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ACCEPTED MANUSCRIPT

Yiqi Yangyin and Huatan Quyu granule can improve skeletal muscle energy metabolism in a type 2 diabetic rat model by promoting the AMPK/SIRT/PGC-1α signalling pathway

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ABSTRACT

Objective: To investigate how *Yiqi Yangyin and Huatan Quyu* granule (YYHQ) improves skeletal muscle insulin resistance in a type 2 diabetic rat model and to discover whether the molecular mechanism is related to the promotion of the AMPK/SIRT/PGC-1α signalling pathway.

Methods: Rats were randomly divided into 4 groups: the normal group, the model group, the YYHO granule group, and the pioglitazone group. The type 2 diabetic rat model was established by feeding a high-fat diet for 5 weeks along with a single intraperitoneal injection of 30 mg/kg streptozotocin (STZ). After modelling successfully, the appropriate drug was intragastrically administered to diabetic rats for 2 weeks, once per day. The YYHQ granule group was given a dose of 4.8 g/kg body weight per day, the pioglitazone group was given a dose of 1.35 mg/kg body weight per day. The doses for both groups were equivalent to the clinical equivalent dose based on a previous study. Other groups were gavaged with the same amount of saline water. Body weight, food intake, water intake, urine volume and grip strength were recorded weekly. The fasting blood glucose(FBG) was determined weekly using blood glucose test strips. The related glucose and lipid metabolism indexes, e.g., fasting insulin (Fins), glycated haemoglobin (GHb), HOMA-IR, ISI, triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and free fatty acid (FFA), were determined using biochemical method. The mRNA expression levels of adenosine monophosphate-activated protein kinase (AMPK), peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1α), carnitine palmitoyl transterase-1 (CPT-1), Sirtuin 1 (SIRT1), and Sirtuin 3 (SIRT3) were assessed using quantitative real-time PCR (qRT-PCR). The protein expression levels of creatine kinase (CK), Ca²⁺ ATPase, α-Actin, AMPK, PGC-1α and CPT-1 were determined using enzyme-linked immunosorbent assay

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