METHODS Foam cells were made by RAW 264.7 macrophages with oxLDL for 24 h. RAW 264.7 macrophages were divided into five groups: control group (RAW264.7 macrophages), oxLDL group (RAW 264.7 macrophages + 40 μg/mL oxLDL), CML group (RAW 264.7 macrophages + 40 μg/mL oxLDL+ 10 μmol/L CML), CD36 knock down group (RAW 264.7 macrophages + 40 μg/mL oxLDL+ 10 μmol/L CML+CD36 siRNA) and Vav1 knock down group (RAW 264.7 macrophages + 40 μg/mL oxLDL+ 10 μmol/L CML+Vav1 siRNA).Cholesterol ester measurement, oil red O staining, wound scratch assay, modified boyden chamber migration assay, western blot analysis and immunofluorescence staining were then performed.

RESULTS Western blot analysis and immunofluorescence staining indicated that CML could efficiently up-regulate the expression of CD36 and p-Vav1.Oil red O staining and cholesterol ester measurement suggested that CML could dramatically induce RAW 264.7 macrophages transdifferentiating into foam cells and CD36 and Vav1 knock down group show that inhabitation of CD36/Vav1 pathway can reverse this process . Wound scratch assay and modified boyden chamber migration assay demonstrated that CML significantly inhibits the migration of RAW264.7 macrophages ($p<0.05$), By inhibiting the CD36 / Vav1 pathway, this process can be alleviated.

CONCLUSIONS CML could inhibit the migration of RAW264.7-derived foam cells via CD36/Vav1 pathway.

GW28-e0443

The extract of Syringa pinnatifolia Hemsl., one of representative folk Mongolian medicine, exerts anti-myocardial ischemia through anti-apoptosis mediated by P53 pathway in mice

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OBJECTIVES Syringa pinnatifolia Hemsl (SP), one of the most representative Mongolian medicine has been widely used for treatment of "He-Yi" related diseases especially coronary heart disease in Inner Mongolian religion of China for hundreds of years. Our previous study has demonstrated that SP possessed the cardio-protective effects against acute myocardial infarction (AMI) by pretreatment in mice underlying an anti-inflammation mechanism through COXs pathway. The present study is to investigate the cardio-protective effect of a major fraction (M) in mice, which obtained phytochemically from total extract of SP with 81 % of total weight, and explore its mechanism of action in anti-apoptosis pathway mediated by P53.

METHODS Left anterior descending (LAD) artery was ligated to produce myocardial infarction to evaluate the anti-myocardial ischemia effect of M. Male ICR mice were randomly divided into six groups (n = 10 per group): a sham group, a model group, group treated with M at three dosages (17 mg/kg, 33 mg/kg, and 65 mg/kg, intragastrically), and a positive control group (captopril, 20 mg/kg, intragastrically). Heart function was determined mainly by ejection fraction (EF) and fractional shortening (FS) that were gained through echocardiography. In serum, creatine kinase-MB (CK-MB), lactate dehydrogenase (LDH), and hypersensitive C-reactive protein (hs-CRP) were detected as indicated components in AMI. Levels of protein in the heart tissue related to apoptosis, such as P53, bax, and cytochrome C, were tested by western-blot. And mRNA expressions of P53 was detected through RT-PCR. Moreover, infiltration of inflammatory cells of infarction area edge and cardiomyocyte necrosis were observed by HE staining.

RESULTS Compared with total extract of SP, M showed equal, even slightly better efficacy that improved heart function by increasing values of EF and FS. The levels of serum CK-MB, LDH, and hs-CRP decreased obviously, and the same effect observed also in captopril group. Western-blot analysis showed decreased expression of protein related to P53 pathway, including P53, bax, caspase-9, caspase-3, and cytochrome C. HE staining showed that there was an obvious effect on reducing infiltration of inflammatory cells and necrosis of cardiomyocyte after administration of M compared with model group.

CONCLUSIONS The major fraction of SP extract showed efficacy of anti-myocardial ischemia by down-regulating mRNA and protein expressions related to P53 pathway. These results validated the determined effect of SP in AMI through anti-apoptosis way, which brought evidence for SP in treating coronary heart disease in clinical.

GW28-e0446

Traditional Tibetan medicine Corydalis hendersonii exerts anti-myocardial ischemia effect by attenuating inflammation and fibrosis in acute myocardial infarction mice

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OBJECTIVES Corydalis hendersonii Hemsl. (CH) has been used for centuries in China largely for the treatment of high altitude polycythemia, hypertension, hepatitis, edema, gastritis, and other infectious diseases, but never employed for coronary heart diseases. The current study is to investigate the cardioprotective effects of CH extract in an ICR mouse model of myocardial ischemic injury.

METHODS CH ethanol extract was orally administrated to AMI mice that was established by ligation of the left ventricular dysfunction (LAD) coronary artery. Mice were randomly divided into six groups (n = 12 per group): sham group, model group, CH groups treated with three doses of CH (100–400 mg/kg, intragastrically), and captopril group (positive control, 16.67 mg/kg, intragastrically). Measurement by echocardiography of ejection fraction (EF) and fractional shortening (FS) to evaluate the heart function. Inflammatory cell infiltration in collagen deposition in the myocardial ischemic heart tissues were observed by histopathological examination. Creatine kinase-MB (CK-MB) and lactate dehydrogenase (LDH) levels in serum, AngII, TNF-α, and IL-6 in plasma, and expressions of proteins MMP-2 and MMP-9, expressions of signal-transduction proteins, p65, IκBα, JAK2, and STAT3 were measured by ELISA and Western blot analyses.

RESULTS A dose-dependent cardioprotective effect was observed by CH treatment in AMI mice. As compared to those in the model group, LVEDs and LVEDd were significantly reduced, and EF and FS were improved in CH groups; inflammatory cell infiltration in the myocardial infarct was attenuated in all CH treated groups. Serum levels of CK-MB and LDH were decreased; expressions of AngII, TNF-α, and IL-6 in plasma were reduced, and MMP-2 and MMP-9 expressions, expressions of p-p65, p-IκBα, p-JAK2, p-STAT3, MMP-2, and MMP-9 in AMI mice were decreased.

CONCLUSIONS CH extract showed a cardio protective effect against myocardial ischemic injury in an anti-inflammation and anti-myocardial fibrosis way. The present finding is the first discovery of cardio protection of CH against AMI injury for the first time.

GW28-e0449

Temporal expressions of cell cycle regulators during cardiac hypertrophy and effects of triptolide

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OBJECTIVES Cardiomyocytes proliferate rapidly during fetal life but exit the cell cycle soon after birth in mammals and become terminally differentiated. Recent studies indicated that postnatal cardiomyocytes are still capable of cell cycle reentry, which results in cardiac hypertrophy, Triptolide (TP) can regulate the expressions of various cell cycle regulators in tumor cells. However, the effects of TP on cell cycle regulators in myocardial hypertrophy and its mechanism are at present poorly understood.

METHODS Neonatal rat ventricular myocytes (NRVM) were isolated and coincubated with 1.0 μmol/L angiotensin II (Ang II) and 1.0 μg/L TP for scheduled times (0, 5, 10, 30 min, or 1, 2, 3, 6, 12, 24, 48 h). Mice were randomly divided into isoprenaline (ISO) and TP treated group, and administrated with ISO (10mg/kg, sc. bid) or ISO plus TP (10 μg/kg, ip. q.d.) for 1, 3, 7, 14, 21 days, respectively. NRVM myocytes were analyzed with flow cytometry to detect the cell cycle, and myocytes area was measured by immunofluorescence assay. The pathological morphology changes were observed after HE, lectin and Masson's trichrome staining. The mRNA expression levels of β-myosin heavy chain (β-MHC) and cyclin A, B, D, E, CDK 1, 2, 4, 6, and p21, p27 were detected by real-time PCR, and the protein expression levels of β-MHC and cyclin D, CDK 4, 6, p21 were detected by WB.

RESULTS The cell size and β-MHC expression level increased dramatically after stimulation with Ang II. Cell cycle analysis indicated that the myocytes number in phase of S+G2 increased and that in G1 phase decreased significantly after Ang II stimulation. The mRNA expressions of cyclin A, p21 and p27 increased soon after stimulation for 5 min, after mRNA expressions of all cell cycle factors