

Immune and Metabolic Regulation Mechanism of Dangguiliuhuang Decoction against Insulin Resistance and Hepatic Steatosis.

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Abstract

Dangguiliuhuang decoction (DGLHD) is a traditional Chinese medicine (TCM) formula, which mainly consists of angelica, radix rehmanniae, radix rehmanniae praeparata, scutellaria baicalensis, coptis chinensis, astragalus membranaceus, and golden cypress, and used for the treatment of diabetes and some autoimmune diseases. In this study, we explored the potential mechanism of DGLHD against insulin resistance and fatty liver *in vivo* and *in vitro*. Our data revealed that DGLHD normalized glucose and insulin level, increased the expression of adiponectin, diminished fat accumulation and lipogenesis, and promoted glucose uptake. Metabolomic analysis also demonstrated that DGLHD decreased isoleucine, adenosine, and cholesterol, increased glutamine levels in liver and visceral adipose tissue (VAT) of ob/ob mice. Importantly, DGLHD promoted the shift of pro-inflammatory to anti-inflammatory cytokines, suppressed T lymphocytes proliferation, and enhanced regulatory T cells (Tregs) differentiation. DGLHD also inhibited dendritic cells (DCs) maturation, attenuated DCs-stimulated T cells proliferation and secretion of IL-12p70 cytokine from DCs, and promoted the interaction of DCs with Tregs. Further studies indicated that the changed PI3K/Akt signaling pathway and elevated PPAR- γ expression were not only observed with the ameliorated glucose and lipid metabolism in adipocytes and hepatocytes, but also exhibited in DCs and T cells by DGLHD. Collectively, our results suggest that DGLHD exerts anti-insulin resistant and antisteatotic effects by improving abnormal immune and metabolic homeostasis. And DGLHD may be a novel approach to the treatment of obesity-related insulin resistance and hepatic steatosis.