation threshold (VFT), myocardial infarction (MI) rats. However, the mechanisms remain unclear. Therefore, we sought to explore the mechanisms.

**METHODS** MI was induced in 30 male Sprague-Dawley rats. 2 weeks later, animals were randomized to receive 5×10⁶ CSCs labeled with PKH26 in phosphate buffer solution(PBS)(20 rats) or PBS (10 rats) alone injection into the infarcted anterior ventricular free wall. After that, 10 rats with CSCs transplantation received PHA665752 (Hepatocyte Growth Factor/c-Met Inhibitor, 15μg/kg) in PBS and DMSO (PHA665752 group), 10 rats with CSCs transplantation received PBS and DMSO (CSC group) and 10 rats with PBS injection received PBS and DMSO (PBS group) via tail vein injection every day for 2 weeks. Then the VFTs were measured. Labeled CSCs were observed in μm cryostat sections from each heart to detect the myocardial fibrosis.

**RESULTS** Comparisons of CSC group, the VFTs were deteriorative in PHA665752 group (PHA665752 group vs. CSC group vs. PBS group; infarct zone: 3.9±1.7mA vs. 10.3±1.9mA vs. 3.4±0.7mA p<0.05; infarct marginal zone: 4.2±1.4mA vs. 9.7±1.4mA vs. 2.9±0.7mA p<0.05). Masson detection showed that the myocardial fibrosis in PHA665752 group was obviously more severity than that in CSCs group.

**CONCLUSIONS** PHA665752, hepatocyte growth factor/c-Met inhibitor, reduces the VFT, and enhances the myocardial fibrosis.

**GW26–e1492**

Changes of Small-conductance calcium-activated K⁺ channels 3 (SK3) in Patients with Persistent Atrial Fibrillation

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**OBJECTIVES** We had reported that the current density of apamin-sensitive SK channels was significantly increased in AF group with persistent atrial fibrillation than SR group. The purpose of this study was to investigate whether the current density increase of SK channels in patients with persistent atrial fibrillation was because of its differential expression between the sinus rhythm (SR) and persistent atrial fibrillation patients and whether SK3 channel is involved in electrical remodeling of human persistent atrial fibrillation.

**METHODS** The right atrial appendage myocytes were obtained from 16 sinus rhythm (SR) and 14 persistent atrial fibrillation patients.