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Antioxidative effects of complementary therapy with Salvia miltiorrhiza in ischemic heart disease

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Abstract

Background: Salvia miltiorrhiza (SM) is a Chinese herb widely used for ischemic heart diseases (IHD), yet little is known about the cellular mechanisms. The aims of this study were to investigate mechanisms of SM.

Methods: The rat A10 cells line, a vascular smooth muscle cells line isolated from rat thoracic embryonic aorta was as a study model. The SM roots aqueous extract , MTT assay, cytotoxicity assay, two-dimensional electrophoresis coupled with MALDI-TOF mass spectrometry , western blot analysis, and biological network analysis were applied for the elucidation of protein changes characterizing the response of the rat A10 cells into the homocysteine(Hcy) -induced oxidative stress.

Results: Our study showed that a low dose (0.015 mg/mL) of the SM significantly inhibited growth (>60%, $p < 0.05$) of the Hcy stimulated rat A10 cells. In addition, concentration of intracellular reactive oxygen species obviously decreased in the rat A10 cells after its incubation with SM in terms of catalase increasing activity. Next, marked down-regulation of protein kinase C beta-1 and phosphorylated mitogen-activated protein kinase expression suggest that observed inhibitory effect of the SM on the Hcy-induced growth of rat A10 cells was realized via the PKC/p44/42 MAPK- dependent pathway. The intensity changes of 10 protein spots in response of the rat A10 cells to the Hcy-induced oxidative damage as alpha-4-tropomyosin, vimentin, F1F0- ATP synthase (beta subunit), glucose regulated protein 75, actin (fragment), prohibitin, capping protein, plakoglobin, endoplasmic reticulum protein 29, and peptidylprolyl isomerase A, were detected with statistical significance ($p < 0.05$). Meanwhile, it was showed that used here SM resist carbonylation of vimentin, alpha-4-tropomyosin and GRP75, respectively, leading to phenotype transformations in the rat A10 cells.

Conclusion: These data suggest that SM may exert its protective effect in IHD through circulating ROS suppression and subsequent modulation of protein carbonylation in rat aortic smooth muscle cells.

Coronary heart disease (CHD) is the leading cause of death in the world. The number of CHD patients will reach 82 million in 2020. CHD still cannot be cured and present treatment prevents symptom development and reduces the incidences of heart attacks. CHD therapy mainly includes exercise-based cardiac rehabilitation, the changes of the dietary patterns (stopping alcohol consumption), and medication as well as aortic valve replacement and coronary-artery bypass graft surgery. Therefore, due to the lack of effective therapy, it is necessary to discover new treatments for preventing CHD risk.

Traditional Chinese medicine (TCM) has a profound history and has been practiced in many diseases. It is an approach to exploring new medicine and mechanism for CHD therapy. Danshen (Salvia miltiorrhiza), a form of TCM, is often applied in the therapy for coronary heart disease. The results of a number of publications pointed to antioxidant, anti-inflammatory, protective, or antiplatelet properties of Danshen and its active compounds. A salvianolic acid B (SaB), an important bioactive ingredient in the root of Danshen, is being suggested to be responsible for its antioxidant property. Other active water-soluble compounds, such as protocatechuic aldehyde (PAl), 3,4-dihydroxyphenyl lactic acid (DLA), and SaB with peroxides scavenging activities, were able to prevent the expression of adhesion molecules in vascular endothelium and inhibit vascular damage and the components such as tanshinone IIA and tanshinone IIB can inhibit the activity of NADPH oxidase and the aggregation of platelet. This may explain the medicine usage for treating various microcirculatory disturbances. Anti-inflammatory properties of major ingredients SaB, tanshinone IIA (Tansh), and protocatechuic acid preventing the expression of adhesive molecules, cytokines, chemokines, and platelet P-selectin were also observed. Furthermore, low-concentration Danshen was able to protect human umbilical vein endothelial cells (HUVECs) and improve their functions. Its main components, rosmarinic acid, lithospermic acid, SaB, salvianolic acid C (SaC), D (SaD), and and H/I (SaHI), have also antiplatelet potential.