

## **Green tea prevents hyperglycemia by preventing expression of insulin resistant-related proteins in adipose tissue of high-fat diet-fed mice**

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### **Summary**

An intake of a high-fat (HF) diet causes insulin resistance accompanying by body weight gain, resulting in hyperglycemia. In this study, we investigated the prevention mechanism of green tea on hyperglycemia in C57BL/6J mice fed the HF diet. Green tea delayed body weight gain during a feeding period compared with water-given control and lowered the white adipose tissue weight in HF diet-fed mice. Green tea also lowered the level of blood glucose in HF diet-fed mice. To clarify the preventive effect of green tea, we investigated that the expression levels of insulin resistance-related proteins in mesenteric white adipose tissue. Green tea suppressed the expression levels of leptin and RBP4 in HF diet-fed mice and increased the expression levels of IGFBP-1 in control and HF diet-fed mice. In conclusion, green tea possibly improves hyperglycemia through down-regulation of insulin resistance-related proteins.

### **Introduction**

Green tea has health promoting effects such as anti-obesity effect. Our previous study showed that an intake of green tea for 3 weeks decreased the white adipose weight of rats and decreased glucose uptake in adipose tissue (Ashida, *et al.*, 2004). It has reported that green tea improved GLUT4 expression in Sprague-Dawley rats fed with a high fructose diet, elevated blood pressure and fasting hyperinsulinemia (Wu, *et al.*, 2004). It has showed that green tea improved the white adipose tissue weight and glucose tolerance in rats fed a high fructose diet, and decreased the metabolic gene expression such as PPAR $\gamma$  and CEBP $\beta$  in adipose tissue (Chen, *et al.* 2009). Although these reports suggest that green tea decreases the white adipose tissue weight and prevent hyperglycemia, the preventive mechanism of green tea is not fully understood to date.

In this study, we demonstrated that green tea decreased the white adipose weight and blood glucose level of mice fed the HF diet. We also demonstrated that green tea prevented expression levels of insulin resistant-related proteins in adipose tissue of mice fed the HF diet.

### **Materials and methods**

All animal treatments was approved by the Institutional Animal Care and Use Committee and carried out according to the Kobe University Animal Experimentation Regulations. Male C57BL/6 mice (5 weeks old, Japan SLC, Shizuoka, Japan) were housed in an air-conditioned room ( $25 \pm 1^\circ\text{C}$ ) under a 12-h light-dark cycle with free access to water and commercial chow, and acclimatized for 1 week. Mice were divided at random into four groups of 4 each. Two groups were given control diet based on AIN-93M and another two groups were given HF (30% lard) diet. Each group was given freshly prepared green tea or water *ad libitum*. After 14 weeks, mice were sacrificed under anesthesia and obtained bloods and white adipose tissues. Blood glucose levels were detected by LabAssay<sup>TM</sup> Glucose (Wako, Osaka, Japan). The expression levels of insulin resistant-related proteins were detected by Proteome profiler<sup>TM</sup> Array Mouse obesity Array Kit (R & D Systems, Minneapolis, USA).

### **Results and discussion**

Population of obesity and diabetes is alarmingly high in most of the affluent countries, and it seems to be still increasing. Many reports showed that green tea have anti-obesity and anti-diabetes effects. In this study, we demonstrated that the effects of green tea on body and white adipose tissue weight of

mice (Fig. 1). In HF diet-fed mice, green tea significantly decreased the body and white adipose tissue weight

compared with water-given

mice. In control diet-fed mice,

green tea did not affect the body and white adipose tissue weight. We also demonstrated that green tea significantly lowered the level of blood glucose compared with water-given mice in control and HF diet-fed mice (data not shown).

To clarify the preventive effect of green tea, we investigated that the expression levels of insulin resistance-related proteins in mesenteric white adipose tissue. Green tea suppressed the expression levels of leptin and RBP4 in HF diet-fed mice (data not shown). Interestingly, green tea increased the expression levels of IGFBP-1 in both control and HF diet-fed mice (data not shown). It has reported that IGFBP-1 closely related with obesity and diabetes. Rajkumar *et al.*, showed that overexpression of IGFBP-1 decreased the white adipose tissue weight and the expression level of leptin. Siddals *et al.*, showed that IGFBP-1 prevented the differentiation of 3T3-L1 adipocytes by inhibiting the effect of IGF-1. Therefore, further investigation will be needed to examine the mechanism of green tea on regulating the expression of IGFBP-1 in adipose tissue.

In conclusion, green tea decreased white adipose tissue weight and lowered the blood glucose level in HF diet-fed mice through promoting expression of IGFBP-1, resulting in preventing expression of insulin resistant-related proteins.

## References

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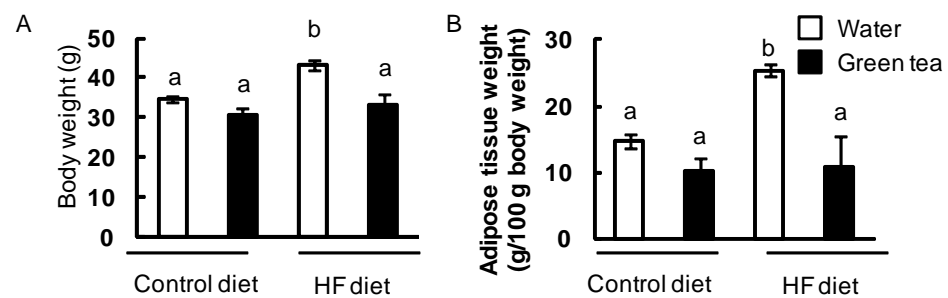


Figure 1. The effects of green tea on body and white adipose tissue weight of mice. Control and HF diet-fed mice were given green tea or water. The body weight (A) and adipose tissue weight of mice (B) were measured at 14 weeks. Data are expressed as the mean  $\pm$  SE (n=4). Different letters indicate statistically significant differences,  $p < 0.05$  by Tukey-Kramer multiple comparison test.