

Anti-obesity Effects of Tea Catechins in Humans

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Abstract : To examine the anti-obesity effects of tea catechins in humans, a trial study using healthy male subjects (27-47 years). Comprising in equal number a low dose catechin (LDC) group ($n=11$) and high dose catechin (HDC) group ($n=12$). The groups were administered catechins at 118.5 mg and 483.0 mg a day for 12 weeks, respectively. At 4 and 12 weeks, effect evaluation was made based on change in weight, body mass index (BMI), waist circumference, body fat ratio and abdominal fat as determined by computed tomography (CT) and triacylglycerol, total cholesterol, free fatty acid, glucose, insulin and total plasminogen activator inhibitor-1 (PAI-1) in serum. In the HDC group, at 12 weeks, weight, BMI, waist circumference, body fat ratio, abdominal fat and total cholesterol, glucose, insulin, PAI-1 in serum were noted to have significantly decreased from values at 0 week. In the LDC group, only weight, BMI and insulin had changed. In the HDC group, BMI had decreased significantly in $25 \leq \text{BMI} \leq 27$ subjects compared to $25 > \text{BMI}$ subjects. In the $25 \leq \text{BMI} \leq 27$ subjects, BMI decreased significantly more in the HDC group. Tea catechins are thus shown here for the first time to have the anti-obesity effects in humans.

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Key words : catechin, human, obesity, BMI, visceral fat

Abstract

We investigated the anti-obesity effects of tea catechins in humans. Healthy men (27-47 years old) were given either a low dose (118.5 mg, n=11) or a high dose (483.0 mg, n=12) of tea catechins for 12 weeks. The effects were evaluated after 4 and 12 weeks based on change in body weight, body mass index (BMI), waist circumference, body fat ratio, abdominal fat measured by computed tomography, and serum concentrations of triglycerides, total cholesterol, free fatty acids, glucose, insulin and total plasminogen activator inhibitor-1 (PAI-1). At the high dose, body weight, BMI, waist circumference, body fat ratio and abdominal fat and serum concentrations of total cholesterol, glucose, insulin and PAI-1 at 12 weeks were significantly lower than at baseline. At the low dose, only body weight, BMI and serum insulin concentration changed. At the high dose, BMI decreased significantly in the obese subjects ($BMI \geq 25$) when compared with the subjects whose body weight was normal ($BMI < 25$). In the obese subjects, the decrease in the BMI was significantly greater in those who took the high dose. These findings show for the first time that tea catechins have anti-obesity effects in humans.

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1. Introduction

Catechin is a general term for flavan-3-ol and is found in many plants as the structural unit of condensed tannins. Tea contains particularly high levels of catechins, which make up 14% to 18% of the dry weight of tea-leaves. The catechins found in tea-leaves include catechin, epicatechin, gallicatechin, epigallicatechin, catechin gallate, epicatechin gallate, gallicatechin gallate and epigallicatechin gallate. Tea catechins are reported to have a variety of physiologic effects, including antioxidant activity,¹ antiviral activity,² inhibition of plaque formation,³ antiallergic effects,⁴ anticancer effects,⁵ radioprotective effects,⁶ antihypertensive activity,⁷ and reduction of blood glucose levels.⁸ Animal studies of the effects of tea catechins on fat metabolism have also shown that oral ingestion of catechins decreases blood concentrations of triglycerides^{9,10} and total cholesterol,¹⁰ reduces fat accumulation in the liver,^{11,12} and inhibits increase in body fat.¹² The only study of the effects of tea catechins on fat metabolism in humans has been a study by Matsumoto et al.¹³ showing that catechins increase blood concentrations of high-density-lipid cholesterol. Dulloo et al. recently reported that a green tea extract promotes energy consumption in animal tissue¹⁴ and in humans,¹⁵ suggesting that green tea extracts may have anti-obesity effects in humans. However, no-one has directly demonstrated that tea catechins actually reduce obesity in humans. In a previous study, we showed that tea catechins have anti-obesity effects in an animal model of obesity, using body weight and visceral fat weight as indicators.¹⁶

The aim of the present study was to investigate the effects of long-term tea catechin intake on obesity and body fat metabolism in humans.

2. Methods

2.1 Test substance

Tea catechins were used as the test substance. The catechins were prepared in accordance with the method of Yayabe et al.¹⁷ and taken as a 500-ml drink. The effects were investigated at a low dose (catechin content: 118.5 mg) and a high dose (catechin content: 483.0 mg). The catechins in each drink were analysed as described by Saijyo et al.¹⁸ and total polyphenols were analysed according to the method of Ikegaya et al.¹⁹ The composition of the catechins is shown in Table 1. The tea catechins used in the study were a mixture of catechin, epicatechin, gallocatechin, epigallocatechin, catechin gallate, epicatechin gallate, gallocatechin gallate and epigallocatechin gallate. The total polyphenol content was 180.0 mg at the low dose and 625.0 mg at the high dose. The caffeine content was 75.0 mg at the low dose and 75.5 mg at the high dose.

Table 1 Catechin Compositions of Test Diets.

	Low dose Catechin	High dose Catechin
Catechin	5.5	6.5
Epicatechin	5.5	8.0
Gallocatechin	22.0	22.0
Epigallocatechin	15.5	17.0
Catechin gallate	4.5	8.0
Epicatechin gallate	7.5	72.0
Gallocatechin gallate	26.0	49.0
Epigallocatechin gallate	32.0	300.5
Total catechin	118.5	483.0
Polyphenols	180.0	625.0
Caffeine	75.0	75.5

mg/500ml

2.2 Subjects and Methods

The study conformed with the spirit of the Declaration of Helsinki and the stipulations of the Kao Corporation Ethics Committee.

The subjects were 23 healthy men who were aged between 27 and 47 years old and ranged from normal weight to obese (grade 1) based on body mass index (BMI) in accordance with the criteria of the Japanese Society for the Study of Obesity.²⁰ Before the test substance was taken, physical measurements were taken and blood chemistry studies were conducted. The subjects were then assigned to two groups such that the physical measurements and test values were virtually the same in the two groups. One group received the low dose of catechins and the other received the high dose. The characteristics of the subjects in each group are shown in Table 2. There were no significant differences between the two groups for any of the variables at baseline.

Table 2 Characteristics of Subjects.

	Low dose Catechin (n=11)	High dose Catechin (n=12)
Age (y)	38.6 ± 1.7	38.7 ± 1.5
Weight (kg)	73.8 ± 2.9	73.0 ± 1.9
Height (cm)	171.9 ± 0.9	173.9 ± 1.8
Body mass index (kg/m ²)	25.0 ± 0.9	24.2 ± 0.6
Waist circumference (cm)	87.8 ± 1.5	87.0 ± 1.1
Body fat ratio (%)	25.0 ± 1.5	24.3 ± 1.3
Total fat area (cm ²)	274.5 ± 18.8	256.8 ± 18.4
Visceral fat area (cm ²)	114.6 ± 12.9	106.9 ± 9.8
Subcutaneous fat area (cm ²)	159.9 ± 8.9	149.8 ± 11.4
Triacylglycerol (mg/100 ml)	135.6 ± 24.3	145.5 ± 16.2
Total cholesterol (mg/100 ml)	217.0 ± 11.3	216.0 ± 9.8
Free fatty acid (mEq/l)	0.38 ± 0.05	0.51 ± 0.07
Glucose (mg/100 ml)	94.9 ± 1.2	96.5 ± 3.5
Insulin (μU/ml)	8.5 ± 1.4	8.5 ± 1.2
Plasminogen activator inhibitor-1 (ng/ml)	31.7 ± 7.2	42.9 ± 9.0

Values are means ± SEM

The subjects were required to take the test substance at each evening meal and to keep a diary showing whether or not they had taken it. At 4 and 12 weeks after dosing was started, blood samples were collected, physical measurements were taken and abdominal computed tomography (CT) was performed and the images were analysed. The physician determined whether any of the blood chemistry values were abnormal during the study period.

Subjects with stable eating habits were selected for the study based on an oral questionnaire conducted beforehand. The subjects were instructed not to change their eating or lifestyle habits after the start of the study, apart from taking the test substance. At completion of the study, eating habits, health status, alcohol intake, smoking and use of medication during the study period were determined by oral questionnaire.

2.3 Collection of blood samples, physical measurements and measurement of body fat ratio

The subjects were required to refrain from consuming alcohol the day before blood samples were taken, to finish their evening meal by 21:00 and to refrain from drinking or eating anything other than water after the evening meal until blood samples had been collected. Blood samples were taken from a vein in the flexor portion of the upper arm and the serum and plasma from the blood samples were used for the blood chemistry studies. Physical measurements comprised height, body weight and waist circumference. The waist circumference was measured at the level of the navel with the subject

standing, as specified in the Japanese Society for the Study of Obesity criteria.²⁰

The body fat ratio of each subject was measured with a body fat meter using the leg impedance method (TBF-401 Tanita Body Fat Analyser, Tanita, Tokyo) at the time the physical measurements were taken.

2.4 Analysis of serum and plasma samples

The concentrations of triglycerides, total cholesterol, free fatty acids, glucose, insulin and total plasminogen activator inhibitor-1 (PAI-1) in the serum and plasma were measured at SRL (Tokyo). Triglycerides, total cholesterol, free fatty acids and glucose were measured by the enzyme method, insulin was measured by radioimmunoassay using two antibodies and total PAI-1 was measured by latex photometric immunoassay.

2.5 Abdominal CT scan

Abdominal CT scans were performed the day before or after physical measurements (Yabuki Clinic: Shiga-gun, Tochigi Prefecture, TCT-300 CT scanner, Toshiba Medical; and Juntendo University Hospital: Bunkyo-ku, Tokyo, Toshiba X-Vision CT scanner, RIAL). Navel-level CT scans were obtained during exhalation in accordance with the criteria of the Japanese Society for the Study of Obesity.²⁰ The total fat area, visceral fat area and subcutaneous fat area of the abdomen were then determined from the CT images using the method described by Tokunaga et al.²¹

2.6 Statistical analysis

The data are reported as the mean \pm standard error of the mean. The values for the two groups at baseline, at 4 weeks and at 12 weeks were compared by paired *t*-test. The significance of differences between the means for the groups was analysed by *t*-test. Differences were considered significant at $P<0.05$.

3. Results

3.1 Test substance intake and change in the eating and lifestyle habits of the subjects during the study period

During the study period, the test substance was taken $93.8 \pm .7\%$ of the time by the subjects overall, $94.6 \pm 2.6\%$ by the low-dose group and $93.0 \pm 2.4\%$ by the high-dose group. There was no significant difference between the low- and high-dose groups. The results of the oral questionnaire at the end of the study also showed that there were no changes in eating habits, health status, alcohol consumption, smoking or use of medication in any of the subjects during the study period. There were no abnormal blood chemistry values in any of the subjects during the study period.

3.2 Changes in physical measurements and body fat ratio

At the low dose, body weight changed by -0.1 kg (-0.17%) at 4 weeks and -0.6 kg (-0.88%) at 12 weeks when compared with baseline. At the high dose, body weight changed by -0.5 kg (-0.72%) at 4 weeks and -1.1 kg

(-1.48%) at 12 weeks. At the low dose, only body weight at 12 weeks was significantly lower than at baseline ($P<0.05$). However, at the high dose, body weight was significantly lower at both 4 weeks ($P<0.05$) and 12 weeks ($P<0.01$).

Table 3 Changes in Rate of Variation in Body Composition (Total).

	Low dose Catechin (n=11)			High dose Catechin (n=12)		
	0 week	4 weeks	12 weeks	0 week	4 weeks	12 weeks
Weight	100	99.83±0.3	99.12±0.4*	100	99.28±0.4*	98.52±0.5**
Body mass index	100	99.83±0.3	99.12±0.4*	100	99.28±0.4*	98.52±0.5**
Waist circumference	100	99.82±0.3	99.32±0.4	100	98.66±0.5*	98.32±0.5**
Body fat ratio	100	99.03±1.6	97.67±1.8	100	97.19±1.9	93.47±1.5***
Total fat area	100	96.91±1.8*	96.78±5.3	100	94.97±3.0	93.29±2.6*
Visceral fat area	100	94.50±4.4	98.73±7.1	100	95.03±5.9	91.33±4.1*
Subcutaneous fat area	100	97.78±1.9	95.24±5.1	100	94.99±2.3*	95.01±3.1

Values are means±SEM

Significantly different from the value at 0 week, * $p<0.05$, ** $p<0.01$, *** $p<0.001$

BMI, waist circumference and body fat ratio at 4 and 12 weeks are expressed as a percentage of the baseline value (Table 3). At both the high and low doses, the BMI, waist circumference and body fat ratio decreased over time when compared with baseline. All three measurements tended to be lower in the high-dose group. At the low dose, none of the values except the BMI were significantly lower than at baseline. At the high dose, however, the BMI and waist circumference at 4 weeks and all of the variables at 12 weeks were significantly lower than at baseline. Changes at 4 and 12 weeks (compared with baseline) were as follows: the BMI changed by $-0.17 \pm 0.3\%$ and $-0.88 \pm 0.4\%$ ($P<0.05$) at the low dose and $-0.72 \pm 0.4\%$ ($P<0.05$) and $1.48 \pm 0.5\%$ ($P<0.01$) at the high dose; the waist circumference changed by $-0.18 \pm 0.3\%$ and $-0.68 \pm 0.4\%$ at the low dose and $-1.34 \pm 0.5\%$ ($P<0.05$) and $1.68 \pm 0.5\%$ ($P<0.01$) at the high dose; and the body fat ratio changed by $-0.97 \pm 1.6\%$ and $-2.33 \pm 1.8\%$ at the low dose and $-2.81 \pm 1.9\%$ and $-6.53 \pm 1.5\%$ ($P<0.001$) at the high dose.

Table 4 Changes in Rate of Variation in Body Composition (BMI <25, 25≤BMI).

	BMI	Low dose Catechin (n=11)			High dose Catechin (n=12)			
		0 week	4 weeks	12 weeks	BMI	0 week	4 weeks	
Weight	<25 (n=5)	100	99.80±0.5	99.20±0.5	<25 (n=5)	100	99.70±0.4	99.90±0.3
	25≤ (n=6)	100	99.90±0.3	99.10±0.6	25≤ (n=7)	100	99.00±0.4*	97.50±0.6**.b
Body mass index	<25 (n=5)	100	99.80±0.5	99.20±0.5	<25 (n=5)	100	99.70±0.4	99.90±0.3
	25≤ (n=6)	100	99.90±0.3	99.10±0.6	25≤ (n=7)	100	99.00±0.4*	97.50±0.6**.b
Waist circumference	<25 (n=5)	100	100.40±0.5	99.20±0.4	<25 (n=5)	100	98.80±0.7	98.80±0.7
	25≤ (n=6)	100	99.30±0.4	99.40±0.8	25≤ (n=7)	100	98.60±0.6*	97.90±0.4**
Body fat ratio	<25 (n=5)	100	98.40±3.1	99.30±3.1	<25 (n=5)	100	100.00±2.2	91.50±1.4**
	25≤ (n=6)	100	99.60±1.8	96.30±2.2	25≤ (n=7)	100	95.20±2.0*	94.90±1.9*
Total fat area	<25 (n=5)	100	99.00±3.1	91.20±11.2	<25 (n=5)	100	97.10±3.3	93.50±2.5
	25≤ (n=6)	100	95.20±2.1*	101.40±3.2	25≤ (n=7)	100	93.40±3.5	93.20±3.6
Visceral fat area	<25 (n=5)	100	96.70±8.7	96.50±15.5	<25 (n=5)	100	99.80±7.5	98.20±3.8
	25≤ (n=6)	100	92.70±4.5	100.60±4.9	25≤ (n=7)	100	91.60±5.3	86.50±5.1**
Subcutaneous fat area	<25 (n=5)	100	99.80±1.0	87.60±9.9	<25 (n=5)	100	94.60±0.6*	89.90±2.2*
	25≤ (n=6)	100	96.10±3.4	101.60±3.5	25≤ (n=7)	100	95.30±4.0	98.70±4.3

Values are means±SEM

Significantly different from the value at 0 week, *p<0.05, **p<0.01

Significantly different from normal body weight subjects (BMI <25) at 12 weeks, #p<0.05

Significantly different from low dose catechin subjects at 12 weeks, b <0.05

Table 4 shows changes in body weight, BMI, waist circumference and body fat ratio when the subjects were divided into a normal body weight group (n=5; BMI: ≥18.5 and <25) and an obese group (grade 1; n=6-7; BMI: ≥25 and <30) based on baseline BMI as specified in the criteria of the Japanese Society for the Study of Obesity.²⁰ At the low dose, there were no significant changes in any of the variables in either the obese group (grade 1) or the normal weight group. At the high dose, there were no significant decreases in any of the variables, except the body fat ratio at 12 weeks, in the normal weight group, but all of the variables were significantly lower at 4 and 12 weeks in the obese group (grade 1) when compared with baseline. In the subjects in the obese group (grade 1) given the high dose, the BMI was 25.64 ± 0.21 kg/m² at baseline, 25.39 ± 0.25 kg/m² at 4 weeks (-1.0%, significantly different from baseline at P<0.05) and 25.01 ± 0.29 kg/m² at 12 weeks (-2.5%, significantly different from baseline at P<0.01), indicating a decrease with time. In the subjects in the normal weight group who received the high dose, the BMI was 22.18 ± 0.97 kg/m² at baseline,

22.08 ± 0.90 kg/m² at 4 weeks (-0.4%, ns) and 22.16 ± 0.97 kg/m² at 12 weeks (-0.1%, ns). There was therefore no significant decrease in the BMI with time in the subjects whose body weight was normal. The BMI at 12 weeks differed significantly between the obese group and the normal weight group given the high dose ($P<0.05$). The body weight and BMI in the obese group and the body fat ratio in the normal weight group at 12 weeks also differed significantly between the low and high doses ($P<0.05$).

3.3 Changes in amount of abdominal fat determined by CT scan

Table 3 shows changes in the relative amount of abdominal fat determined from the navel-level scans. At the low dose, total fat area, visceral fat area and subcutaneous fat area tended to be lower, except for total fat area at 4 weeks, but no significant differences were noted. At the high dose, however, all of the variables were lower than at the low dose and the subcutaneous fat area at 4 weeks ($P<0.05$) and the total fat area and visceral fat area at 12 weeks ($P<0.05$) were significantly lower than at baseline.

Table 4 shows changes in the amount of abdominal fat as a percentage of the baseline values when the subjects were divided into a normal body weight group (n=5; BMI: ≥18.5 and <25) and an obese group (grade 1; n=6-7; BMI: ≥25 and <30) based on the BMI at baseline and as specified in the Japanese Society for the Study of Obesity criteria.²⁰ At the low dose, the only significant decrease relative to baseline was the total

fat area in the obese group at 4 weeks ($P<0.05$). At the high dose, however, the visceral fat area in the obese group at 12 weeks ($P<0.05$) and the subcutaneous fat area in the normal body weight group at 4 and 12 weeks ($P<0.05$) were significantly lower than at baseline. The visceral fat area at 12 weeks also differed significantly between the obese subjects given the low dose and the obese subjects given the high dose ($P<0.05$ respectively).

3.4 Changes in blood chemistry values

Table 5 Changes in Rate of Variation in Serum Metabolic Indexes.

	Low dose Catechin (n=10)			High dose Catechin (n=12)		
	0 week	4 weeks	12 weeks	0 week	4 weeks	12 weeks
Triacylglycerol	100	125.56±13.0	129.17±15.5	100	91.18± 9.9	102.84± 6.4
Total cholesterol	100	98.45± 3.3	95.81± 3.3	100	96.41± 2.5	94.58± 1.2***
Free fatty acid	100	150.96±27.0*	119.44±15.8	100	113.91±13.6	130.40±21.9*
Glucose	100	95.45± 2.3*	97.62± 1.9	100	96.61± 1.9*	96.82± 1.6*
Insulin	100	100.84± 8.6	88.51± 6.3*	100	96.21± 8.9	90.78± 7.6*
Plasminogen activator inhibitor-1	100	107.37±18.6	114.75±22.4	100	83.63±16.1	77.63± 9.5*

Values are means±SEM

Significantly different from the value at 0 week, * $p<0.05$, *** $p<0.001$
Significantly different from low dose catechin subjects at 12 weeks, b <0.05

Table 5 shows the blood chemistry values at 4 and 12 weeks expressed as a percentage of the baseline values. At the high dose, glucose at 4 weeks ($P<0.05$) and total cholesterol ($P<0.001$), glucose ($P<0.05$), insulin ($P<0.05$) and PAI-1 ($P<0.05$) at 12 weeks were significantly lower than at baseline. Total cholesterol decreased from 216.0 ± 9.8 mg/100 ml at baseline to 203.9 ± 8.9 mg/100 ml at 12 weeks; glucose decreased from 96.5 ± 3.5 mg/100 ml at baseline to 93.0 ± 2.5 mg/100 ml at 12 weeks; insulin decreased from 8.5 ± 1.2 μ U/ml at baseline to 7.2 ± 0.9 μ U/ml at 12 weeks; and PAI-1 decreased from 42.9 ± 9.0 ng/ml at baseline to 29.3 ± 4.5 ng/ml at 12 weeks.

At the low dose, the free fatty acid concentration at 4 weeks was significantly higher than at baseline ($P<0.05$) and the glucose concentration at 4 weeks ($P<0.05$) and the insulin concentration at 12 weeks ($P<0.05$) were significantly lower than at baseline. The serum concentration of free fatty acids at 12 weeks (0.60 ± 0.1 mEq/l) was significantly higher at the high dose than at the low dose but was within the normal range. The data from one of the subjects in the low-dose group were not included in the totals because this subject consumed alcohol the day before blood samples were taken.

4. Discussion

We investigated the anti-obesity effects of catechins in humans, using body weight, BMI, waist circumference, body fat ratio and the results of abdominal CT image analysis as indicators, and also determined whether catechins reduce blood concentrations of total cholesterol, glucose, insulin and PAI-1. This is the first study to investigate the anti-obesity effects of catechins in humans. It has been suggested that the anti-obesity effects of tea extracts may be due to caffeine as well as to catechins.²²⁻²⁶ However, the caffeine content of the catechins used in the present study was virtually the same for both the high and low doses, suggesting that the differences in efficacy were attributable to the catechin content rather than to caffeine.

BMI is used worldwide as a criterion for obesity²⁷ and the Japanese Society for the Study of Obesity has also

specified criteria for obesity based on BMI.²⁰ The dose-dependent decrease in BMI seen in our subjects over time therefore shows that tea catechins have anti-obesity effects in humans (Table 3). In the Japanese population, a BMI of 22 is considered normal and is associated with the lowest incidence of concurrent disease. The incidence of concurrent disease increases in obese individuals with a high BMI (≥ 25) and in underweight individuals with a low BMI (< 18.5).^{20,28} In our study, catechins administered at a high dose had significant anti-obesity effects in the subjects who were obese (grade 1; BMI: ≥ 25 and < 30) but minimal effect in the subjects whose body weight was normal (BMI: ≥ 18.5 and < 25) (Table 4). This not only shows that tea catechins are effective in reducing obesity but also demonstrates that individuals of normal body weight are at little risk of becoming underweight (BMI < 18.5) as a result of catechin consumption, another observation suggesting that tea catechins are safe.

Obesity is classified into visceral fat obesity and subcutaneous fat obesity based on body fat distribution. Visceral fat obesity is a risk factor for lifestyle-related diseases such as diabetes mellitus, hyperlipidemia, hypertension and arteriosclerosis.^{20,21,29} Our results showed that administration of tea catechins at a high dose resulted in a significant decrease in waist circumference, a diagnostic indicator of visceral fat obesity,²⁰ at 4 and 12 weeks and a significant decrease in the visceral fat area at 12 weeks (Table 3). We also saw a significant reduction in the serum concentration of PAI-1 (Table 5), an adipocytokine produced by adipose tissue that is strongly correlated

with visceral fat levels.³⁰ These results show that intake of tea catechins reduces visceral fat obesity. This, and the fact that tea catechin intake significantly reduced the serum concentrations of total cholesterol, glucose and insulin at 12 weeks (Table 5), strongly suggests that catechins would be effective for reducing obesity and preventing lifestyle-related diseases. However, daily catechin intake of greater than 118.5 mg is required to reduce obesity and visceral fat obesity in humans, since our results showed no significant change in body weight, BMI, waist circumference or visceral fat area in obese subjects (grade 1; BMI: ≥25 and <30) who received the low dose.

Accumulation of body fat is determined by the balance between energy intake and expenditure. Studies of the mechanisms by which tea catechins reduce energy intake by inhibiting fat and sugar absorption have shown that tea catechins increase excretion of total fat and cholesterol into the feces in rats³¹ and decrease sugar absorption through inhibition of α-amylase and sucrase in the gastrointestinal tract.⁸ Ikeda et al.³² showed that tea catechins inhibit absorption of cholesterol and triglycerides and that the reduction in cholesterol absorption is the result of decreased solubilisation of cholesterol in micelles. The anti-obesity effects and reduction in blood concentrations of total cholesterol and glucose produced by tea catechins in our study may have been partly attributable to these mechanisms.

Many studies have confirmed that the absorption of catechins into the body after oral intake in humans is related to blood and urinary concentrations.³³⁻³⁸ Kao et

al.^{39,40} recently showed that intraperitoneal administration of epigallocatechin gallate in rats is followed by an increase in blood concentrations and inhibits weight gain. Borchardt et al.⁴¹ also reported that tea catechins inhibit activity of catechol-O-methyltransferase, a catecholamine-degrading enzyme involved in fat metabolism. Dulloo et al. showed that a green tea extract promotes fat oxidation in animal tissue¹⁴ and in humans¹⁵ by increasing energy expenditure and decreasing the respiratory quotient and suggested that this may be due to inhibition of catechol-O-methyltransferase activity by tea catechins. The results of these studies strongly suggest that the anti-obesity effects of tea catechins may be attributable not only to reduced energy intake as a result of inhibited fat and sugar absorption in the gastrointestinal tract, but also to increased energy expenditure due to promotion of metabolism after tea catechins are absorbed into the body.

The findings of the present study show that tea catechins have anti-obesity effects in humans and suggest that intake of catechins may assist in the prevention and treatment of lifestyle-related diseases for which obesity and visceral fat obesity are risk factors.

- References**
- Yoshino, K., Hara, Y., Sano, M. & Tomita, I. (1994) *Biol. Pharm. Bull.*, **17**, 146-149.
 - Nakayama, M., Suzuki, K., Toda, M., Okubo, S., Hara, Y. & Shimamura, T. (1993) *Antiviral Research*, **21**, 289-299.
 - Hattori, M., Kusumoto, I. T., Namba, T., Ishigami, T. & Hara, Y. (1990) *Chem. Pharm. Bull.*, **38**, 717-720.
 - Kakegawa, H., Mitsumoto, H., Endo, K., Sato, T., Nonaka, G. & Nishioka, I. (1985) *Chem. Pharm. Bull.*, **33**, 5079-5082.
 - Katiyar, S.K. & Mukhtar, H. (1996) *Int. J. Oncol.*, **8**, 221-238.
 - Uchida, S., Ozaki, M., Suzuki, K. & Shikita, M. (1992) *Life Sci.*, **50**, 147-152.
 - Henry, J.P. & Stephen-Larson, P. (1984) *Hypertension*, **6**, 437-444.
 - Matsumoto, N., Ishigaki, F., Ishigaki, A., Iwashima, H. & Hara, Y. (1993) *Biosci. Biotech. Biochem.*, **57**, 525-527.
 - Nanjo, F., Hara, Y. & Kiuchi, Y. (1994) *ACS Symp. Ser.*, **547**, 76-82.
 - Chan, P.T., Fong, W.P., Cheung, Y.L., Huang, Y., Ho, W.K.K. & Chen, Z.Y. (1999) *J. Nutr.*, **129**, 1094-1101.
 - Chaudhari, P.N. & Hatwalne, V.C. (1977) *Ind. J. Nutr. Diet.*, **14**, 136-139.
 - Muramatsu, K., Fukuyo, M. & Hara, Y. (1986) *J. Nutr. Sci. Vitaminol.*, **32**, 613-622.
 - Ikeda, I., Imasato, Y., Sasaki, E., Nakayama, M., Nagao, H., Takeo, T., Yayabe, F. & Sugano, M. (1992) *Biochimica et Biophysica Acta*, **1127**, 141-146.
 - He, Y. H. & Kies, C. (1994) *Plant Foods Hum. Nutr.*, **46**, 221-229.
 - Nakagawa, K., Okuda, S. & Miyazawa, T. (1997) *Biosci. Biotechnol. Biochem.*, **61**, 1981-1985.
 - Pietta, P.G., Simonetti, P., Gardana, C., Brusamolino, A., Morazzoni, P. & Bombardelli, E. (1998) *Biofactors*, **8**, 111-118.
 - Pietta, P., Simonetti, P., Gardana, C., Brusamolino, A., Morazzoni, P. & Bombardelli, E. (1998) *Biofactors*, **8**, 111-118.
 - Ishigaki, A., Tonooka, F., Matsumoto, N. & Hara, M. (1991) *Proc. Int. Sympo. On Tea Science*, **309**-313.
 - Matsumoto, N. & Hara, Y. (1995) *Syokuhinkogyo*, **3**, 81-84.
 - Dulloo, A.G., Seydoux, J., Girardier, L., Chantre, P. & Vandermander, J. (2000) *Int. J. Obes.*, **24**, 252-258.
 - Dulloo, A.G., Duret, C., Rohrer, D., Girardier, L., Mensi, N., Fathi, M., Chantre, P. & Vandermander, J. (1999) *Am. J. Clin. Nutr.*, **70**, 1040-1045.
 - Meguro, S., Mizuno, T., Onizawa, K., Kawasaki, K., Nakagiri, H., Komine, Y., Suzuki, J., Matsui, Y., Hase, T., Tokimitsu, I., Shimasaki, H. & Itakura, H. *J. Oleo Science*, in press.
 - Yayabe, F., Kinugasa, H., & Takeo, T. (1989) *Nippon Nogeikagaku Kaishi*, **63**, 845-847.
 - Saijyo, R. & Takeda, Y. (1999) *Nippon Shokuhin Kagaku Kogaku Kaishi*, **46**, 138-147.
 - Ikegaya, K., Takayanagi, H. & Anan, T. (1990) *Chagyousenkyuhoukoku*, **71**, 43-74.
 - Matsuzawa, Y., Inoue, S., Ikeda, Y., Sakata, T., Saito, Y., Sato, Y., Shirai, K., Ohno, M., Miyazaki, S., Tokunaga, K., Fukagawa, K., Yamanouchi, K. & Nakamura, T. (2000) *J. Jap. Soc. Study Obes.*, **6**, 18-28.
 - Tokunaga, K., Matsuzawa, Y., Ishikawa, K. & Tarui, S. (1983) *Int. J. Obes.*, **7**, 437-445.
 - Nilsson-Ehle, P. (1980) *Annu. Rev. Biochem.*, **49**, 667-693.
 - Holland, M.A., Arch, J.R.S., Phil, D. & Cawthorne, M.A. (1981) *Am. J. Clin. Nutr.*, **34**, 2291-2294.
 - Spindel, E.R., Wurtman, R.J., McCall, A., Carr, D.B., Conlay, L. & Arnold, M.A. (1984) *Clin. Pharmacol. Ther.*, **36**, 402-407.
 - Yoshioka, K., Yoshida, T., Kamanaru, K., Hiraoka, N. & Kondo, M. (1990) *J. Nutr. Sci. Vitaminol.*, **36**, 173-178.
 - Han, L-K., Takaku, T., Li, J., Kimura, Y. & Okuda, H. (1999) *Int. J. Obes.*, **23**, 98-105.
 - WHO/NUT/NCD (1998) Report of a WHO Consultation on Obesity: Obesity-preventing and managing the global epidemic.
 - Yoshiike, N., Nishi, N., Matsushima, S., Itoh, C., Ikeda, Y., Kashihara, H., Yoshinaga, H., Ogura, H., Komine, S., Sato, Y., Sato, N., Sasaki, Y., Fujioka, S., Oku, J., Amemiya, T., Sakata, T. & Inoue, S. (2000) *J. Jap. Soc. Study Obes.*, **6**, 4-17.
 - Fujioka, S., Matsuzawa, Y., Tokunaga, K. & Tarui, S. (1987) *Metabolism*, **36**, 54-59.
 - Shimomura, I., Funahashi, T., Takahashi, M., Maeda, K., Kotani, K., Nakamura, T., Yamashita, S., Miura, M., Fukuda, Y., Takemura, K., Tokunaga, K. & Matsuzawa, Y. (1996) *Nature Medicine*, **2**, 800-803.
 - Yang, C.S., Chen, L., Lee, M.J., Balentine, D., Kuo, M.C. & Schantz, S.P. (1998) *Cancer Epidemiol. Biomarkers Prev.*, **7**, 351-354.
 - Li, C., Lee, M.J., Sheng, S., Meng, X., Prabhu, S., Winnik, B., Huang, B., Chung, J.Y., Yan, S., Ho, C.T. & Yang, C.S. (2000) *Chem. Res. Toxicol.*, **13**, 177-184.
 - Kao, Y.H., Hipakka, R.A. & Liao, S. (2000) *Endocrinology*, **141**, 980-987.
 - Kao, Y.H., Hipakka, R.A. & Liao, S. (2000) *Am. J. Clin. Nutr.*, **72**, 1232-1233.
 - Borchardt, R.T. & Huber, J.A. (1975) *J. Med. Chem.*, **18**, 120-122.