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Effects and mechanisms of Danshen-Shanzha herb-pair for atherosclerosis treatment using network pharmacology and experimental pharmacology[1]

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ABSTRACT

*Ethnopharmacological relevance:*The danshen (the root of *Salvia miltiorrhiza* Bge.)-shanzha (the fruit of *Crataegus pinnatifida* Bge. var. *major* N.E.Br.) (DS) herb combination is a commonly used traditional Chinese medicine with cardiovascular disease (CVD) treatment potential.
Materials and methods:In this study, we investigated the anti-atherosclerotic effects and mechanisms of DS by the integration of network pharmacology and polypharmacology. Eight main components were selected for target fishing by PharmMapper.
Results: The network pharmacological study indicated that DS may target 41 proteins and 16 pathways associated with inflammation, lipid metabolism and endothelial protection, which indicates that DS probably adjusts these processes as part of its anti-atherosclerotic activities. Furthermore, this hypothesis was verified by polypharmacology using an atherosclerotic model. Histopathological

DS, danshen-shanzha; CVD, cardiovascular disease; IMT, intima-media thickness; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; IL-1β, interleukin-1β; NO,nitric oxide; 6-keto-$PGF_{1\alpha}$, 6-keto-prostaglandin $F_{1\alpha}$; ET, endothelin; TXB_2, thromboxane B_2; AS, atherosclerosis; TCM, Traditional Chinese medicine; SBP, Shenxiang Baoxin Pill; TXB_2, thromboxane B_2; Hs-CRP, high-sensitivity C-reactive protein; CA, chlorogenic acid; PB, procyanidin B_2; EC, (-)-epicatechin ; RA, rosmarinic acid; LA, lithospermic acid; SAB, salvianolic acid B; SAA, salvianolic acid A; GSK3β, glycogen synthase kinase-3β; MAPK10, mitogen-activated protein kinase 10; ACE, angiotensin-converting enzyme; CA2, carbonic anhydrase 2; PDE4B, CAMP-specific 3, 5-cyclic phosphodiesterase 4B; GSTP1, Glutathione S-transferase P; SOD2, superoxide dismutase 2; GSTT2, glutathione S-transferase theta-2; GSTM2, glutathione S-transferase Mu 2; INSR, Insulin receptor; ESR1, estrogen receptor; ESR2, estrogen receptor beta; PPARG, Peroxisome proliferator activated receptor gamma; HSPA1A, Heat shock protein; BACE, 1Protease β-site APP-cleaving enzyme 1.