Effect of tea catechins on body fat accumulation in rats fed a normal diet

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(Received 4 October 2007; and accepted 14 November 2007)

ABSTRACT

Although it is known that tea catechins exert potent effects in obese subjects, there is scant information concerning these effects on body weight gain and body fat accumulation in the non-obese. We studied normal rats fed a normal diet and water containing either 0.1% or 0.5% tea catechins to examine the effects on body fat content and serum cholesterol levels, as well as evaluating whether the effect is related to bile acids, which in recent years have emerged as an inducer of energy expenditure. The administration of 0.5% catechins decreased the accumulation of body fat and the serum levels of cholesterol and bile acids. These results indicate that tea catechins modulate lipid metabolism not only in obese subjects, but also in the non-obese.

Green tea, a popular beverage in Asian countries, contains a series of polyphenols known as catechins, in particular epicatechin (EC), epicatechin gallate (ECG), epigallocatechin (EGC) and epigallocatechin gallate (EGCG) (3, 14, 15, 21). There is considerable interest in the anti-obesity potential of green tea (24), as several reports have shown that administration of polyphenols resulted in a significant reduction in body weight gain and body fat accumulation induced by a high-fat diet in animal models (9, 16, 20). But despite the great interest, there is scant information concerning the effects of tea catechins on body weight gain and body fat accumulation in non-obese subjects.

Bile acids are synthesized from cholesterol in the liver, and secreted after meals to promote absorption of fat from the intestine. Although it has been shown that bile acids also mitigate diet-induced obesity (11), that finding has attracted limited attention. Recently, Watanabe et al. (23) confirmed and expanded this observation, showing that feeding mice with cholic acid moderated the effects of a high-fat diet. The novel metabolic effect of bile acids is critically dependent on inducing energy expenditure by promoting intracellular thyroid hormone activation (23). It is unclear whether the tea catechins-induced reduction in body weight gain is related to increased metabolism induced by bile acids.

Therefore, we performed a study in normal rats fed a normal diet to examine the effects on body fat content and the levels of serum cholesterol and bile acids.

MATERIALS AND METHODS

Tea catechins. We used a crude catechin extract (Teafuran 90S; Itoen Ltd, Tokyo, Japan) containing 55.5% (w/w) EGCG and 19% others (EC, ECG, EGC). According to the manufacturer, the total polyphenol content was 94%, and caffeine content was 0.6%.

Animals. Male Wistar rats (200–250 g) were purchased at 7 weeks of age (Clea Japan Inc., Tokyo,
Japan) and maintained at 24 ± 1°C under a 12-h light-dark cycle (light on from 08:00 to 20:00 hours). They were divided into 6 groups of 6 animals each and all were fed a normal diet (Clea Rodent Diet CE-2: 24.5% crude protein, 4.8% crude fat, 51.4% nitrogen-free extract, 3.7% crude fiber). The control group was given tap water, and the treatment groups were given 0.1% or 0.5% solution of catechins.

The studies were carried out according to the Guidelines for the Treatment of Experiment Animals of Kitasato University School of Medicine.

Body weight and food intake. Body weight was measured at day 0 (start of catechin administration) and days 14 and 21. Daily intakes of food and water were measured on the 7th day after beginning the study.

Blood analysis. Following 24-h fasting, blood was collected via the heart from anesthetized rats at 22 days (3 weeks) after the start of the experiments. The serum levels of total cholesterol (TC), serum triglycerides (TG), total protein (TP) and albumin (Alb) were determined using Fuji-Drichem biochemical analysis equipment (Fujifilm Medical Co., Tokyo, Japan). The serum total bile acid concentration was analyzed using an automatic clinical biochemistry analyzer (JCA-BM2250, JEOL, Tokyo, Japan).

Weight and lipid content of the mesenterium and liver. After the animals were sacrificed with CO₂ gas inhalation, the wet weights of the mesenterium and liver were measured after rinsing and washing them with saline. Their respective lipid contents were measured after extraction with a chloroform-methanol mixture (2:1, v/v), as described by Folch et al. (7), and drying with nitrogen gas. Determinations of cholesterol ester and triglyceride were used with the accompanying protocols (2) (Wako Pure Chemical Industries, Ltd., Osaka, Japan).

Statistical analysis. All values are expressed as means ± SD, and one-way analysis of variance (ANOVA) with Scheffe’s test was used for statistical analysis. A difference of P < 0.05, with a two-tailed test, was considered as significant.

RESULTS

Body weight, food intake and fluid consumption
The changes in the body weight of the rats in each experimental group after having free access to food and water for 3 weeks are shown in Fig. 1. The body weight gain of the catechin groups was less than that of the corresponding control group. Mean body weight of the 0.5% catechins group after 3-week-treatment was significantly lower than that of the control.

Food intake of the rats did not differ between the control and catechin groups. Fluid intake was significantly increased by catechin administration in the rats as compared with the control group (Fig. 2).

Lipid content of mesenterium and liver
In the 7-week-old rats administration of 0.1% and 0.5% catechin for 3 weeks significantly reduced both the mesenteric and hepatic lipid content (Fig. 3). Figure 4 shows the lipid profiles of the mesenteries and livers of the animals. The cholesterol ester and TG concentrations in the control liver were 4.9 ± 0.5 and 16.0 ± 2.3 mg/g of tissue, respectively. Likewise, their levels in the control mesenterium were 106.0 ± 9.1 and 280.7 ± 28.3 mg/g of tissue. The cholesterol and TG concentrations were significantly decreased in both the tissues of the rats given catechins.

Serum levels of TC, TG, TP and Alb
After 3 weeks of catechin treatment the serum TG values for the rats did not differ from those of the corresponding control rats, however the serum TC level was significantly lower in the 0.5% catechin...
DISCUSSION

In the previous study (28) with normal mice fed a normal diet, the combination of catechins and caffeine was reported to induce strong suppression of body fat accumulation. In this study, we proved marked alterations in the lipid content of both the mesenteric and hepatic tissues of non-obese rats given drinking water containing crude catechin extract at doses (0.1% and 0.5%) within the normal limits for routine daily green tea drinking (3, 16), and

**Fig. 2** Average daily food intake (a) and fluid consumption (b) measured on the 7th day after beginning catechin treatment. Each value indicates mean ± SD for 6 animals. *P < 0.01 vs control.

**Fig. 3** Effect of tea catechins on mesenteric (a) and hepatic lipid (b) contents in 7-week-old rats. Each value indicates mean ± SD for 6 animals. **P < 0.01 vs control, ##P < 0.01 vs 0.1% catechin.

group. The serum TP and Alb levels of all the catechin-treated rats did not differ from those of the respective control animals (Table 1).

**Serum level of bile acids**

Serum bile acids concentrations in the rats given catechins treatment for 3 weeks were significantly and dose-dependently decreased compared with untreated control (Fig. 5).
catechins on visceral fat accumulation has been extensively studied in experimental models using a high-caloric diet (4, 9, 16, 20, 25). The present study using normal rats fed a normal diet showed a meaningful reduction in intra-abdominal fat storage with ad libitum drinking water containing tea catechins. Several studies have demonstrated regional differences in lipid metabolism, particularly between the mesenteric and hepatic fat depots (8, 17), and our present results are consistent with the previous finding that tea catechins reduce the accumulation of both visceral and hepatic fat. Although the species difference should be kept in mind, it is likely that long-term intake of tea catechins can potentially influence body fat accumulation in non-obese subjects.

Adipose tissue is amorphous and widely distributed throughout the body, however the recent focus is on intra-abdominal fat as a risk factor for the so-called “metabolic syndrome” (1). The effect of tea catechins on visceral fat accumulation has been extensively studied in experimental models using a high-caloric diet (4, 9, 16, 20, 25). The present study using normal rats fed a normal diet showed a meaningful reduction in intra-abdominal fat storage with ad libitum drinking water containing tea catechins. Several studies have demonstrated regional differences in lipid metabolism, particularly between the mesenteric and hepatic fat depots (8, 17), and our present results are consistent with the previous finding that tea catechins reduce the accumulation of both visceral and hepatic fat. Although the species difference should be kept in mind, it is likely that long-term intake of tea catechins can potentially influence body fat accumulation in non-obese subjects.

Tea catechins have anti-obesity effects, such as reducing body weight gain (9, 16). Kao et al. reported that an intraperitoneal injection of EGCG

![Fig. 4](image-url) The lipid profiles (cholesterol ester (a) and TG (b) levels) of the mesenteries and livers of the 7-week-old rats. Values are expressed as percentages of controls and represent means ± SD for 6 animals. **P < 0.01 vs control, ##P < 0.01 vs 0.1% catechin.

**Table 1** Effect of catechin administration for 3 weeks on serum nutrient levels in the 7-week-old rats

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<thead>
<tr>
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<th>7-week-old rats</th>
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<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td>Total protein (g/dL)</td>
<td>5.9 ± 0.2</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.7 ± 0.2</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>108 ± 6</td>
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<tr>
<td>Total cholesterol (mg/dL)</td>
<td>65 ± 1</td>
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Each value represents the mean ± SD. (n = 4) **P < 0.01 vs control
Tea catechin reduces body fat

(85 mg/kg body weight) reduced body weight and food intake in Sprague-Dawley rats via a central appetite-regulating network pathway (13). Our data show that the body weight of the rats treated with tea catechins tended to be lower than that of the control subjects, even though the average daily food intake did not differ between the groups during the experimental period. Although the difference in administration routes should be kept in mind, it is unlikely that the doses of catechins used in the present study modulated appetite and thus reduced the body weight gain. Other studies using models of obesity (9, 16) have documented that animals showed significantly accelerated weight gain when fed a high-fat diet, and that tea or tea components prevented this. There is compelling evidence that lipid catabolism is stimulated in obese rodents by long-term feeding with tea components (4, 9, 16, 25). The changes in body weight with administration of tea catechins may be attributed to changes in body fat stores.

In obese experimental animals, the reduction in body fat and weight by green tea is presumably caused by an increase in energy expenditure and fat oxidation (4, 5) through stimulation of brown adipose tissue thermogenesis (6). Murase et al. demonstrated that long-term feeding of tea catechins significantly upregulated expression of acyl-CoA oxidase, which is a peroxisosomal β-oxidation enzyme, and medium-chain acyl-CoA dehydrogenase, which is a mitochondrial β-oxidation enzyme, in the murine liver (16). Although bile acids have long been known to be essential in dietary lipid absorption and cholesterol catabolism, in recent years, they have emerged as an inducer of energy expenditure in rodent models (23). In the present study, administration of tea catechins caused a decrease in the serum concentration of bile acids. Our results do not allow the inference that bile acids may contribute directly to the catechins-induced reduction in body fat and weight. Teddy et al. reported that tea catechins increased the fecal excretion of bile acids in rats with diet-induced hypercholesterolemia (26). Thus, the decrease in the serum bile acids level may have resulted from an increment in fecal bile acids excretion induced by tea catechins.

Our data show that administration of 0.5% tea catechins reduced the serum level of TC. Several studies using obese rodent models have indicated that tea catechins can markedly decrease plasma lipid levels (1, 16, 22, 26, 27), especially TC, without affecting plasma protein concentrations (13). These findings support those of recent epidemiological studies that consumption of green tea is associated with a reduced risk for metabolic syndrome (12, 18). In diet-induced obesity, green tea polyphenols increase fecal excretion of cholesterol and bile acids and reduce cholesterol absorption from the intestine (10). Although it is difficult to evaluate the fecal excretion of cholesterol in normal rats fed a normal diet, we consider that the tea catechins reduced the serum TC level by increasing fecal elimination of cholesterol. The present evidence strongly indicates that tea catechins modulate lipid metabolism not only in obese animals, but also in non-obese subjects.

In summary, we present two important findings regarding tea catechins. First, oral administration of green tea extract at in vivo doses caused significant decrements in both visceral and hepatic fat accumulation of non-obese rats fed a normal diet. Second, the tea catechin treatment caused a decrease in the serum levels of cholesterol and bile acids. These results prove that tea catechins have a notable effect on lipid metabolism in non-obese subject as well as obese ones.

Acknowledgments

Part of this work was supported by Grants-in-Aid for Scientific Research from the Japanese Ministry of Education, Science, and Culture and by the Integrative Research Program of the Graduate School of Medical Sciences, Kitasato University. This study
REFERENCES


