일반 1

Anti-diabetic effect and mechanism of Korean red ginseng extract in C57BL/KsJ db/db mice

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Purpose: Ginseng is a well-known medical plant used in traditional Oriental medicine. Korean red ginseng (KRG) has been known to have potent biological activities such as radical scavenging, vasodilating, anti-tumor and anti-diabetic activities. However, the mechanism of the beneficial effects of KRG on diabetes is yet to be elucidated. The present study was designed to investigate the anti-diabetic effect and mechanism of KRG extract in C57BL/KsJ db/db mice.

Methods: The db/db mice were randomly divided into six groups: diabetic control group (DC), red ginseng extract low dose group (RGL, 100 mg/kg), red ginseng extract high dose group (RGH, 200 mg/kg), metformin group (MET, 300 mg/kg), glipizide group (GPZ, 15 mg/kg) and pioglitazone group (PIO, 30 mg/kg), and treated with drugs once per day for 10 weeks. During the experiment, body weight and blood glucose levels were measured once every week. At the end of treatment, we measured Hemoglobin A1c (HbA1c), blood glucose, insulin, triglyceride (TG), adiponectin, leptin, non-esterified fatty acid (NEFA). Morphological analyses of liver, pancreas and white adipose tissue were done by histological observation through hematoxylin-eosin staining. Pancreatic islet insulin and glucagon levels were detected by double-immunofluorescence staining. To elucidate an action of mechanism of KRG, DNA microarray analyses were performed, and western blot and RT-PCR were conducted for validation.

Results: Compared to the DC group mice, body weight gain of PIO treated group mice showed 15.2% increase, but the other group mice did not showed significant differences. Compared to the DC group, fasting blood glucose levels were decreased by 19.8% in RGL, 18.3% in RGH, 67.7% in MET, 52.3% in GPZ, 56.9% in PIO-treated group. With decreased plasma glucose levels, the insulin resistance index of the RGL-treated group was reduced by 27.7% compared to the DC group. Insulin resistance values for positive drugs were all markedly decreased by 80.8%, 41.1% and 68.9%, compared to that of DC group. HbA1c levels in RGL, RGH, MET, GPZ and PIO-treated groups were also decreased by 11.0%, 6.4%, 18.9%, 16.1% and 27.9% compared to that of DC group, and these figure revealed a similar trend

shown in plasma glucose levels. Plasma TG and NEFA levels were decreased by 18.8% and 16.8%, respectively, and plasma adiponectin and leptin levels were increased by 20.6% and 12.1%, respectively, in the RGL-treated group compared to those in DC group. Histological analysis of the liver of mice treated with KRG revealed a significantly decreased number of lipid droplets compared to the DC group. The control mice exhibited definitive loss and degeneration of islet, whereas mice treated with KRG preserved islet architecture. Compared to the DC group mice, KRG resulted in significant reduction of adipocytes. From the pancreatic islet double-immunofluorescence staining, we observed KRG has increased insulin production, but decreased glucagon production. KRG treatment resulted in stimulation of AMP-activated protein kinase (AMPK) phosphorylation in the db/db mice liver. To elucidate mechanism of action of KRG extract, microarray analysis was conducted in the liver tissue of mice treated with KRG extract, and results suggest that red ginseng affects on hepatic expression of genes responsible for glycolysis, gluconeogenesis and fatty acid oxidation. In summary, multiple administration of KRG showed the hypoglycemic activity and improved glucose tolerance. In addition, KRG increased glucose utilization and improved insulin sensitivity through inhibition of lipogenesis and activation of fatty acid β-oxidation in the liver tissue. In view of our present data, we may suggest that KRG could provide a solid basis for the development of new anti-diabetic drug.

Keywords: Korean red ginseng, C57BL/KsJ db/db mice, Diabetes, DNA microarray

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