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Research Article

Mechanisms Underlying the Therapeutic Effects of Huangqi, Gegen, Renshen and Sangye in Treating Diabetic Cardiomyopathy Based on Data Mining, Network Pharmacology and Molecular Docking

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ABSTRACT

Objective: To evaluate the therapeutic effects of traditional Chinese medicines Radix astragali (Huangqi, HQ), Ginseng (Renshen, RS), Radix puerariae (Gegen, GG), and Mulberry leaf (Sangye, SY) on diabetic cardiomyopathy (DC) based on bioinformatics and network pharmacology, through gene expression analysis of geo clinical samples, molecular docking of compounds and targets, and molecular dynamics simulation, and to discover new targets for prevention or treatment of DC, in order to facilitate and better serve the discovery of new drugs as well as their application in the clinic.

Materials and Methods: For the initial selection of ingredients and targets using the TCMSP as a starting point, we performed a primary screening of ingredients and targets of the four herbs using tools including Cytoscape, Tbtools, R 4.0.2, Autodock Vina, PyMOL, and GROMACS. To further screen the effective ingredients and targets, we performed protein interaction network (PPI) analysis (gene = 12), gene expression analysis (n = 24) by clinical samples of DCs from the gse26887 dataset, biological process (BP) analysis (FDR ≤ 0.05, gene = 7), KEGG pathway analysis (FDR ≤ 0.05, gene = 7), and ingredient target pathway network analysis (gene = 7) by applying these targets from the screen, Biological processes, disease pathways regulated by targets and the relationship between each component target and pathway were obtained. We further screened the targets and visualized the docking results by precision molecular docking of ingredients and targets, after which we performed molecular dynamics simulation and consulted a large number of relevant literature for validation of the results.

Results: Through screening, analysis and validation of the data, we finally confirmed the presence of 36 active ingredients in HQ, RS, GG, and SY, which mainly act on AKT1, ADRB2, GSK3B, PPARG, and BCL2 targets, and these five targets mainly regulate PI3K-Akt, Adrenergic signaling in cardiomyocytes, AGE-RAGE signaling pathway in diabetic complications, JAK-STAT, cGMP-PKG, AMPK, and mTOR signaling pathway exert preventive or therapeutic effects on DCM. Molecular dynamics (MD) simulations revealed that the complex formed by Calycosin, Frutinone A, Puerarin, Inophyllum E, the four active components of HQ, RS, GG, and SY, and the four target proteins ADRB2, PPARG, AKT1, and GSK3B acting on DCS is able to exist in a very stable tertiary structure under human environment.

Conclusion: Our study successfully explains the effective mechanism of HQ, RS, GG, and SY in ameliorating DC, while predicting the potential targets and active components of HQ, RS, GG, and SY in treating DC, which provides a new basis for investigating novel mechanisms of action at the network pharmacology level and a great support for subsequent DC research.

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