

Antihyperglycemic effect of carvacrol in combination with rosiglitazone in high-fat diet-induced type 2 diabetic C57BL/6J mice

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Abstract Thiazolidinediones constitute a family of anti-diabetic drugs, and rosiglitazone (RSG) has an extensive usage in treating the complications of type 2 diabetes mellitus. Carvacrol (CVL), a monoterpene phenol that occurs in many essential oils of the family Labiatae including *Origanum*, *Satureja*, *Thymbra*, *Thymus*, and *Corydanthus* species, possess a wide variety of pharmacological properties including antioxidant potential. We hypothesized that carvacrol in combination with RSG would prove beneficial to ameliorate the dysregulated carbohydrate metabolism in high-fat diet (HFD)-induced type 2 diabetic C57BL/6J mice. Mice were divided into six groups and fed HFD, for 10 weeks. CVL (20 mg/kg BW) and RSG (4 mg/kg BW) were administered post-orally, daily for 35 days. HFD mice showed an elevation in plasma glucose, insulin, glycosylated hemoglobin and a decrease in hemoglobin. The activities of carbohydrate metabolic enzymes such as glucose-6-phosphatase and fructose-1,6-bisphosphatase increased whereas glucokinase and glucose-6-phosphate dehydrogenase activities decreased in the liver of HFD mice. The activities of hepatic marker enzymes such as aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and gamma-glutamyl transpeptidase increased in HFD mice. Combination of CVL and RSG prevented the above changes toward normalcy. Histopathological analysis of H&E stained pancreas was also in agreement with the biochemical findings. These major findings provide evidence that combination of CVL with RSG has better antidiabetic properties.

Keywords High-fat diet · Carvacrol · Rosiglitazone · Insulin resistance · Diabetes mellitus

Introduction

Diabetes mellitus (DM) is characterized by the derangements in carbohydrate, protein, and fat metabolism caused by defective insulin action and secretion. The increase in DM epidemic can be attributed to many factors, including a stressful lifestyle as well as improper dietary habits. The world prevalence of diabetes among adults (aged 20–79 years) was 6.4 %, affecting 285 million adults in 2010, and will increase to 7.7 % and 439 million adults by 2030 [1]. Insulin resistance often precedes the onset of hyperglycemia and causes adverse health effects, depending on dietary conditions [2]. Increased mobilization of stored lipids in cells elevates free fatty acids in the blood plasma. Elevated blood fatty acid concentrations [associated with insulin resistance and type 2 diabetes mellitus (T2DM)], reduced muscle glucose uptake, and increased liver glucose production all contribute to elevated blood glucose levels [3]. High plasma levels of insulin and glucose due to insulin resistance are major components of the metabolic syndrome. On the existence of insulin resistance, more insulin needs to be secreted by the pancreas.

High saturated fat, high calorie, processed carbohydrate, and low-fiber diets increase the incidence of insulin resistance [4]. The model of high-fat diet-induced glucose intolerance had been extensively used by others and was shown to impair carbohydrate metabolism, increase hepatic glucose production, and induce insulin resistance [5]. It is generally accepted that high-fat diets can be used to generate a valid rodent model for the metabolic syndrome with insulin resistance and compromised β -cell function [6].

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