## Isoflavone Regulates Lipid Metabolism *via* Expression of Related Genes in OVX Rats Fed on a High-fat Diet<sup>1</sup>

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**Objective** To investigate the effects of isoflavone on body weight, fat mass, and gene expression in relation to lipid metabolism. **Methods** Thirty-six female SD rats were ovariectomized or sham-operated and fed on a high-fat diet. Two months later, abdominal incision was made, blood was collected to separate serum, and the liver and adipose tissue were immediately collected and weighed. Some portions of these tissues were frozen in liquid nitrogen and stored at -80°C. **Results** Ovariectomy (OVX) with a high-fat diet could induce obesity in rats, while treatment with isoflavone significantly inhibited the increase in body weight and fat mass in abdomen. Serum total cholesterol and leptin were significantly decreased in isoflavone group, compared with the OVX group. The mRNA expression of liver fatty acid synthase (FAS) in the OVX group was significantly higher than that in sham-operated group, while this difference was not observed in the isoflavone group. The mRNA expression of liver hormone-sensitive lipase (HSL) in the OVX rats tended to be lower than that in the sham-operated rats. Furthermore, a large amount of isoflavone maintained the mRNA expression at a sham level. **Conclusion** Isoflavone may prevent obesity induced by ovariectomy with a high-fat diet, in part by modulating gene expression related to lipid metabolism.

Key words: Isoflavone; Lipid metabolism; Ovariectomy; Obesity; Gene expression

## REFERENCES

factors in postmenopausal women. J Nutr 131, 1202-1206.

- Goodman-Gruen D, Kritz-Silverstein D (2003). Usual dietary isoflavone intake and body composition in postmenopausal women. *Menopause* 10, 427-432.
- Kamei Y, Suzuki M, Miyazaki H, et al. (2005). Ovariectomy in mice decreases lipid metabolism-related gene expression in adipose tissue and skeletal muscle with increased body fat. J Nutr Sci Vitaminol (Tokyo) 51, 110-117.
- 2. Genazzani A R, Gambacciani M (2006). Effect of climacteric transition and hormone replacement therapy on body weight and body fat distribution. *Gymecol Endocrinol* **22**, 145-150.
- Dixon R A (2004). Phytoestrogens. Annu Rev Plant Biol 55, 225-261.
- Kim S, Sohn I, Lee Y S, *et al.* (2005). Hepatic gene expression profiles are altered by genistein supplementation in mice with diet-induced obesity. *J Nutr* 135, 33-41.
- Banz W J, Davis J, Peterson R, *et al.* (2004). Gene expression and adiposity are modified by soy protein in male Zucker diabetic fatty rats. *Obesity Res* 12, 1907-1913.
- Bhathena S J, Velasquez M T (2002). Beneficial role of dietary phytoestrogens in obesity and diabetes. *Am J Clin Nutr* 76, 1191-1201.
- 7. Goodman-Gruen D, Kritz-Silverstein D (2001). Usual dietary isoflavone intake is associated with cardiovascular disease risk

- Reeves P G, Nielsen F H, Fahey G C (1993). AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutrition adhoc writing committee on the reformulation of the AIN-76A rodent diet. J Nutr 123, 1939-1951.
- Naaz A, Yellayi S, Zakroczymski M A, et al. (2003). The soy isoflavone geniatein decreases adipose deposition in mice. *Endocrinology* 144, 3315-3320.
- 11.Kim H K, Nelson-Dooley C, Della-Fera M A, *et al.* (2006). Genistein decreases food intake, body weight, and fat pad weight and causes adipose tissue apoptosis in ovariectomized female mice. *J Nutr* **136**, 409-414.
- 12.Ali A A, Velasquez M T, Hansen C T, et al. (2004). Effects of soybean isoflavones, probiotics, and their interactions on lipid metabolism and endocrine system in an animal model of obesity and diabetes. J Nutr Biochem 15, 583-590.
- Wu J, Wang X, Chiba H, et al. (2004). Combined intervention of soy isoflavone and moderate exercise prevents body fat elevation and bone loss in ovariectomized mice. *Metabolism* 53, 942-948.
- Yamori Y (2004). Worldwide epidemic of obesity: hope for Japanese diets. *Clin Exp Pharmacol Physiol* 31, S2-4.
- 15. Mori M, Aizawa T, Tokoro M, et al. (2004) Soy isoflavone tablets

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reduce osteoporosis risk factors and obesity in middle-aged Japanese women. *Clin Exp Pharmacol Physiol* **31**, S39-41.

- 16.D'Eon T M, Souza S C, Aronovitz M, et al. (2005). Estrogen regulation of adiposity and fuel partitioning. J Biol Chem 280, 35983-35991.
- 17.McInnes K J, Corbould A, Simpson E R, et al. (2006). Regulation of adenosine 5', monophosphate-activated protein kinase and lipogenesis by androgens contributes to visceral obesity in an estrogen-deficient state. Endocrinology 147, 5907-5913.
- Kraemer F B, Shen W J (2006). Hormone-sensitive lipase knockouts. *Nutr Metab* (Lond) 3, 12.
- Yeaman S J (2004). Hormone-sensitive lipase new roles for an old enzyme. *Biochem J* 379, 11-22.
- 20.Kraemer F B, Shen W J (2002). Hormone-sensitive lipase: control of intracellular tri-(di-)acylglycerol and cholesteryl ester hydrolysis. J Lipid Res 43, 1585-1594.
- 21.Palin S L, McTernan P G, Anderson L A, et al. (2003). 17Beta-estradiol and anti-estrogen ICI:compound 182,780 regulate expression of lipoprotein lipase and hormone-sensitive lipase in isolated subcutaneous abdominal adipocytes. *Metabolism* 52, 383-388.
- 22. Braissant O, Foufelle F, Scotto C (1996). Differential

expression of peroxisome proliferator-activated receptors (PPARs): tissue distribution of PPAR-alpha, -beta, and -gamma in the adult rat. *Endocrinology* **137**, 354-366.

- 23. Schoonjans K, Staels B, Auwerx J (1996). The peroxisome proliferator activated receptors (PPARs) and their effects on lipid metabolism and adipocyte differentiation. *Biochim Biophys Acta* **1302**, 93-109.
- 24.Campbell S E, Mehan K A, Tunstall R J (2003). 17β-Estradiol upregulates the expression of peroxisome proliferator-activated receptor-alpha and lipid oxidative genes in skeletal muscle. J Mol Endocrinol **31**, 37-45.
- 25.Mezei O, Banz W J, Steger R W, et al. (2003). Soy isoflavones exert antidiabetic and hypolipidemic effects through the PPAR pathways in obese Zucker rats and murine RAW 264.7 cells. J Nutr 133, 1238-1243.
- 26.Kawakami Y, Tsurugasaki W, Nakamura S, et al. (2005). Comparison of regulative functions between dietary soy isoflavones aglycone and glucoside on lipid metabolism in rats fed cholesterol. J Nutr Bio 16, 205-212.

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