by quantitative real-time polymerase chain reaction (PCR) and enzyme-linked immunosorbent assay (ELISA). Macrophage polarization and its mechanism were evaluated by flow cytometry and western blot. Additionally, toll-like receptor 4 (TLR4) small interfering RNA androgen-activated protein kinase (MAPK) inhibitors were used to further confirm the molecular mechanism of curcumin on macrophage polarization.

**RESULTS** Curcumin dose-dependently inhibited M1 macrophage polarization and the production of TNF-α, IL-6, and IL-12. It also decreased TLR4 expression, which regulates M1 macrophage polarization. Furthermore, curcumin significantly inhibited the phosphorylation of ERK, JNK, p38, and nuclear factor (NF)-κB. In contrast, siTLR4 in combination with p-JNK, p-ERK, and p-p38 inhibition reduced the effect of curcumin on polarization.

**CONCLUSIONS** Curcumin can modulate macrophage polarization through TLR4-MAPK/NF-κB pathway inhibition, indicating that its effect on macrophage polarization is related to its anti-inflammatory and anti-atherosclerotic effects. Our data suggest that curcumin could be used as a therapeutic agent in atherosclerosis.

**Effects of Niacin on ApoE-/- Mice' Adipose Tissue, Serum Lipid and Atherosclerosis**

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**OBJECTIVES** To investigate the effects of Niacin on ApoE-/- mice’ adipose tissue, serum lipid and atherosclerosis, and furthermore to explore the potential relation among them.

**METHODS** Total 28 male ApoE-/- mice were randomly divided into 3 groups: control group (n = 8), model group (n = 10), and Niacin treatment group (n = 10), respectively fed with normal diet, high cholesterol diet, and 1% Niacin diet, respectively. The content of cholesterol in subcutaneous adipose tissue in groin was quantitated by high percent-aeticin eosin. The content of cholesterol and apoA-I was measured by enzymatic method and by level (total triglyceride, total cholesterol, HDL cholesterol, LDL cholesterol, apoA-I) was measured by enzymatic method and by immunoturbidimetry. Lesions of aortic arteries were stained with hematoxylin eosin. The content of cholesterol in arterial wall and subcutaneous adipose tissue in groin was quantitated by high performance liquid chromatography. The expression of LXRa, ABCA1 and ABCG1 mRNA in subcutaneous adipose tissue was determined by RT-PCR.

**RESULTS** The content of cholesterol in subcutaneous adipose tissue in control group, model group, and Niacin treatment group was (3.13 ± 0.19), (20.81 ± 1.97) and (4.00 ± 0.81) mg/g, respectively. Compared with model group, Niacin treatment could increase the expression of LXRa, ABCA1 and ABCG1 mRNA 144%, 47.3% and 73.8%, respectively. And furthermore, it could also downregulate the level of serum total triglyceride, total cholesterol and LDL cholesterol, upregulate the level of serum HDL cholesterol, and apoA-I. Pearson correlation test showed that there is a positive relationship between the content of cholesterol in arterial wall and the ratio of intima/media thickness (r = 0.58, P < 0.05). In addition to those above, Niacin treatment could thin the intima thickness, decrease the ratio of intima/media thickness and downregulate the sub-endothelium lipid-accumulation, especially cholesterol -accumulation.

**CONCLUSIONS** Niacin treatment may promote the reverse cholesterol transport of peri-adipose tissue, bring the changes of serum lipid profile, and furthermore influence the sub-endothelium lipid-accumulation, especially cholesterol -accumulation, and subsequently reverse the aortic atherosclerosis.

**Renalase Protects the Cardiomyocytes of Sprague-Dawley Rats Against Ischemia and Reperfusion Injury by Reducing Myocardial Cell Necrosis and Apoptosis**

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**OBJECTIVES** Renalase, a novel flavoprotein expressed in the kidney and heart, reduces renal tubular necrosis and apoptosis, which suggests that it might protect against myocardial ischemia reperfusion injury (MIRI) in the same manner. This experiment sought to explore the effects of renalase on Sprague-Dawley (SD) rats subjected to MIRI.

**METHODS** We used Lentivirus-mediated RNA interference (RNAi) to inhibit the renalase gene expression in the heart tissue via pericardial cavity injection. The MIRI animal model was established by blocking the left anterior descending artery for 45ms followed by 4h of reperfusion. Real-time PCR and western blotting were used to detect renalase expression in the heart tissue. Double staining and TUNEL were used to detect the necrosis and apoptosis in the myocardial cells, respectively.

**RESULTS** All rats subjected to MIRI exhibited lower levels of renalase in the heart tissue than did the sham-operated group (P < 0.05). The (RNAi) group rats exhibited lower renalase levels than did the controls and also exhibited more serious necrosis (7.12 ± 0.56% vs. 3.32 ± 0.93%, P < 0.05, n = 6) and apoptosis (15.18 ± 8.2% vs. 66.8 ± 6.5%, P < 0.05, n = 6); however, pretreatment with the recombinant renalase significantly reduced myocardial cell necrosis (4.31 ± 0.12% vs. 4.13 ± 0.02%, P < 0.05, n = 6) and apoptosis (21.3 ± 5.0% vs. 52.6 ± 10.4, P < 0.05, n = 6) relative to the control rats.

**CONCLUSIONS** Exogenous recombinant renalase protein reduced myocardial cell necrosis and apoptosis. Recombinant renalase protein might be a new cardiovascular drug for ischemia/IR injury.
surgery without LAD ligation; b). Sham-H-PHC group. The rats were administered with high dose of peneclidine hydrochloride (H-PHC; 1 mg/kg bodyweight)by i.v. 30min before sham surgery; c) Ischemia reperfusion (I/R) group: The rats were subjected to a 30min LAD coronary artery ligation followed by 3h reperfusion; d) I/R-H-PHC group: The rats were administered with low dose of PHC (0.3 mg/kg bodyweight, oral i.d.); e) ISchemia-H-PHC group: The rats were administered with moderate dose of PHC (M-PHC; 0.3 mg/kg bodyweight) 30min before I/R; f) I/R-H-PHC group: The rats were injected with H-PHC (1 mg/kg bodyweight) 30min 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/TTC 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-IkB, IkB 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) compared to superoxide dismutase (SOD) activities. 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-IkB and IkB were downregulated, and the ratio of p-IκB to IkB was upregulated. 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-IkB.

**CONCLUSIONS** PHC presented significantly dose dependent effects on myocardial I/R by inhibiting inflammatory, oxidative stress and apoptosis, and reducing the level of nuclear NF-κB and p-IkB.

**GW26-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 III (ATIII) 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 × 10^10 platelets/ml for platelet aggregation. ATII, ATIII and Atractylenolic 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 fibrinogen, platelets were incubated with ATII and ATIII respectively for 3 min and allowed to spread on immobilized fibrinogen. The cell reaction was done as following, human platelet-depleted plasma was mixed with washed human platelets to a concentration of 4 × 10^10/ml and was incubated with ATII and ATIII for 3 min respectively. Plasma was induced to coagulate with 0.4U/ml thrombin. We examined clot retraction formation by FeCl3-induced carotid artery injury murine thrombosis model. After mice were treated with ATII/ATIII at 60mg/kg dose by oral administration, carotid artery blood flow was monitored.

**RESULTS** Compared to Atractylenolic acid, ATII/ATIII inhibited platelet aggregation with lower concentration(10μM) 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 Ser473 phosphorylation levels were significantly diminished for ATII/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 1904.0 ± 409.86 pixels for ATII/ATIII, 1687.07 pixels for ATII/ATIII versus 6706.50 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 6.76 min for ATIII mice. In contrast to 6.76min in control mice. The average ratio of clot retraction of ATII with platelets was 0.1659 ± 0.0145, 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/AT 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) in 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 × 10^5 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 5μm 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 non-infarct zone: 2.9 ± 0.9mA vs. 9.1 ± 1.1mA vs. 2.6 ± 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 in MI rats treated with CSCs transplantation, which indicates that CSCs paracing hepatocyte growth factor ameliorate myocardial fibrosis leading to VFT improvement.

**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