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Troxerutin suppresses lipid abnormalities in the heart of high-fat–high-fructose diet-fed mice

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Abstract The reversal effect of troxerutin (TX) on obesity, insulin resistance, lipid accumulation, oxidative damage, and hypertension induced in the high-fat–high-fructose diet (HFFD)-fed mice model of metabolic syndrome was investigated. Adult male *Mus musculus* mice of body weight 25–30 g were fed either control diet or HFFD. Each group was divided into two and treated or untreated with TX (150 mg/kg bw, p.o.) from the 16th day. Assays were done in plasma and heart after 30 and 60 days of the experimental period. Significant increase in the levels of glucose and insulin, blood pressure (BP), and oxidative stress were observed after 30 days of HFFD feeding as compared to control. Animals fed HFFD for 60 days developed more severe changes in the above parameters compared to those fed for 30 days. Hearts of HFFD-fed mice registered downregulation of peroxisome proliferator-activated receptor-α and peroxisome proliferator-activated receptor gamma coactivator-1α, carnitine palmitoyl transferse-1b and AMP-activated protein kinase; and upregulation of cluster of differentiation 36, fatty acid-binding protein-1, and sterol regulatory element-binding protein-1c after 60 days. TX administration restricted obesity (as seen by Lee's index); improved whole body insulin sensitivity; reduced BP, lipid accumulation, and oxidative damage; upregulated fatty acid (FA) oxidation; and downregulated FA transport and lipogenesis. Histology of heart revealed that TX diminishes inflammatory cell infiltration and fatty degeneration in HFFD-fed mice. The antioxidant property of TX and its ability to influence lipid regulatory genes could be the underlying mechanisms for its beneficial effects.

Keywords High-fat–high-fructose diet · Heart lipids · Oxidative stress · Troxerutin

Introduction

Metabolic syndrome (MS) is a constellation of physical conditions and metabolic abnormalities characterized by central obesity, insulin resistance, dyslipidemia, and hypertension [1]. It increases an individual's risk for development of type 2 diabetes and cardiovascular disease [2]. Epidemiological studies relate the prevalence of obesity-associated insulin resistance and MS to adaptation of a sedentary lifestyle with a shift from habitual diet to "Western- type" diet rich in fat and sugar [3–6].

Diet rich in fat and fructose represents the unhealthy human Western diet and is used extensively by researchers to induce obesity, insulin resistance, and metabolic disturbances in experimental animals. Rodents fed high-carbohydrate and/or high-fat diet for 2–4 months are observed to develop insulin resistance, hypertension, fatty liver, and cardiac changes like cardiac stiffness, cardiac contractile dysfunction, cardiovascular remodeling, lipid accumulation, oxidative stress, depletion of antioxidants, and myocardial apoptosis [7–9].

Defects in lipid metabolism and lipid accumulation in tissues are cardinal features of obesity and insulin resistance. Under these conditions, myocardial glucose uptake is diminished and to meet the energy demand, fatty acid (FA) uptake and metabolism are enhanced. FA uptake in

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