Methods: We established low-estrogen atherosclerotic animal model by feeding ovariectomized mice a high-fat diet, and oxidative-injured cells model were induced by ox-LDL in HUV-ECs. Tanshinone IIA (mice: 30mg/kg, 60mg/kg, cells: 0.1μM, 1μM, 10μM) was given to the mice and cells, and estrogen (mice: 0.13mg/kg/ d, cells: 0.01μM) and estrogen receptor antagonist (ICI182780, mice: 65μg/kg, cells: 0.1μM) were also designed to be given. The levels of NF-κB, iNOS, MCP-1, AP-1, E- selectin and 17βestradiol in serum and the levels of NF-κB, iNOS, MCP-1, AP-1, and E-selectin in supernatant were measured by ELISA. The expression of P-EK1/2 in cells and mice aorta and expression of ERα in cells were assessed by Western blotting.

Results: Tanshinone IIA could not significantly increase the serum E2 level of ovariectomized mice (P>0.05). Interestingly, it significantly inhibited the levels of NF-κB, AP-1, iNOS, MCP-1, E-selectin and 17βestradiol in serum and the levels of NF-κB, iNOS, MCP-1, AP-1, and E-selectin in supernatant were measured by ELISA. The expression of P-EK1/2 in cells and mice aorta and expression of ERα in cells was assessed by Western blotting. Furthermore, Nox-4 siRNA silencing and treatment with an anti-LOX-1 antibody attenuated the effects of Ox-LDL induced both apoptosis and protein expression of LOX-1 and Nox-4 proteins and mRNAs were analysed by Western blotting and RT-PCR, respectively.

Conclusions: Curcumin inhibited cardiac fibrosis in rats and mice, by inhibiting myofibroblast differentiation.

Curcumin inhibits cardiac fibrosis in vitro and in vivo by inhibiting myofibroblast differentiation

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Objectives: To study the changes of calreticulin-STAT3 signaling pathway and its effect on cardiac mitochondria damage in selenium deficiency rat hearts.

Methods: Twenty male Sprague-Dawley rats were randomized into normal control group (n=8) and selenium deficiency model group (n=12). When rats were fed for 20 weeks, the cardiac function was measured by hemodynamic studies. The signal molecules involved in the calreticulin-STAT3 pathway were measured using real-time PCR and western-blot. The mitochondrial structure and function were assessed.

Results: Compared with the control group, the rats in the model group had reduced systolic and diastolic function. Cardiac C-reactive protein expression was 4.6-fold higher in the model group than that in the control group, and the protein level of calreticulin was 3.3-fold higher than that in the control group (P<0.05). The protein expression of STAT3 and P-STAT3 in the whole myocardium and cardiac mitochondria were both significantly down-regulated in the model group (P<0.05). The mRNA and protein levels of manganese superoxide dismutase (MnSOD), downstream to STAT3, were also significantly decreased in the model group (P<0.05). Under electron microscopic observation, the cardiac mitochondria in the model group were swelling with fractured or dissolved cristae. The mitochondrial membrane potential level of the isolated fresh cardiac mitochondria, and the enzyme activities of succinate dehydrogenase and cytochrome c oxidase in the model group were all significantly decreased as compared with the control group (P<0.05).

Conclusions: The development of selenium deficiency induced cardiomyopathy in rats, might be due to the up-regulated expression of calreticulin, which inhibits STAT3 phosphorylation in both the whole cell and mitochondrial fraction.