

Tea Catechins with a Galloyl Moiety Reduce Body Weight and Fat

Osami Kajimoto,^{*,a} Yoshitaka Kajimoto,^b Mitsuharu Yabune,^b Tadashi Nakamura,^c Kazuaki Kotani,^{c,d} Yuko Suzuki,^e Ayumu Nozawa,^e Kozo Nagata,^e Tomonori Unno,^e Yuko Mitane Sagesaka,^e Takami Kakuda,^e and Toshikazu Yoshikawa^f

^aHealth Management Center, Osaka University of Foreign Studies, 8–1–1 Higashi Awaumatani, Minou-shi, Osaka 562–8558, Japan, ^bDepartment of Clinical Trial and Research, Soiken Inc., 1–4–2 Shinshisato Higashimachi, Toyonaka-shi, Osaka 560–0082, Japan, ^cGraduate School of Medical Research Molecular Control Internal Medicine, Osaka University, 2–2 Yamadaoka, Suita-shi, Osaka 565–0871, Japan, ^dOsaka Kenkou Club, Sekiyama Clinic, 4–10–1 Esaka-cho, Suita-shi, Osaka 564–0063, Japan, ^eCentral Research Institute, ITOEN, Ltd., 21 Meoto, Aira-cho, Haruhara-gun, Shizuoka 421–0516, Japan, and ^fFirst Department of Internal Medicine, Kyoto Medical School, 465 Kajii-cho, Hirokoji-noboru, Kawaharamachi-dori, Kamikyo-ku, Kyoto 602–8566, Japan

(Received October 26, 2004; Accepted December 22, 2004; Published online December 27, 2004)

We investigated the effect of consumption of a catechin-containing drink on body fat level and its safety in healthy adults. The beverage (250 ml/bottle) contained 215.3 mg of tea catechins mostly possessing a galloyl moiety, which included (–)-epigallocatechin gallate 74.6 mg, (–)-epicatechin gallate 34.1 mg, (–)-galocatechin gallate 77.8 mg, (–)-catechin gallate 24.5 mg. We conducted a double-blind study with three parallel groups. Healthy subjects (98 men and 97 women) aged from 20 to 65 years old with $22.5 < \text{body mass index (BMI)} \leq 30 \text{ kg/m}^2$ were assigned to consume 3 bottles of placebo drink (control group), 2 bottles of catechin-containing drink and 1 bottle of placebo drink (low-dose group), or 3 bottles of catechin-containing drink (high-dose group), per day at mealtimes for 12 week (daily consumption of catechins was 41.1, 444.3 or 665.9 mg respectively). Compared to the value at 0 week, consumption of two or three bottles of catechin-containing drink results in significant decrease in body weight and BMI at 8 and 12 or 4, 8 and 12 week, respectively. Body weight and BMI was significantly decreased in both catechin groups compared with the control group from 4 to 12 week. The measurements of abdominal fat areas indicated significant reduction of total fat area and visceral fat area in both catechin groups compared with the control group at 12 week. Thus our present observations suggest that consumption of a catechin-containing drink may be useful for the prevention of obesity-related disorders.

Key words — tea catechin, body fat, obesity, clinical trial

INTRODUCTION

An increase in the hyperlipidemic population in Japan is probably due to changes in eating habits and lack of exercise. In particular, an increase in fat intake despite a decrease in total calorie intake contributes considerably to the increase. There is a report that the relative amount of fat in a diet may influence adiposity.¹⁾ The accumulation of fat, especially visceral fat, leads to metabolic disorders such as glucose intolerance and hyperlipidemia,²⁾ which are risk factors for coronary artery disease.³⁾

Green tea is rich in polyphenols, which contribute to its astringent/bitter taste. Green tea polyphenols mainly consist of catechins including (–)-epigallocatechin gallate (EGCg), (–)-epicatechin gallate (ECg), (–)-epigallocatechin (EGC) and (–)-epicatechin (EC). In the process of manufacturing canned and bottled tea beverages, parts of these authentic catechins were easily epimerized, and their corresponding epimers, (–)-galocatechin gallate (GCg), (–)-catechin gallate (Cg), (–)-galocatechin (GC) and (–)-catechin (C) were formed.^{4,5)} Green tea catechins have several physiological activities such as antioxidative action,^{6–8)} cancer-inhibiting action,⁹⁾ hypoglycemic action,¹⁰⁾ and anti-hypertensive action,¹¹⁾ and have been recognized as important components of green tea.¹²⁾

The authors have recently reported that a 12 week consumption of a tea catechin-containing

*To whom correspondence should be addressed: Health Management Center, Osaka University of Foreign Studies, 8–1–1 Higashi Awaumatani, Minou-shi, Osaka 562–8558, Japan. Tel.: +81-727-30-5152; Fax: +81-727-30-5153; E-mail: kajimoto@soiken.com

Table 1. Catechin Compositions of Study Drinks

	Catechin drink	Placebo drink
	mg/ bottle (250 ml)	
(-)-Epigallocatechin gallate	74.6	3.1
(-)-Epicatechin gallate	34.1	ND ^{a)}
(-)-Gallocatechin gallate	77.8	2.5
(-)-Catechin gallate	24.5	2.7
(-)-Epigallocatechin	0.7	2.5
(-)-Epicatechin	1.6	0.4
(-)-Gallocatechin	1.1	1.4
(-)-Catechin	0.9	1.1
Total catechins	215.3	13.7

a) Abbreviations used: ND, not detected.

drink effectively decreased serum total cholesterol in subjects with borderline or mild hypercholesterolemia.¹³⁾ Animal studies have also provided evidence that tea catechins or green tea extract modulate lipid metabolism, through reduction of triacylglycerols,¹⁴⁻¹⁶⁾ inhibition of fat accumulation^{17,18)} and enhancement of energy expenditure.¹⁹⁾ In addition, an epidemiological study showed an inverse association between the number of cups of tea consumed and body fat content²⁰⁾ and intervention study showed tea catechins reduced body fat.²¹⁾ Therefore, green tea, or its major constituents, tea catechins, have attracted much attention in regard to body fat reducing action. In the present study, we investigated the effectiveness of 12 week consumption of a tea catechin-containing drink with a little caffeine on body fat reduction and evaluated its safety in healthy adult men and women showing $22.5 < \text{BMI} \leq 30 \text{ kg/m}^2$.

MATERIALS AND METHODS

Subjects — The subjects, who were volunteers living in Osaka, were recruited by Soiken Inc. (Osaka, Japan) Four weeks prior to the study, preliminary screening was conducted and 197 subjects showing a $\text{BMI} < 22.5 < \text{BMI} \leq 30 \text{ kg/m}^2$ were selected. Excluded from the subjects were those who were taking medicines or health foods which may affect lipid metabolism, who had a history of food allergy, who had had 200 ml blood withdrawn within 1 month or 400 ml within 3 months, or who were judged to be inappropriate by the study investigator. The study subjects meeting the criteria were 98 men and 99 women ranging in age from 20 to 65 years old. Only 2 subjects discontinued participation in

this study at 12 week for personal reasons. The final effective number of subjects was 195 (including 98 men and 97 women, mean age: 43.0 ± 12.0 years old). The present study was initiated upon approval by the joint investigational review board of the Soiken Inc. and Soiken Clinic (Osaka, Japan). According to the Helsinki Declaration, the subjects were fully informed regarding the content and method of this study, and informed consent in writing was obtained prior to the study.

Study Drink — The study drink contained mainly tea catechins with a galloyl moiety (EGCg, ECg, GCg and Cg) derived from tea extract, THEA-FLAN 90S produced by ITO EN, Ltd. (Shizuoka, Japan) (hereinafter referred to as the catechin drink). This drink also included catechin-free green tea extract, which was made to remove catechin with polyvinyl-pyrrolidone,²²⁾ in order to adjust its taste, cyclodextrin and vitamin C. The ingredients of the placebo drink were the same as those of the catechin drink except that the latter contained the tea extract, THEA-FLAN 90S. The catechin composition of the study drink is shown in Table 1. Both test drinks contained nearly equal amounts of caffeine (catechin drink: 16.4 mg and placebo drink 17.4 mg). Prior to initiation of the study, it was confirmed that the catechin drink could not be distinguished from the placebo drink by flavor, taste or packaging. Catechins and caffeine in study drinks were analyzed by the modified method of Goto *et al.*²³⁾

Protocol — We conducted a double-blind study with three parallel arms. The study period consisted of a 2 week run-in period, 12 week intake period, and an 8 week withdrawal period. The subjects were divided into 3 groups based on the results of the preliminary screening (blood tests and physical examinations) so that the three groups were uniform in

background, including age, BMI and waist/hip ratio. The study drinks were consumed according to the following method.

Control Group: Each subject consumed 1 bottle of placebo drink at mealtimes, breakfast, lunch and dinner, for a total of 3 placebo bottles/day. Total intake of catechins: 41.1 mg/day.

Low-Dose Group: Each subject consumed 1 bottle of the catechin drink at breakfast and dinner and a placebo drink at lunchtime, for a total of 2 catechin bottles and 1 placebo bottle. Total intake of catechins: 444.3 mg/day.

High-Dose Group: Each subject consumed 1 bottle of the catechin drink at mealtimes, breakfast, lunch and dinner, for a total of 3 catechin bottles. Total intake of catechins: 665.9 mg/day.

The subjects were instructed not to change daily activities including eating habits, smoking and exercise except for drinking the assigned bottles of drink on a daily basis.

Nutrition Survey and Determination of Physical Activity — The subjects were instructed to record the contents of daily meals, snacks and beverages in a dietary diary for 3 consecutive days prior to the following examination days: on the first day of intake (0 week), and every 4 week after beginning of intake period. The respective daily intake of energy, protein, fat, carbohydrate, cholesterol, and dietary fiber was calculated from the diary record by nutritionists using HealthMaker Pro 501 (MushroomSoft Co, Ltd., Okayama, Japan). Physical activity was measured by the number of steps taken using a pedometer. The subjects were instructed to record daily alcohol intake in a diary whenever alcohol drinks were consumed during the study period.

Anthropometric Measurements — All measurements were performed by investigators trained in anthropometric measurements. Height was measured without shoes to the nearest 0.1 cm. Body weight was measured without shoes or heavy outer clothing and recorded to the nearest 0.1 kg using a scale (Tanita TBF-614, Tanita, Tokyo, Japan). Waist circumference was measured as the smallest location of the midsection, and hip circumference was measured at the location of the greatest gluteal mass. Both waist and hip circumferences were measured to the nearest 0.1 cm in the standing position. These measurements were performed at 2 week prior to the first day of intake (–2 week), on the first day of intake (0 week), and every 4 week after beginning of intake period.

Measurement of Fat by Computed Tomography (CT) — Except for women less than 35 years old, all subjects underwent abdominal fat analysis using computed tomography (CT) scanning. Based on the images taken by abdominal CT across the 4th and 5th lumbar vertebrae cross-sections, the total fat area (TFA), visceral fat area (VFA) and subcutaneous fat area (SFA) were estimated using PC software Fat Scan (N2 System K.K., Hyogo, Japan). CT analysis was performed at 0, 12, and 20 week. On the day of the examination, the subjects fasted for at least 4 hr and were not allowed to drink for 2 hr prior to the examination. CT analysis was performed with either Asteion Super 4 Edition or Xlead (Toshiba Medical Systems Corporation, Tochigi, Japan).

Blood Sampling and Clinical Analysis — After a 12 hr fast, blood samples were collected for hematological and biochemical analysis at –2, 0, 4, 8, 12, 16 and 20 week. Measurement parameters were blood cell components (leukocytes, erythrocytes, hemoglobin, hematocrit, platelet counts), triacylglycerol, total cholesterol, low-density lipoprotein-cholesterol (LDL-cholesterol), high-density lipoprotein-cholesterol (HDL-cholesterol), ketone body fractions, ferritin, amylase, cholinesterase, aspartate aminotransferase, alanine aminotransferase, γ -glutamyl transpeptidase, lactate dehydrogenase, alkaline phosphatase, uric acid, urea nitrogen, creatinine, total proteins, albumin, total bilirubins, direct bilirubin, fasting glucose level, glycated hemoglobin, creatinine phosphokinase, insulin, unsaturated iron binding capacity (UIBC), Fe, IP, Na, K, Cl, Ca, and Mg. The analyses were all outsourced to specialized clinical testing companies: SRL, Inc. (Tokyo, Japan) and Osaka Serum Microbiology Institute (Osaka, Japan).

Adverse Events — Adverse events were measured by questionnaires at –2, 0, 4, 8, 12, 16 and 20 week. Incidence of subjective symptoms such as systemic fatigue, lack of appetite, nausea, diarrhea, vomiting, and headache, and other adverse events were reported.

Statistical Analysis — Values are expressed as means \pm scanning electron microscope (SEM). Variation patterns in the physical examination and serum lipids during the administration periods, and the interactions between the administration periods and the study groups were analyzed by two-way repeated-measure analysis of variance (ANOVA) between the control group and the low-dose group or between the control group and the high-dose group. Significant differences among study groups for the

same period were determined by the Bonferroni method. To compare the differences with 0 week within the study groups paired *t*-tests were performed for abdominal fats. To compare the differences with 0 week within the study groups, the Bonferroni method was used for nutrient intakes, physical activity, anthropometric measurements and blood tests. These statistical calculations were performed with SPSS Ver. 11.5 (SPSS Inc., Chicago, Illinois, U.S.A.).

RESULTS

Nutrient Intake, Alcohol Consumption and Physical Activity

Table 2 shows nutrient intake, alcohol consumption and physical activity. There were no significant differences among the study groups in any parameters tested. No significant variations were found during the intake period.

Anthropometric Measurements

The repeated-measure ANOVA revealed significant differences in body weight ($p < 0.001$), BMI ($p < 0.001$) and waist circumference ($p < 0.05$) between the control group and the low-dose group; and in the body weight ($p < 0.001$) and BMI ($p < 0.001$) between the control group and the high-dose group (Table 3). Body weight and BMI increased significantly in the control group at 8, 12, 16 and 20 week compared to the value at 0 week ($p < 0.001$ for all), whereas body weight and BMI decreased significantly in both catechin groups (low-dose group: 8 week $p < 0.05$, 12 week $p < 0.001$; high-dose group: 4, 8, and 12 week $p < 0.001$ for all) (Table 3). Waist circumference and waist/hip ratio decreased significantly in both catechin groups at 12 week (waist: $p < 0.05$ in the low-dose group; $p < 0.01$ in the high-dose group; waist/hip ratio: $p < 0.01$ for both) (Table 3). Hip circumference did not change in any group (Table 3). Figure 1 shows the change in Body weight and BMI. Compared with the control group, Body weight and BMI was significantly lowered in both catechin groups between 4 and 20 week. There were also significant differences between the low-dose group and the high-dose group at 4 and 8 week in Body weight and BMI (Fig. 1).

Body Fat Analysis

Table 4 shows body fat composition. TFA was significantly increased at 12 week compared with

the value at 0 week in the control group ($p < 0.01$), whereas in both catechin groups it was significantly decreased ($p < 0.05$ for both). VFA demonstrated a significant increase at 12 week compared with the value at 0 week in the control group ($p < 0.05$). However, it was significantly decreased in both low- and high-dose groups ($p < 0.01$ for both). There were no significant variations in SFA in any group. Figure 2 shows the changes of TFA and VFA, which indicated significant differences between the control group and both catechin groups at 12 week in all subjects.

Serum Lipids

Table 5 shows change in serum lipids. ANOVA indicated significant differences in total cholesterol ($p < 0.01$), LDL-cholesterol ($p < 0.05$) between the control group and the low-dose group, and in total cholesterol ($p < 0.001$) and LDL-cholesterol ($p < 0.01$) between the control group and the high-dose group. Total cholesterol significantly increased in the control group at 8 week ($p < 0.05$) and 16 week ($p < 0.01$) compared with the value at 0 week, whereas it significantly decreased in the high-dose group at 12 week ($p < 0.01$). In the high-dose group, total cholesterol significantly decreased from 4 to 16 week compared with the control group. In the low-dose group, it significantly decreased at 8 and 12 week compared with the control group. Significant increases of HDL cholesterol were noted in the low-dose group at 4 and 20 week ($p < 0.01$ for both) compared with the value at 0 week. There were also significant increases in the control group at 8 week ($p < 0.05$). LDL-cholesterol was significantly lowered in the high-dose group at 8 and 12 week compared with the control group, and significantly lowered in the low-dose groups at 12 week compared with the control group. Triacylglycerol was significantly lowered in the high-dose group at 16 week compared with the control group.

Changes in General Blood Biochemical Test Data and Blood Test Data (Data not Shown)

There was a significant increase in blood glucose with fasting in the control group at 12 week (5.16 ± 0.06 mmol/l) compared with that at 0 week (4.99 ± 0.05 mmol/l) ($p < 0.01$). In the low-dose group, serum amylase demonstrated a significant increase at 12 week (62.8 ± 3.1 μ U/l) compared with that at 0 week (58.3 ± 2.7 μ U/l) ($p < 0.05$), whereas the inorganic phosphorus and urea nitrogen levels showed significant decreases (inorganic phospho-

Table 2. Intake of Nutrient Components and Alcohol Consumption, and Physical Activity of Men and Women Consuming Tea Catechins for 12 week^{a)}

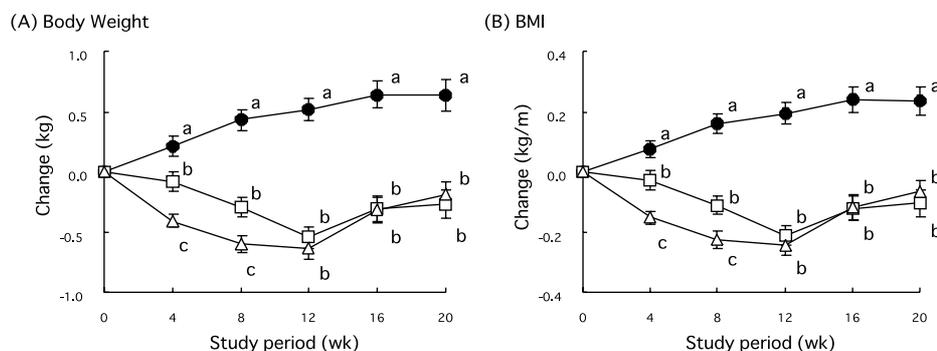
	group	Intake period		
		0 week	4 week	8 week
Energy, kJ/day	Control	8647 ± 248	8540 ± 221	8697 ± 245
	Low-dose	8157 ± 202	8332 ± 213	8271 ± 214
	High-dose	8353 ± 212	8506 ± 233	8661 ± 275
Protein, g/day	Control	76.6 ± 2.3	77 ± 2.5	80.1 ± 2.7
	Low-dose	77.6 ± 2.4	79.3 ± 2.6	78.3 ± 2.5
	High-dose	77.6 ± 2.5	81.3 ± 2.8	82.2 ± 3.2
Fat, g/day	Control	59 ± 2.2	58.1 ± 2.1	61.4 ± 2.3
	Low-dose	55 ± 2.1	58.9 ± 2.2	59.7 ± 2.3
	High-dose	58.7 ± 2.2	59 ± 2.2	62.5 ± 2.6
Carbohydrate, g/day	Control	267 ± 8.2	266 ± 8.0	263 ± 8.4
	Low-dose	255 ± 6.7	254 ± 6.7	254 ± 7.0
	High-dose	253 ± 7.9	258 ± 8.5	256 ± 8.8
Cholesterol, mg/day	Control	380 ± 17	368 ± 18	400 ± 19
	Low-dose	386 ± 19	410 ± 21	406 ± 19
	High-dose	387 ± 20	433 ± 24	446 ± 23
Dietary fiber, g/day	Control	13.5 ± 0.5	14 ± 0.5	14 ± 0.6
	Low-dose	13.6 ± 0.6	13.6 ± 0.6	13.5 ± 0.6
	High-dose	13.3 ± 0.5	13.1 ± 0.5	13.8 ± 0.6
Alcohol, g/day	Control	21.8 ± 3.7	19 ± 3.3	18.1 ± 3.3
	Low-dose	14.2 ± 2.7	15.5 ± 2.9	13.3 ± 2.5
	High-dose	20.7 ± 3.6	18.2 ± 3.3	18 ± 3.3
Physical activity ^{b)}	Control	9471 ± 482	9653 ± 489	8948 ± 466
	Low-dose	10185 ± 1635	9124 ± 609	8497 ± 439
	High-dose	9646 ± 547	9640 ± 647	9728 ± 547
	group	Intake period		Withdrawal
		12 week	16 week	20 week
Energy, kJ/day	Control	8389 ± 209	8520 ± 249	8533 ± 250
	Low-dose	8370 ± 225	7877 ± 199	8159 ± 241
	High-dose	8775 ± 263	8574 ± 216	8353 ± 243
Protein, g/day	Control	76.7 ± 2.4	80.5 ± 2.9	80.5 ± 3.0
	Low-dose	78.2 ± 2.6	74.5 ± 2.3	79.3 ± 2.8
	High-dose	81.2 ± 3.2	80.4 ± 2.7	75.5 ± 2.7
Fat, g/day	Control	61.7 ± 2.3	60 ± 2.4	60.1 ± 2.4
	Low-dose	57.1 ± 1.8	55.7 ± 1.9	58 ± 2.2
	High-dose	60.1 ± 2.4	58.7 ± 2.1	56 ± 2.2
Carbohydrate, g/day	Control	254 ± 7.9	259 ± 8.7	258 ± 8.0
	Low-dose	260 ± 8.0	251 ± 7.4	250 ± 7.7
	High-dose	269 ± 8.2	260 ± 7.8	259 ± 7.6
Cholesterol, mg/day	Control	397 ± 16	413 ± 21	415 ± 21
	Low-dose	378 ± 17	379 ± 20	423 ± 22
	High-dose	420 ± 21	408 ± 20	393 ± 21
Dietary fiber, g/day	Control	13.4 ± 0.6	13.5 ± 0.5	13 ± 0.5
	Low-dose	13.8 ± 0.6	13.4 ± 0.5	13.4 ± 0.6
	High-dose	14.2 ± 0.6	13.5 ± 0.5	13.6 ± 0.5
Alcohol, g/day	Control	16.5 ± 3.0	22.1 ± 3.5	16.5 ± 3.0
	Low-dose	19.7 ± 8.1	13.4 ± 2.6	11.9 ± 2.5
	High-dose	17.9 ± 3.3	22 ± 3.8	17.9 ± 3.3
Physical activity ^{b)}	Control	8914 ± 436	9184 ± 1118	8378 ± 412
	Low-dose	8647 ± 419	8366 ± 403	8337 ± 408
	High-dose	10344 ± 923	9220 ± 509	9947 ± 732

a) Values are means ± SEM, n = 66 (Control group), 65 (Low-dose group) or 64 (High-dose group). b) Number of steps per day.

Table 3. Anthropometric Measurements of Men and Women Consuming Tea Catechins for 12 week^(a,b)

	group	Run in		Intake period		ANOVA
		-2 week	0 week	4 week	8 week	
BW, kg	Control	68.6 ± 1.1	68.7 ± 1.1	69.0 ± 1.1	69.2 ± 1.1***	
	Low	68.4 ± 1.1	68.4 ± 1.1	68.3 ± 1.1	68.1 ± 1.1*	
	High	68.5 ± 1.1	68.4 ± 1.1	68.0 ± 1.1***	67.8 ± 1.1***	
BMI, kg/m ²	Control	25.7 ± 0.3	25.7 ± 0.3	25.8 ± 0.3	25.9 ± 0.3***	
	Low	25.6 ± 0.2	25.6 ± 0.2	25.5 ± 0.2	25.5 ± 0.2*	
	High	25.7 ± 0.2	25.7 ± 0.2	25.5 ± 0.2***	25.5 ± 0.2***	
WC, cm	Control	83.4 ± 1.0	83.3 ± 1.0	83.6 ± 1.0	83.4 ± 0.9	
	Low	83.7 ± 1.0	83.6 ± 1.0	83.6 ± 1.0	83.3 ± 1.0	
	High	83.6 ± 0.8	83.5 ± 0.8	83.4 ± 0.8	83.1 ± 0.8	
HC, cm	Control	99.2 ± 0.6	98.9 ± 0.6	99.0 ± 0.6	99.1 ± 0.6	
	Low	98.9 ± 0.6	98.5 ± 0.6	98.8 ± 0.7	98.6 ± 0.6	
	High	98.7 ± 0.5	98.5 ± 0.6	99.0 ± 0.5	98.6 ± 0.5	
Waist/hip	Control	0.840 ± 0.007	0.842 ± 0.007	0.844 ± 0.007	0.841 ± 0.007	
	Low	0.846 ± 0.007	0.848 ± 0.007	0.845 ± 0.008	0.843 ± 0.007	
	High	0.846 ± 0.007	0.848 ± 0.007	0.843 ± 0.006	0.842 ± 0.007	
	group	Intake period		Withdrawal		ANOVA
		12 week	16 week	20 week		
BW, kg	Control	69.3 ± 1.1***	69.4 ± 1.1***	69.4 ± 1.1***		
	Low	67.9 ± 1.2***	68.1 ± 1.1	68.1 ± 1.1	<i>p</i> < 0.001	
	High	67.8 ± 1.1***	68.1 ± 1.1	68.3 ± 1.1	<i>p</i> < 0.001	
BMI, kg/m ²	Control	25.9 ± 0.3***	26.0 ± 0.3***	26.0 ± 0.2***		
	Low	25.4 ± 0.2***	25.4 ± 0.2	25.5 ± 0.2	<i>p</i> < 0.001	
	High	25.5 ± 0.2***	25.6 ± 0.2	25.6 ± 0.2	<i>p</i> < 0.001	
WC, cm	Control	83.4 ± 0.9	83.6 ± 0.9	83.6 ± 0.9		
	Low	82.7 ± 1.0*	83.4 ± 1.0	83.3 ± 1.0	<i>p</i> < 0.05	
	High	82.7 ± 0.8**	83.4 ± 0.8	83.4 ± 0.8		
HC, cm	Control	99.0 ± 0.5	99.1 ± 0.5	99.1 ± 0.5		
	Low	98.7 ± 0.6	98.8 ± 0.6	98.7 ± 0.6		
	High	98.8 ± 0.5	98.7 ± 0.5	98.6 ± 0.5		
Waist/hip	Control	0.841 ± 0.007	0.843 ± 0.007	0.843 ± 0.007		
	Low	0.837 ± 0.007**	0.843 ± 0.007	0.843 ± 0.007		
	High	0.837 ± 0.007**	0.844 ± 0.006	0.845 ± 0.006		

a) Values are means ± SEM, *n* = 66 (Control group), 65 (Low-dose group) or 64 (High-dose group). Significantly different from the value at 0 week: **p* < 0.05, ***p* < 0.01, ****p* < 0.001. b) Abbreviations used: BW, body weight; WC, waist circumference; HC, hip circumference; Control, control group; Low, low-dose group; High, high-dose group; ANOVA, two-way repeated-measure ANOVA.

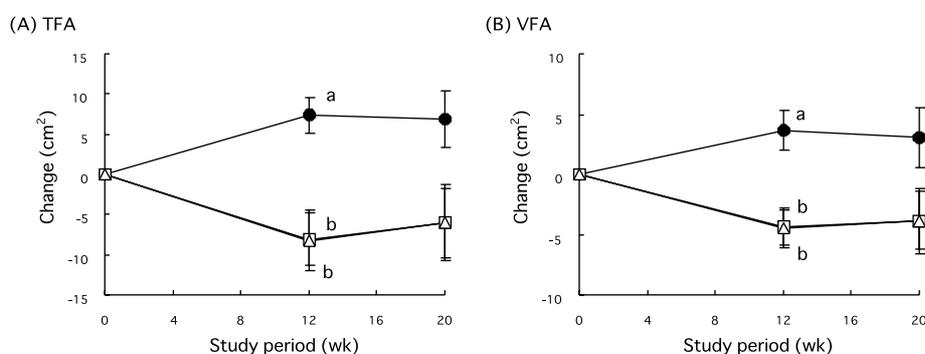
**Fig. 1.** Change of Body Weight (A) and BMI (B) in Men and Women Consuming Tea Catechins for 12 week

●, control group (*n* = 66); □, low-dose group (*n* = 65); △, high-dose group (*n* = 64). Each point represents the mean ± SEM. Those in the same study period not sharing a letter differ, *p* < 0.05.

Table 4. Body Fat Composition of Men and Women Consuming Tea Catechins for 12 week^{a)}

	group	Intake period		Withdrawal
		0 week	12 week	20 week
Total fat area, cm ²	Control	293 ± 7	300 ± 8**	300 ± 8
	Low	293 ± 8	285 ± 8*	287 ± 8
	High	293 ± 7	285 ± 8*	287 ± 8
Visceral fat area, cm ²	Control	107 ± 4	111 ± 4*	110 ± 4
	Low	107 ± 4	103 ± 4***	103 ± 5
	High	108 ± 4	103 ± 4***	104 ± 5
Subcutaneous fat area, cm ²	Control	185 ± 7	189 ± 7	189 ± 8
	Low	186 ± 7	183 ± 7	184 ± 7
	High	185 ± 7	182 ± 7	183 ± 7

a) Values are means ± SEM, control group (n = 58), low-dose group (n = 56), high-dose group (n = 56). Significantly different from the value at 0 week: *p < 0.05, **p < 0.01.

**Fig. 2.** Change of TFA (A) and VFA (B) in Men and Women Consuming Tea Catechins for 12 week

●, control group (n = 58); □, low-dose group (n = 56); △, high-dose group (n = 56). Each point represents the mean ± SEM. Those in the same study period not sharing a letter differ, p < 0.05.

rus: 1.06 ± 0.02 mmol/l; urea nitrogen: 4.53 ± 0.13 mmol/l) at 4 week compared with those values at 0 week (inorganic phosphorus: 1.12 ± 0.02 mmol/l; urea nitrogen: 4.98 ± 0.15 mmol/l) (inorganic phosphorus: p < 0.01 and urea nitrogen p < 0.001). Direct bilirubin was significantly decreased at 12 week (4.71 ± 0.21 μmol/l) in the low-dose group compared with the value at 0 week (5.55 ± 0.25 μmol/l) (p < 0.01). Erythrocyte counts showed a significant reduction at 12 week ($4.58 \pm 0.05 \times 10^{12}$ /l) in the high-dose group compared with the value at 0 week ($4.71 \pm 0.04 \times 10^{12}$ /l) (p < 0.001). There was a significant increase in the hemoglobin level in the control group at 8 week (14.3 ± 0.2 g/l) compared with the value at 0 week (14.1 ± 0.2 g/l) (p < 0.01), whereas there was a significant decrease at 12 week (13.8 ± 0.2 g/l) in the high-dose group compared with the value at 0 week (14.2 ± 0.2 g/l) (p < 0.01). There were no clinically significant decreases in Fe, UIBC or ferritin in any group. Although significant changes were found in the study period for other

items tested, the variations were similar to those in the control group; they were within the normal range without exception.

Adverse Events

During the study periods, 34 cases of cold-like symptoms (control group, 15; low-dose group, 12; high-dose group, 7), 3 cases of eczema (1 in each group), 7 cases of diarrhea or soft stools (control group, 1; low-dose group, 4; high-dose group, 2), and 1 case of lack of appetite (high-dose group) were reported. Recovery from each of these symptoms was spontaneous in the course of the study.

DISCUSSION

Obesity is defined as an excess of adipose tissue, and many people suffer from it in modern society. In Japan, obesity is specified as a BMI ≥ 25 kg/m², and the ratio of obesity was 25.5% ac-

Table 5. Concentration of Serum Lipids of Men and Women Consuming Tea Catechins for 12 week^{a,b)}

	Group	Intake period			
		Run in -2 week	0 week	4 week	8 week
TC, mmol/l	Control	5.69 ± 0.11	5.55 ± 0.10	5.67 ± 0.10	5.82 ± 0.11*
	Low	5.67 ± 0.15	5.65 ± 0.13	5.60 ± 0.13	5.66 ± 0.14
	High	5.64 ± 0.12	5.61 ± 0.12	5.45 ± 0.12	5.48 ± 0.11
Change, ^{c)} mmol/l	Control			0.11 ± 0.06 ^{d)}	0.27 ± 0.08 ^{d)}
	Low			-0.05 ± 0.06 ^{d,e)}	0.01 ± 0.07 ^{e)}
	High			-0.16 ± 0.06 ^{e)}	-0.14 ± 0.06 ^{e)}
HDL-C, mmol/l	Control	1.40 ± 0.04	1.39 ± 0.04	1.44 ± 0.04	1.46 ± 0.04*
	Low	1.38 ± 0.04	1.37 ± 0.03	1.46 ± 0.04**	1.43 ± 0.04
	High	1.42 ± 0.04	1.42 ± 0.04	1.45 ± 0.04	1.43 ± 0.04
Change, mmol/l	Control			0.04 ± 0.02	0.06 ± 0.02
	Low			0.09 ± 0.02	0.06 ± 0.02
	High			0.03 ± 0.02	0.01 ± 0.02
LDL-C, mmol/l	Control	3.47 ± 0.10	3.47 ± 0.09	3.50 ± 0.10	3.60 ± 0.10
	Low	3.46 ± 0.13	3.56 ± 0.12	3.39 ± 0.12	3.48 ± 0.12
	High	3.46 ± 0.11	3.50 ± 0.11	3.34 ± 0.11	3.32 ± 0.10
Change, mmol/l	Control			0.03 ± 0.06	0.13 ± 0.07 ^{d)}
	Low			-0.17 ± 0.06	-0.08 ± 0.07 ^{d,e)}
	High			-0.16 ± 0.06	-0.18 ± 0.07 ^{e)}
TG, mmol/l	Control	1.98 ± 0.11	1.79 ± 0.09	1.85 ± 0.11	1.91 ± 0.12
	Low	1.95 ± 0.12	1.80 ± 0.10	1.89 ± 0.17	1.89 ± 0.15
	High	1.89 ± 0.10	1.92 ± 0.12	1.74 ± 0.10	1.87 ± 0.16
Change, mmol/l	Control			0.06 ± 0.10	0.12 ± 0.10
	Low			0.09 ± 0.14	0.09 ± 0.11
	High			-0.18 ± 0.10	-0.05 ± 0.13

a) Values are means ± SEM, $n = 66$ (Control group), 65 (Low-dose group) or 64 (High-dose group). Significantly different from the value at 0 week: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. d, e) Values not sharing a superscript are significantly different among the groups for the same time ($p < 0.05$). b) Abbreviations used: TC, total cholesterol; HDL-C, HDL-cholesterol; LDL-C, LDL-cholesterol; TG, triacylglycerol; Control, control group; Low, low-dose group; High, high-dose group; ANOVA, two-way repeated-measure ANOVA. c) Four-, 8-, 12-, 16- and 20-week values minus 0-week value.

according to the 2001 National Nutrition Survey²⁴⁾ and the ratio of obesity among the general population is increasing year by year. Obesity is one of the serious risk factors for 'lifestyle-related diseases' mentioned by the Ministry of Health and Welfare in Japan in 1996. Lifestyle-related diseases included hypertension, diabetes, hyperlipidemia and atherosclerotic disease.

In the present study, using adult men and women showing $22.5 < \text{BMI} \leq 30$ as subjects, we investigated the effectiveness of tea catechin-containing beverages on the reduction of body fats and its safety when the drinks were consumed for 12 week at two dosage levels. The results revealed significant decreases in body weight, BMI, waist circumference and waist/hip ratio in both the low- and high-dose groups. Measurement of the abdominal fat area indicated significant decreases in TFA and VFA in both low- and high-dose groups. In both the low- and

high-dose groups, there were no significant differences in the body fat reducing effect at 12 week, but the expression of the effect was definitely earlier in the high-dose group.

Two types of obesity are currently known: the subcutaneous type in which fat accumulates predominantly in the subcutis, and the visceral type which is characterized by a marked fat accumulation in the abdominal cavity and frequent association with metabolic aberrations such as glucose intolerance and hyperlipidemia.²⁾ Yamashita *et al.* referred to this condition as "visceral fat syndrome," which includes visceral fat accumulation, glucose intolerance, hyperlipidemia, and hypertension as a highly atherogenic state with a cluster of risk factors based upon visceral fat accumulation, irrespective of body weight.²⁵⁾ Therefore, it is very important to reduce body fat, especially visceral fat, for the prevention of lifestyle-related diseases.

Table 5. Continued

	Group	Intake period	Withdrawal		ANOVA
		12 week	16 week	20 week	
TC, mmol/l	Control	5.76 ± 0.11	5.88 ± 0.12**	5.74 ± 0.11*	<i>p</i> < 0.01
	Low	5.54 ± 0.10	5.77 ± 0.13	5.76 ± 0.13	
	High	5.39 ± 0.10**	5.64 ± 0.12	5.60 ± 0.12	
Change, ^{c)} mmol/l	Control	0.21 ± 0.07 ^{d)}	0.32 ± 0.07 ^{d)}	0.19 ± 0.06	<i>p</i> < 0.001
	Low	-0.11 ± 0.07 ^{e)}	0.13 ± 0.06 ^{d,e)}	0.11 ± 0.07	
	High	-0.23 ± 0.06 ^{e)}	0.03 ± 0.08 ^{e)}	-0.02 ± 0.08	
HDL-C, mmol/l	Control	1.43 ± 0.04	1.40 ± 0.04	1.44 ± 0.04	<i>p</i> < 0.05
	Low	1.39 ± 0.04	1.42 ± 0.04	1.44 ± 0.04**	
	High	1.41 ± 0.04	1.44 ± 0.05	1.42 ± 0.04	
Change, mmol/l	Control	0.03 ± 0.02	0.01 ± 0.02	0.04 ± 0.02	<i>p</i> < 0.01
	Low	0.02 ± 0.02	0.05 ± 0.02	0.07 ± 0.02	
	High	0.00 ± 0.03	0.02 ± 0.02	0.00 ± 0.03	
LDL-C, mmol/l	Control	3.59 ± 0.10	3.60 ± 0.10	3.53 ± 0.11	<i>p</i> < 0.05
	Low	3.39 ± 0.11	3.57 ± 0.11	3.57 ± 0.11	
	High	3.31 ± 0.10	3.43 ± 0.11	3.41 ± 0.11	
Change, mmol/l	Control	0.12 ± 0.07 ^{d)}	0.14 ± 0.06	0.06 ± 0.06	<i>p</i> < 0.01
	Low	-0.17 ± 0.06 ^{e)}	0.01 ± 0.06	0.01 ± 0.07	
	High	-0.19 ± 0.06 ^{e)}	-0.07 ± 0.09	-0.09 ± 0.09	
TG, mmol/l	Control	1.92 ± 0.27	1.93 ± 0.14	1.77 ± 0.09	<i>p</i> < 0.05
	Low	1.98 ± 0.29	1.65 ± 0.09	1.60 ± 0.09	
	High	1.74 ± 0.12	1.65 ± 0.11	1.76 ± 0.15	
Change, mmol/l	Control	0.13 ± 0.27	0.14 ± 0.13 ^{d)}	-0.02 ± 0.08	<i>p</i> < 0.05
	Low	0.18 ± 0.28	-0.15 ± 0.10 ^{d,e)}	-0.20 ± 0.08	
	High	-0.18 ± 0.11	-0.27 ± 0.10 ^{e)}	-0.16 ± 0.15	

In the control group, body weight and BMI increased during the administration of drinks. It was reported that body weight and total cholesterol generally increase from summer to winter.²⁶⁾ The increase in body weight in the control group may be attributable to the effects of seasonal factors since the study was conducted during the period from fall to winter (intake period: from 9/20/2003 to 12/13/2003).

Tea, as well as coffee is a popular drink, and has been regarded as a drink for a healthy life. With the advancement of modern science, ingredients such as caffeine and catechins were identified, and their physiological functions have been investigated. In Japan, green tea is a popular drink, and catechins, which are major components of tea, have been reported to have valuable physiological functions.⁶⁻¹²⁾ Animal and human studies indicate that catechins, for example, accelerate energy expenditure.^{19,27)} Oolong tea, which is made from the same plant (*Camellia sinensis* L.) as green tea, is also reported to be involved in energy expenditure in humans, suggesting caffeine is major ingredient of increasing

energy expenditure.²⁸⁾ Single application of caffeine at a level of 100 to 300 mg was reported to significantly increase the energy metabolism.^{29,30)} In the present study, since the drinks included caffeine at a low level of about 50 mg/day in all groups, its effects were considered to be minimal.

It was also reported in an *in vitro* study that green tea extract inhibits gastric and pancreatic lipase,³¹⁾ and EGCg significantly decreased fat absorption in rats.¹⁶⁾ When hamsters were fed a high fat diet supplemented with tea catechins, an increase in serum triacylglycerol was suppressed, and there was no effect on lipogenesis in the liver.¹⁵⁾ Recently, the drug orlistat, which inhibits lipase activity and the intestinal absorption of dietary fats, has been used for the treatment of obesity.³²⁾ It seems reasonable to suppose that tea catechins reduce body fat by inhibiting lipid absorption from meals.

The catechin drink used in this study mainly contained the following four ingredients: EGCg, GCg, ECg and Cg, but catechin content without a galloyl moiety was extremely low. Although catechins with a galloyl moiety demonstrated a pan-

creatic lipase inhibiting action, catechins without a galloyl moiety have little effect,³³⁾ and it is important to consider the catechin composition. Previously, the authors reported a serum cholesterol reducing action of catechins in humans.¹³⁾ In this study, the subjects showed mild and borderline hypercholesterolemia, and total cholesterol and LDL-cholesterol were found to be significantly reduced in both the low- and high-dose groups. The result supports the previous investigation.

At the doses used in this study, catechins did not induce abnormal changes in hepatic functions, renal functions or electrolytes. In addition, phenolic compounds such as catechins are considered to interfere with iron absorption by complex formation with iron in the gastro-intestinal lumen, making the iron less available for absorption.³⁴⁾ The results based on all subjects of either sex indicated no significant decrease in the serum Fe levels, UIBC and ferritin during the administration, and no onset of anemic subjects was reported as an adverse event. Among 195 subjects, the only symptoms reported in this study were 34 cases of cold-like symptoms, 3 cases of eczema, 7 cases of diarrhea and soft stools and only one case of lack of appetite, and they were found in all groups. Because of its pancreatic lipase inhibiting action, it is presumable that diarrhea and soft stools were brought by the catechin drink. However, these symptoms were mild, temporary, disappeared spontaneously during the study period and reported in all groups. From medical perspective, the catechin drink was unlikely to bring diarrhea and soft stools. Other symptoms were also judged to be unrelated to the catechin drink. Based on these facts, we considered the catechin drink safe when consumed over a long period.

In summary, our present study demonstrated that a drink containing tea catechins was effective in reducing body fat and safe when given continuously for 12 week. Although these effects were milder than those of medicines, it is useful because of its safety and availability for long-term intake. Therefore the tea catechin-containing drink may be beneficial for many people in whom moderate or mild overweight may increase the risk of life-style related disorders such as diabetes and hyperlipidemia.

REFERENCES

- 1) Nelson, L. H. and Tucker, L. A. (1996) Diet composition related to body fat in a multivariate study of 203 men. *J. Am. Diet Assoc.*, **96**, 771–777.
- 2) Fujioka, S., Matsuzawa, Y. and Tokunaga, K. (1987) Contribution of intra-abdominal fat accumulation to the impairment of glucose and lipid metabolism in human obesity. *Metabolism*, **36**, 54–59.
- 3) Kobayashi, H., Nakamura, T. and Miyaoka, K. (2001) Visceral fat accumulation contributes to insulin resistance, small-sized low-density lipoprotein, and progression of coronary artery disease in middle-aged non-obese Japanese men. *Jpn. Circ. J.*, **65**, 193–199.
- 4) Chen, Z. Y., Zhu, Q. Y., Tsang, D. and Huang, Y. (2001) Degradation of green tea catechins in tea drinks. *J. Agric. Food Chem.*, **49**, 477–482.
- 5) Seto, R., Nakamura, H., Nanjo, F. and Hara, Y. (1997) Preparation of epimers of tea catechins by heat treatment. *Biosci. Biotechnol. Biochem.*, **61**, 1434–1439.
- 6) Unno, T., Sugimoto, A. and Kakuda, T. (2000) Scavenging effect of tea catechins and their epimers on superoxide anion radicals generated by a hypoxanthine and xanthine oxidase system. *J. Sci. Food Agric.*, **80**, 601–606.
- 7) Unno, T., Yayabe, F., Hayakawa, T. and Tsuge, H. (2002) Electron spin resonance spectroscopic evaluation of scavenging activity of tea catechins on superoxide radicals generated by a phenazine methosulfate and NADH system. *Food Chemistry*, **76**, 259–265.
- 8) Yoshino, K., Hara, Y. and Sano, M. (1994) Antioxidative effects of black tea theaflavins and thearubigin on lipid peroxidation of rat liver homogenates induced by tert-butyl hydroperoxide. *Biol. Pharm. Bull.*, **17**, 146–149.
- 9) Fujiki, H., Suganuma, M., Okabe, S., Sueoka, N., Komori, A., Sueoka, E., Kozu, T., Tada, Y., Suga, K., Imai, K. and Nakachi, K. (1998) Cancer inhibition by green tea. *Mutat. Res.*, **402**, 307–310.
- 10) Valsa, A. K., Sudheesh, S. and Vijayalakshmi, N. R. (1997) Effect of catechin on carbohydrate metabolism. *Indian J. Biochem. Biophys.*, **34**, 406–408.
- 11) Henry, J. P. and Stephens-Larson, P. (1984) Reduction of chronic psychosocial hypertension in mice by decaffeinated tea. *Hypertension*, **6**, 437–444.
- 12) Yang, C. S. and Landau, J. M. (2000) Effects of tea consumption on nutrition and health. *J. Nutr.*, **130**, 2409–2412.
- 13) Kajimoto, O., Kajimoto, Y., Yabune, M., Nozawa, A., Nagata, K. and Kakuda, T. (2003) Tea catechins reduce serum cholesterol levels in mild and border-

- line hypercholesterolemia patients. *J. Clin. Biochem. Nutr.*, **33**, 101–111.
- 14) Nanjo, F., Hara, Y. and Kikuchi, Y. (1994) Effects of tea polyphenols on blood rheology in rats fed a high-fat diet. Food Phytochemicals for Cancer Prevention II. Teas, Spices and Herbs. Washington, DC, USA. *American Chemical Society.*, **547**, 76–82.
- 15) Chan, P. T., Fong, W. P., Cheung, Y. L., Huang, Y., Ho, W. K. K. and Chen, Z. Y. (1999) Jasmine green tea epicatechins are hypolipidemic in hamsters (*Mesocricetus auratus*) fed a high fat diet. *J. Nutr.*, **129**, 1094–1101.
- 16) Raederstorff, D. G., Schlachter, M. F., Elste, V. and Weber, P. (2003) Effect of EGCG on lipid absorption and plasma lipid levels in rats. *J. Nutr. Biochem.*, **14**, 326–332.
- 17) Sayama, K., Lin, S., Zheng, G. and Oguni, I. (2000) Effects of green tea on growth, food utilization and lipid metabolism in mice. *In Vivo*, **14**, 481–484.
- 18) Murase, T., Nagasawa, A., Suzuki, J., Hase, T. and Tokimitsu, I. (2002) Beneficial effect of tea catechins on diet-induced obesity: stimulation of lipid catabolism in the liver. *Int. J. Obes.*, **26**, 1459–1464.
- 19) Dulloo, A. G., Seydoux, J. and Girardier, L. (2000) Green tea and thermogenesis: Interactions between catechin-polyphenols, caffeine and sympathetic activity. *Int. J. Obes.*, **24**, 252–258.
- 20) Wu, C. H., Lu, F. H., Chang, C. S., Chang, T. C., Wang, R. H. and Chang, C. J. (2003) Relationship among habitual tea consumption percent body fat, and body fat distribution. *Obes. Res.*, **11**, 1088–1095.
- 21) Tsuchida, T., Itakura, H. and Nakamura, H. (2002) Reduction of body fat in humans by long-term ingestion of catechins. *Progress in Medicine.*, **22**, 2189–2203.
- 22) Asaka, M., Murai, K., Nakanishi, R. and Aoyama, Y. (2000) An increase in antibacterial activity of green tea infusion by heat-treatment. *Nippon Shokuhin Kagaku Kogaku Kaishi*, **47**, 708–715.
- 23) Goto, T., Yoshida, Y., Kiso, M. and Nagashima, H. (1996) Simultaneous analysis of individual catechins and caffeine in green tea. *J. Chromatogr. A.*, **749**, 295–299.
- 24) Health and Welfare Statistics Association (2003) *Annual Statistical Report of National Health, Welfare Guidelines*, vol. 50, p. 90.
- 25) Yamashita, S., Nakamura, T., Shimomura, I., Nishida, M., Yoshida, S., Kotani, K., Kameda-Takemura, K., Tokunaga, K. and Matsuzawa, Y. (1996) Insulin resistance and body fat distribution. *Diabetes Care*, **19**, 287–291.
- 26) Gordon, D. J., Hyde, J., Trost, D. C., Whaley, F. S., Hannan, P. J., Jacobs, D. R. and Ekelund, L. G. (1988) Cyclic seasonal variation in plasma lipid and lipoprotein levels. The Lipid Research Clinics Coronary Primary Prevention Trial Placebo Group. *J. Clin. Epidemiol.*, **41**, 679–689.
- 27) Dollo, A. G., Duret, C. and Rohrer, D. (1999) Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-hr energy expenditure and fat oxidation in humans. *Am. J. Clin. Nutr.*, **70**, 1040–1045.
- 28) Rumper, W., Seale, J., Clevidence, B., Judd, J., Wiley, E., Yamamoto, S., Komatsu, T., Sawaki, T., Ishikura, Y. and Hosoda, K. (2001) Oolong tea increases metabolic rate and fat oxidation in men. *J. Nutr.*, **131**, 2848–2852.
- 29) Acheson, K. J., Zahorska-Markiewicz, B., Pittet, P., Anantharaman, K. and Jequier, E. (1980) Caffeine and coffee: their influence on metabolic rate and substrate utilization in normal weight and obese individuals. *Am. J. Clin. Nutr.*, **33**, 989–997.
- 30) Astrup, A., Toubro S., Cannon S., Hein, P., Breum, L. and Madsen, J. (1990) Caffeine: a double-blind, placebo-controlled study of its thermogenic, metabolic, and cardiovascular effects in healthy volunteers. *Am. J. Clin. Nutr.*, **51**, 759–767.
- 31) Juhel, C., Armand, M., Pafumi, Y., Rosier, C., Vandermander, J. and Lairon, D. (2000) Green tea extract (AR25) inhibits lipolysis of tryglycerides in gastric and duodenal medium in vitro. *J. Nutr. Biochem.*, **11**, 45–51.
- 32) Hauner, H. (2001) Current pharmacological approaches to the treatment of obesity. *Int. J. Obes. Relat. Metab. Disord.*, **25**(Suppl. 1), S102–S106.
- 33) Ikeda, I., Tsuda, K., Suzuki, Y., Kobayashi, M., Unno, T., Tomoyori, H., Goto, H., Kawata, Y., Imaizumi, K., Nozawa, A. and Kakuda, T. (2005) Tea catechins with galloyl moiety suppress postprandial hypertriacylglycerolemia by delaying lymphatic transport of dietary fat in rats. *J. Nutr.*, **135**, 155–159.
- 34) Hurrell, R. F., Reddy, M. and Cook, J. D. (1999) Inhibition of non-haem iron absorption in man by polyphenolic-containing beverages. *Br. J. Nutr.*, **81**, 289–295.