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学 位 論 文 要 旨
Dissertation Abstract

氏名：
Name　Adhikari Sudhashree

学位論文題目：
Title of Dissertation　Effects of daidzein and its metabolite on lipid and glucose metabolism
（ダイゼインおよびその代謝物が脂質・糖代謝に与える影響）

学位論文要旨：
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We carried out the experiment to investigate the lipid-lowering effect of daidzein and genestein with the contribution of sterol concentration and expression of key genes involved in cholesterol regulation. Six week old non-ovariectomized (non-ovx) and ovariectomized (ovx) SD rats were fed daidzein (D, 150 mg/kg diet), genistein (G, 150 mg/kg diet), daidzein:genistein (D+G, 1:1, 300 mg/kg diet) or casein-based control AIN 76 cholesterol-free diets for four weeks. The daidzein suppresses the cholesterol metabolism by lowering the hepatic and small intestinal HMGCoAR mRNA expression. The suppressed cholesterol synthesis by the dietary daidzein is further evidence by the lower cholesterol precursor levels in the serum.

The second experiment was designed to find the enterohepatic circulation of daidzein and its metabolite S-equol in sham-operated and ovariectomized female rats fed a diet containing 150 mg/kg daidzein or 150 mg/kg equol. Two experiments were run to detect the enterohepatic circulation of daidzein and S-equol in serum, bile, urine and fecal samples. Dietary daidzein significantly increased serum and bile concentrations of S-equol in a time-dependent manner, but not those of daidzein. These results indicated that a substantial proportion of dietary daidzein was converted to S-equol, which underwent efficient enterohepatic circulation and predominantly accumulated there.

The third experiment was proposed to find the hypolipidemic and hypoglycemic effect of daidzein in a control diet based on AIN-93 and high-fat high sucrose (HF/HS) fed rats. After performing the ovariectomy operation, dietary daidzein (300mg/kg diet) was fed in AIN-93 normal and HF/HS diet for 5 weeks of the experimental period. Oral glucose

tolerance test (OGTT) at week 2 and 3 were done to detect the glucose tolerance activity of daidzein in two different diet groups. The dietary daidzein significantly decreased fasting basal blood glucose levels in rats fed the HF/HS diets, but not in rats fed the normal diets. Dietary daidzein also significantly improved glucose tolerance, and trended to decreased serum insulin concentration, regardless of the composition of the diet. The dietary daidzein increased PGC1α and IRS-2 gene expressions in a liver, and preproglucagon gene expression in the intestine. In addition, the dietary daidzein significantly reduced the body weight, food intake, white fat weights and hepatic triglycerides and serum cholesterol levels either fed with normal or HF/HS diet.

And the last study was performed in order to elucidate the food lowering effect of daidzein via gastro-emptying with or without gastric contents. Seven-week-old female ovariectomized (OVX) Sprague Dawley rats were chosen to test the hypothesis that the anorectic effect of dietary daidzein may be attributed to delay gastric emptying. Time-restricted feeding and gastrectomy operation was done to find the gastro emptying effect of daidzein. The time restriction did not alter the food intake but daidzein lowered the food intake after 3 or 4 days of treatment. But delaying in gastric content was found by daidzein in the rats without gastrectomy operation showed that the delays gastric emptying has an anorectic effect with residual gastric contents, but not without gastric contents.