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学 位 論 文 要 旨
Dissertation Abstract

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学位論文題目： Nutritional and physiological effects of soy isoflavone and the mechanisms
Title of Dissertation (大豆イソフラボンの栄養・生理効果とその機構)

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Our previous study showed that daidzein decreased food intake in female rats but not in male rats. The aim of our present work was to obtain more detailed insights into the action of isoflavones on energy homeostasis, body weight, serum and hepatic cholesterol levels in female rats. We initially carried out the experiments in anorectic action of daidzein and estradiol in CCK or leptin receptor deficiency (ObRb) rats with their wild types. After performing the ovariectomy or a sham operation, each rat was divided into three groups: control, daidzein (150 mg/ kg diet), and estradiol (4.2 μg/rat/day) groups for 5 week experiment. The estradiol treatment and the daidzein both decreased the food intake and body weight gain even in CCK1R- and OVX ObRb− deficiency rats, indicated that CCK1R and ObRb signalings were not the key mechanism for the daidzein and estradiol-induced anorectic action.

In order to elucidate the mechanism of anorectic effect of daidzein, we designed the next study in the appetite-mediated gene expression in the hypothalamus and small intestine of SD rats. To the best of our knowledge, no one has examined so far the anorectic effect of daidzein in appetite-mediated gene expression. We examined appetite-mediated gene expression in the hypothalamus and small intestine during the 3 meals per day feeding (MF3) method. Daidzein decreased a feeding-induced increase of NPY and galanin expression in parallel with the suppression of food intake. Daidzein feeding also increased the expression of CRH mRNA in the hypothalamus. In this study, the anorectic effect of daidzein could be due to the suppressing expression of NPY and galanin and increasing expression of CRH in the hypothalamus. Using this MF3 method,

daidzein induced suppression of feeding was observed primarily during the second feeding, while the anorectic effect was reduced during the first and third feeding. The increased CCK mRNA levels in the small intestine by the daidzein, suggesting that CCK may involve in the hypothalamic regulation of this anorectic effect.

In the next experiment, we chose the dietary daidzein and genistein (150 mg/kg diet) in order to confirm that they are responsible for the hypocholesterolemic effect on intact female and ovariectomized SD rats. We also investigated gene expression of the key regulators of cholesterol and bile acid metabolism in the liver and small intestinal mucosa. In this study, daidzein but not genistein decreased the body weight, food intake in Ovx rats only. However, the dietary daidzein significantly reduced serum cholesterol in rats, regardless of Ovx status. The lowering of serum cholesterol by daidzein could be explained by the decreasing effect of ApoB mRNA expression and the increasing effect of fecal bile acid excretion in both non-Ovx and Ovx rats. However, at present, we do not have evidence to support the hypothesis that ApoB is the main factor in reducing the serum and hepatic cholesterol levels, nor do we understand why dietary daidzein increased the fecal excretion. Genistein on the other hand did not exhibit any physiological effects on lipid levels, but did affect genes involved in cholesterol metabolism.

We speculated that the anorectic and hypolipodemic effects of dietary daidzein are caused by equol. Equol is produced from the daidzein in the gastrointestinal tract by gut microflora, which is stronger than daidzein and genistein in its agonistic activity for the estrogen receptors.