論 文 要 旨

Rosmarinic Acid Ameliorates Hyperglycemia and Insulin Sensitivity in Diabetic Rats, Potentially by Modulating the Exepression of PEPCK and GLUT4

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Background

Rosmarinic acid (RA) is a potent antioxidant that is present in many common culinary herbs and was first isolated from a widely used culinary plant, rosemary(Rosmarinus officinalis). Recently, studies examining the utility of administering RA to treat diabetic conditions have suggested that RA may reduce diabetesinduced disorders and complications. Initial studies of RA showed that RA may control plasma glucose by modulating sodium-glucose cotransporter 1 (SGLT1) trafficking to the intestinal brush-border membrane (BBM) to ameliorate postprandial hyperglycemia (HG) by a control over carbohydrate digestion and absorption. However, the mechanism(s) potentially underlying the RA-induced amelioration of DM remain unclear. In an attempt to elucidate the role of RA in diabetes treatment, this study investigated the effects of RA on glucose homeostasis and insulin regulation in rats with streptozocin (STZ)-induced type 1 diabetes and high-fat diet (HFD)-induced type 2 diabetes.

Methods

Wistar rats were induced into two types of diabetes models, STZ-induced type 1- like diabetes and HFD-induced type 2-like diabetes. Two groups of diabetes animal were divided into 4 subgroups (Control group and 3 different doses of rosmarinic acid (120, 160, and 200 mg/kg) and treated for 7 days. Glucose homeostasis was determined using oral glucose tolerance tests (OGTTs) and postprandial glucose tests (PGTs) in STZ-induced type 1 diabetes groups, and insulin activity was evaluated using insulin tolerance tests (ITTs) and the homeostatic model assessment for insulin resistance (HOMA-IR) in HFD-induced type 2 diabetes groups. Meanwhile, the protein expression levels of phosphoenolpyruvate carboxykinase (PEPCK) in liver and glucose transporter type 4 (GLUT4) in skeletal muscle were characterized using Western blot analysis.

Results

RA exerted a marked hypoglycemic effect on PGT in STZ-induced diabetic rats and on OGTT in normal and STZ rats. RA reversed insulin resistant on ITT and HOMA-IR in HFD-induced diabetic rats. Thus, RA improved glucose homeostasis administration in STZ-induced diabetic rats (DM type 1) and enhanced glucose utilization and insulin sensitivity in HFD-fed diabetic rats (DM type 2). These effects of RA were observed at all three different doses (120, 160, and 200 mg/kg) in a dose-dependent manner. Meanwhile, RA administration reversed the STZ- and HFD-induced increase in PEPCK expression in the liver and the STZ- and HFDinduced decrease in GLUT4 expression in skeletal muscle.

Conclusion

RA dose-dependently ameliorates HG and insulin resistance by decreasing PEPCK expression in the liver and increasing GLUT4 expression in muscles.