Effects of Intake of a Mixture of Thiamin, Arginine, Caffeine, and Citric Acid on Adiposity in Healthy Subjects with High Percent Body Fat

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We assessed the effects of intake of thiamin, arginine, caffeine, and citric acid (TACC) on lipid metabolism in healthy subjects. Thirty-one subjects with high percent body fat (≥ 25.0%) were randomly assigned to a 12-wk intervention with daily intake of TACC-supplemented tea (1.1, 1240, 52, and 540 mg, respectively; n = 16) or control tea (n = 15). The percent body fat decreased significantly during the intervention in both groups, especially in the TACC group. A percentage decrease in triceps skinfold was significantly greater in the TACC group than in the control group. The decrease in abdominal visceral fat in obese subjects was significantly greater in the TACC group than in the control group. Serum triglyceride was significantly lower during intervention than that during the non-intervention period in the TACC group. These results suggest that TACC may be effective in reducing body fat in obese subjects.

Key words: thiamin; arginine; caffeine; citric acid; human obesity

Obesity has become prevalent in industrialized countries as a result of changes in lifestyle, especially in eating habits. It is known to be associated with a number of serious medical complications such as non-insulin dependent diabetes mellitus (NIDDM), hyperlipidemia, hypertension, and cardiovascular disease.1,2 Therefore, prevention and treatment of obesity are relevant to health promotion.

Various food components have been reported to influence lipid metabolism and to be effective in the prevention and treatment of obesity.5-7 For example, thiamin (vitamin B1) is essential for energy metabolism. Intake of arginine is known to stimulate secretion of glucagon,8,9 which directly increases the lipolysis of human adipose tissue.10 Caffeine promotes lipolysis of adipose tissue, and in rodents, in vivo caffeine treatment has been shown to decrease body weight in association with a reduction in fat mass through an increase in energy expenditure.11,12 Elevation of the citric acid concentration in muscle may contribute to increased use of intramuscular triglyceride (TG) or extramuscular free fatty acids (or both) at rest and at the beginning of exercise.13 Taking these findings into account, we have developed a mixture of thiamin, arginine, caffeine, and citric acid (TACC) which are useful for reduction of body fat.

We have previously demonstrated that TACC is effective in reducing adipose tissue mass as well as improving disorders in lipid metabolism in non-insulin dependent diabetes KK mice.14 Administered alone, both arginine and caffeine, the main components of TACC, almost completely suppressed the increase of lipogenesis in the liver in fasted-refed mice. Each of these two showed an anti-obesity action in KK mice with diet-induced obesity, but the action was more potent when arginine and caffeine were mixed, and much greater with TACC. Moreover, the hepatic TG content and the plasma insulin concentration were significantly decreased by the intake of TACC in KK mice.14

Caffeine has been reported to promote adipocyte lipolysis not only in mice15 but also in humans.16 Arginine has also been shown to stimulate the secretion of glucagon in humans,17 which leads to the increase of lipolysis in adipose tissue. Therefore, TACC is fully expected to manifest an anti-obesity effect in humans. In this study, we investigated the effects of 12-wk ingestion of TACC on body fat and on the serum lipid profile in healthy subjects with high percent body fat (≥ 25.0%).

Subjects and Methods

Subjects. Twenty-six men and 5 women aged 24–59 y with high percent body fat (≥ 25.0%) and high serum TG levels (1.36 ≤ TG in mmol/l < 3.39) were
Table 1. Descriptive Characteristics of Subjects at Baseline

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>TACC</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender; Male</td>
<td>12</td>
<td>13</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>43.0±3.1</td>
<td>42.8±2.7</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Height, cm</td>
<td>165.2±2.5</td>
<td>167.9±1.9</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>75.1±3.2</td>
<td>75.2±3.0</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.4±0.5</td>
<td>26.5±0.7</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>% Body fat</td>
<td>31.2±1.4</td>
<td>30.2±1.3</td>
<td>&gt;0.10</td>
</tr>
</tbody>
</table>

1 Values represent means±SEM.

Table 2. Composition of TACC-Supplemented Tea

<table>
<thead>
<tr>
<th></th>
<th>Added</th>
<th>Measured</th>
<th>Added</th>
<th>Measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingredient</td>
<td>mg/4 g of powdered tea</td>
<td></td>
<td>mg/4 g of powdered tea</td>
<td></td>
</tr>
<tr>
<td>Thiamin</td>
<td>ND</td>
<td>1.2</td>
<td>ND</td>
<td>1.1</td>
</tr>
<tr>
<td>Arginine</td>
<td>0.1</td>
<td>1260.0</td>
<td>1.1</td>
<td>1240.0</td>
</tr>
<tr>
<td>Caffeine</td>
<td>ND</td>
<td>30.5</td>
<td>ND</td>
<td>52.0</td>
</tr>
<tr>
<td>Citric acid</td>
<td>ND</td>
<td>525.0</td>
<td>ND</td>
<td>544.0</td>
</tr>
<tr>
<td>Green tea extract</td>
<td></td>
<td>1300.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brown rice tea extract</td>
<td></td>
<td>500.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barley tea extract</td>
<td>1800.0</td>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactose</td>
<td>1000.0</td>
<td>383.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dextrin</td>
<td>1200.0</td>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy, kJ</td>
<td>64.9</td>
<td>61.1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 ND = not detected.

included in the study. Before inclusion, the subjects underwent a screening examination (4 wk before randomization), which comprised medical history taking, anthropometric measurements, and routine laboratory tests. The examination was done to ensure that the subjects were in good health, were using no medication or health food known to affect lipid metabolism, and had no history of diabetes, hypercholesterolemia, hepatopathy, or nephropathy.

The subjects were randomly assigned to either a TACC group (n = 16) or to a control group (n = 15). The sex, age, and anthropometric measurements of the subjects at baseline are given in Table 1 (one subject in the control group withdrew before the beginning of intervention). A total of 29 subjects completed the trial, 16 in the TACC group and 13 in the control group. Two subjects dropped out because of a change of address.

Approval of the protocol was obtained from Kunwakai Aiwa Clinic Institutional Review Board (Saitama, Japan), and the study was conducted in agreement with the Declaration of Helsinki (5th version). The procedures had been fully explained to the subjects and written informed consent was obtained from each subject before the start of the study.

Study design. The study was conducted as a 16-wk, parallel-group, randomized controlled trial. After random assignment, the subjects in the TACC group each day consumed 1.1 mg thiamin, 1240 mg arginine, 52 mg caffeine and 540 mg citric acid in the tea provided, while those in the control group received no such supplements in their tea. The mixing ratio of TACC adopted in this study was selected on the basis of the results of the animal experiments in which TACC showed a significant anti-obesity action. Dietary-intervention period set for 12 wk thereafter a 4-wk wash-out period by which carry-over effects of TACC were verified. The subjects were not informed as to which group they belonged. Physical characteristics and biochemical profiles were measured every 4 wk. Abdominal fat distribution and dietary intake were assessed at baseline and at the end of the intervention. The subjects were instructed not to change their dietary habits or physical activity patterns during the study. To encourage compliance with the study protocol, the subjects kept a brief daily record of their food intake and activity patterns during the study.

Intervention. TACC was given to the subjects as a constituent of powdered tea. The composition of the TACC-supplemented powdered tea and control powdered tea is shown in Table 2. The green tea extract and brown rice tea extract were selected as main components of the TACC-supplemented tea to mask the flavor of TACC, especially arginine. Since green tea extract and brown rice extract contain caffeine, we selected barley tea extract, which contains no caffeine, as a main component of the control tea to minimize the effect of control tea on lipid metabolism. Lactose and dextrin were used as diluting agents. Thiamin mononitrate, a food additive, was purchased from BASF Takeda Vitamins (Tokyo, Japan). Arginine was purchased from Kyowa Hakko (Tokyo, Japan). Caffeine, a more than 98.5% pure extract from coffee beans, was purchased from Shiratori Pharmaceutical (Chiba, Japan). Citric acid was purchased from ADM Far East (Tokyo, Japan). The extracts of green tea, brown rice tea, and barley tea were obtained from Sato Food Industries (Aichi, Japan). The subjects were instructed to consume one of the powdered teas (depending on the group to which they were assigned) every morning at a dose of 4 g/d during the intervention period. Each powdered tea was dissolved in 100–150 ml of cold or hot water just before intake.

Dietary intake and walking steps. The subjects were instructed to continue with their habitual diets during the study and to record the contents of meals and snacks in a diet diary for 3 consecutive days just before the beginning of the intervention and for 3 consecutive days just before its end. As verification
of their records, the subjects were instructed to photograph their meals during these periods. The calories of meals and snacks recorded in the diet diary were calculated using the Healthy Diet III software (Tokyo Shoseki, Tokyo, Japan). The subjects were also instructed to continue with their physical activity patterns during the study and to record walking steps by pedometer (Hello-walk 5631, Tanita, Tokyo, Japan) for 3 consecutive days just before the beginning and the end of the intervention.

**Measurements of body fat.** Skinfold thickness was measured at triceps and subcapular on the right side of the body with skinfold calipers (Digital body fat scale, Mitutoyo Corporation, Kanagawa, Japan). For each site, skinfold thickness was adopted as the mean of three measurements in each subject. Percent body fat was assessed by a bioelectric impedance method with a body fat analyzer (BC-118, Tanita). The body impedance was measured through eight polar electrodes, by putting the soles of the feet on two of the electrodes and by holding the grips fitted with two of the electrodes. This measurement was done every 4 wk.

Abdominal visceral and subcutaneous fat areas were assessed by computed tomography scanning (CT scan, X Vision Real, Toshiba Medical, Tokyo, Japan) at the umbilical level. CT scanning was done by Kasukabe Shuwa Hospital (Saitama, Japan) at the baseline and at the end of the intervention.

**Laboratory tests.** Blood and urinary samples were collected from subjects who fasted overnight. The subjects were instructed not to consume alcoholic beverages on the day before the analyses. Serum lipids (TG, total cholesterol, and HDL cholesterol) were analyzed enzymatically by SRL (Tokyo, Japan) using a Hitachi Automatic Analyzer 7170 (Hitachi, Ibaraki, Japan) every 4 wk. Serum leptin was measured by SRL using a commercially available radioimunoassay kit (Linco Research, St Charles, MO) every 4 wk. For safety evaluation, serum chemistry (total protein, albumin, total bilirubin, glutamic oxaloacetic transaminase, glutamic-pyruvic transaminase, alkaline phosphatase, lactate dehydrogenase, γ-glutamyl transpeptidase, creatine phosphokinase, uric acid, blood urea nitrogen, creatinine, blood glucose, non-esterified fatty acid, phospholipid), hematological features (red blood cells, white blood cells, platelets, hemoglobin, hematocrit) and urine (occult blood, urinary glucose, urinary protein) were determined by Aiwa Clinic (Saitama, Japan) at the screening examination and at the end of the intervention. At the same time points, serum iron, total iron-binding capacity, unsaturated iron-binding capacity, ferritin, and transferrin were examined by SRL, also for the sake of safety.

**Statistical analyses.** Values were expressed as means ± SEM. All statistical analyses were done using Dr. SPSS software version 8.01 (SPSS Japan, Tokyo, Japan). Comparisons between the baseline and each time point were done by the paired Student’s t-test within each group. Comparisons of percentage changes from the baseline were done by Student’s t-test between groups. These intragroup and intergroup comparisons for body fat measurements were done on all subjects. Analysis of the correlation between BMI at baseline and changes from the baseline in body fat measurements were done using Pearson’s correlation coefficient. The intragroup and intergroup comparisons for body fat measurements in which changes from baseline were positively correlated with the BMI were done after stratification of subjects by BMI (<27.0 or ≥27.0). The Mann-Whitney U test was used for comparisons between the groups on the stratified subjects. Values of serum lipids and leptin in the TACC group were normalized using the mean value of the control group at the corresponding time point to compensate for seasonal variation, and comparisons between the normalized mean value during the non-intervention period and that during the intervention period were done by the paired Student’s t-test within TACC group. The significance level was set at P<0.05.

**Results**

**Background**

Of the 80 persons who underwent a screening examination, 31 were included in the study. The 31 subjects were randomly assigned to 1 of 2 groups: 15 received control powdered tea and 16 received TACC-supplemented powdered tea. In the control group, 2 subjects did not complete the study because of a change of address, one having withdrawn before the intervention, and the other, after wk 8 of the intervention. The data of the former subject was eliminated from the study, while that of the latter (until wk 8) was used in the analysis. There were no significant differences in baseline values of height, weight, BMI, or percent body fat, or in any demographic variable such as gender or age (Table 1). No side effects were recognized in either group during the study, after analyses of serum chemistry, hematological features, and urine contents (data not shown).

**Calorie intake and walking steps**

Mean calorie intake for 3 d, just before the beginning of the intervention and just before the end of the intervention, showed no difference either between groups or between time points (Means ± SEM, control group: 8836.1 ± 315.9 and 8682.0 ± 543.5 kJ/d, TACC group: 8699.4 ± 503.3 and 8517.4 ± 515.7 kJ/d, respectively). There was also no difference either between groups or between time points in
walking steps for the 3 d (data not shown). Moreover, the subjects seemed not to change their dietary habits or physical activity patterns during the study, as judged from their brief daily records of food intake and activity patterns.

Body fat analysis on all subjects
Percent body fat significantly decreased at wk 8 and 12 of the intervention in the control group \( (P = 0.008 \) and 0.011, respectively), and at wk 12 in the TACC group \( (P < 0.001) \) (Table 3). There was also no difference in its percentage change between the groups at wk 12 of the intervention. However, the proportion of the subjects whose body fat had shown decreases was significantly higher in the TACC group \( (16/16 \) subjects) than in the control group \( (8/13 \) subjects) at wk 12 \( (P = 0.011 \) by chi square test).

Triceps skinfold thickness did not change during the intervention period in the control group, but it was significantly decreased in the TACC group at wk 4, 8, and 12 \( (P = 0.003, 0.027 \) and 0.012, respectively). Percentage decrease from the baseline in the triceps skinfold thickness was significantly greater in the TACC group than in the control group at wk 12 of the intervention \( (P = 0.038) \) (Table 3). Subscapular skinfold thickness in the control group was significantly increased \( (P = 0.037) \) at wk 4 of the intervention, but did not change in the TACC group during the intervention period (Table 3).

Abdominal visceral and subcutaneous fat areas did not show any differences within or between groups after the intervention (Table 4).

### Table 3.  Effects of TACC on Percent Body Fat and Skinfold Thicknesses

<table>
<thead>
<tr>
<th>wk</th>
<th>Control group (n=13 or 14)</th>
<th>TACC group (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( P ) values (vs. baseline)</td>
<td>Percentage change from baseline</td>
</tr>
<tr>
<td>0</td>
<td>31.2 ± 1.4</td>
<td>-3.0 ± 1.9</td>
</tr>
<tr>
<td>4</td>
<td>30.2 ± 1.4</td>
<td>&gt; 0.10</td>
</tr>
<tr>
<td>8</td>
<td>29.9 ± 1.3</td>
<td>0.008</td>
</tr>
<tr>
<td>12</td>
<td>29.7 ± 1.5</td>
<td>0.011</td>
</tr>
<tr>
<td>16</td>
<td>29.3 ± 1.5</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

1 Values represent means ± SEM.

2 The number of subjects in control group was 14 until wk 8.

### Table 4.  Effects of TACC on Abdominal Fat Areas

<table>
<thead>
<tr>
<th>wk</th>
<th>Control group (n=13)</th>
<th>TACC group (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( P ) values (vs. baseline)</td>
<td>Percentage change from baseline</td>
</tr>
<tr>
<td>0</td>
<td>309.6 ± 14.7</td>
<td>0.2 ± 2.8</td>
</tr>
<tr>
<td>12</td>
<td>310.5 ± 17.1</td>
<td>&gt; 0.10</td>
</tr>
<tr>
<td>0</td>
<td>138.9 ± 8.9</td>
<td>0.2 ± 2.8</td>
</tr>
<tr>
<td>12</td>
<td>143.7 ± 12.0</td>
<td>&gt; 0.10</td>
</tr>
<tr>
<td>0</td>
<td>170.7 ± 12.6</td>
<td>0.2 ± 2.8</td>
</tr>
<tr>
<td>12</td>
<td>166.8 ± 12.4</td>
<td>&gt; 0.10</td>
</tr>
</tbody>
</table>

1 Values represent means ± SEM.
the TACC group, decreases in abdominal fat at wk 12 of the intervention were positively correlated with the baseline BMI ($r=0.702$ and $P=0.002$), whereas those correlations were not found either in percent body fat or in triceps or subscapular skinfold thickness (Fig. 1). In the abdominal fat, the decreases were positively correlated with the BMI in both visceral ($r=0.567$, $P=0.022$) and subcutaneous ($r=0.703$, $P=0.002$) fat areas. However, changes in the measurements of body fat did not correlate with the BMI in the control group. Therefore, abdominal fat may have been effectively decreased in obese subjects in the TACC group.

To confirm this supposition, the effects of TACC on abdominal fat were analyzed in the stratified subjects by BMI at baseline ($<27.0$ or $\geq27.0$). In subjects with BMI $\geq27.0$, abdominal total, visceral, and subcutaneous fat areas were significantly

![Image: Correlation between BMI at the Baseline and Changes from the Baseline in Body Fat Measurements at wk 12 of the Intervention Period.](image)

**Fig. 1.** Correlation between BMI at the Baseline and Changes from the Baseline in Body Fat Measurements at wk 12 of the Intervention Period. Correlation analysis was done using Pearson’s correlation coefficient. *Significant correlation for the TACC group.

**Table 5.** Effects of TACC on Abdominal Fat Areas in Obese Subjects with BMI $\geq27.0$

<table>
<thead>
<tr>
<th>BMI $\geq27.0$</th>
<th>Control group</th>
<th>TACC group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Abdominal fat areas, Total, cm²</td>
<td>0.289 ± 0.177</td>
<td>0.283 ± 0.202</td>
</tr>
<tr>
<td>Visceral, cm²</td>
<td>0.148 ± 0.156</td>
<td>0.141 ± 0.173</td>
</tr>
<tr>
<td>Subcutaneous, cm²</td>
<td>0.141 ± 0.173</td>
<td>0.142 ± 0.157</td>
</tr>
<tr>
<td>BMI $&lt;27.0$</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Abdominal fat areas, Total, cm²</td>
<td>0.321 ± 0.208</td>
<td>0.324 ± 0.215</td>
</tr>
<tr>
<td>Visceral, cm²</td>
<td>0.133 ± 0.111</td>
<td>0.142 ± 0.139</td>
</tr>
<tr>
<td>Subcutaneous, cm²</td>
<td>0.188 ± 0.147</td>
<td>0.182 ± 0.159</td>
</tr>
</tbody>
</table>

*Values represent means ± SEM.
Table 6. Effects of TACC on Serum Components

<table>
<thead>
<tr>
<th></th>
<th>Control group (n = 13 or 14)</th>
<th>TACC group (n = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>wk</td>
<td>P values (%)</td>
</tr>
<tr>
<td>Blood parameters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglyceride, mmol/l</td>
<td>0.167±0.17</td>
<td>2.00±0.17</td>
</tr>
<tr>
<td></td>
<td>4 2.30±0.34</td>
<td>0.013</td>
</tr>
<tr>
<td></td>
<td>8 2.08±0.35</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td></td>
<td>12 1.95±0.37</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td></td>
<td>16 1.67±0.15</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Total cholesterol, mmol/l</td>
<td>0 5.50±0.21</td>
<td>5.56±0.14</td>
</tr>
<tr>
<td></td>
<td>4 5.59±0.17</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td></td>
<td>8 5.13±0.23</td>
<td>0.099</td>
</tr>
<tr>
<td></td>
<td>12 5.30±0.16</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td></td>
<td>16 5.06±0.17</td>
<td>0.026</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/l</td>
<td>0 1.36±0.07</td>
<td>1.30±0.06</td>
</tr>
<tr>
<td></td>
<td>4 1.33±0.07</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td></td>
<td>8 1.31±0.07</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td></td>
<td>12 1.32±0.06</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td></td>
<td>16 1.28±0.06</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Leptin, mg/l</td>
<td>0 7.01±0.66</td>
<td>6.65±0.99</td>
</tr>
<tr>
<td></td>
<td>4 5.78±0.73</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>8 6.41±0.67</td>
<td>0.067</td>
</tr>
<tr>
<td></td>
<td>12 7.17±0.95</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td></td>
<td>16 5.64±0.79</td>
<td>0.003</td>
</tr>
</tbody>
</table>

1 Values represent means±SEM.
2 The number of subjects in control group was 14 until wk 8.

Blood analysis

The serum TG level increased significantly (P = 0.013) from the baseline at wk 4 of the intervention in the control group (Table 6). On the other hand, no such increase was observed in the TACC group during the intervention period. As a result, the percentage decrease in the TG was significantly greater (P = 0.043) in the TACC group than in the controls at wk 4. Since seasonal variations in serum TG have been reported in several studies,17-19 normalized values were obtained in the TACC group using the mean value of the control group at the corresponding time points. Comparison of those mean values during the non-intervention period and the intervention period revealed that serum TG was significantly lower (P = 0.009) during the intervention period in the TACC group (Table 7).

Serum total and HDL cholesterol levels did not change in this study. The serum leptin level decreased significantly from the baseline at wk 4 in both groups (Table 6). Comparison of the normalized values revealed that, in the TACC group, the serum leptin level tended to be lower (P = 0.070) during the intervention period than that during the non-intervention period (Table 7).

Discussion

In this study, we investigated the effects of the ingestion of TACC on body fat and the serum lipid profile in healthy subjects with high percent body fat. We have previously shown that the intake of TACC combined with dietary intervention effectively reduced adipose tissue mass in mice.14 In addition, percent body fat was decreased in healthy young women (n = 8; aged from 21 to 22 yr, BMI ranging from 18.4 to 25.7) after daily intake of TACC-
supplemented tea for 5 wk (unpublished data). Therefore, an anti-obesity effect of TACC was fully expected to occur in these subjects. We showed in the present study that intake of TACC-supplemented tea was effective in reducing percent body fat, triceps skinfold thickness and abdominal fat as well as in lowering the serum TG level in healthy subjects. Our results suggest that TACC is useful for reduction of body fat in obese subjects.

In this study, percent body fat significantly decreased at wk 12 of the intervention in both groups (Table 3). Mean calorie intake and walking steps for 3 d, just before the beginning and the end of the intervention, showed no difference either between groups or between time points. Therefore, one possible reason for the decrease in percent body fat in the control group is the seasonal variation of adipose tissue lipoprotein lipase (LPL) that provides free fatty acids for storage in adipocytes. It has been reported that the LPL activity in human is regulated by season, and is significantly higher in winter than in summer.20 Similar seasonal variation has been reported in BMI which is highest in winter and lowest in summer.21 Since this study was done from March to July, it is possible that percent body fat in both groups decreased as a result of the seasonal variation. However, the proportion of the subjects who decreased body fat was significantly higher in the TACC group than in the control group.

We have previously investigated the mechanisms of fat-reducing action by TACC.14 Both arginine and caffeine, the main components of TACC, are effective in suppressing the development of fatty liver in fasted-refed mice. Such inhibitory effects on hepatic lipogenesis are considered to be exerted by glucagon and catecholamines secreted in response to the presence of arginine and caffeine, respectively.5,8,22-26 In addition, arginine and caffeine have been reported to promote lipolysis in human adipocytes.8,15 Moreover, total energy expenditure was significantly higher in mice given TACC (Means ± SD, 191 ± 6.6 kcal/kg14/day) than in control mice (179 ± 5.9 kcal/kg14/day).27 These mechanisms may contribute to the fat-reducing action of TACC. In this study, TACC showed considerable fat-reducing action in the subcutaneous tissues, which are known to be resistant to decrease due to their slow metabolic rate.28 However, the 3-d diet diary just before the beginning and the end of the intervention and the brief daily record during the study were strongly suggested that there was no difference in calorie intake between the groups. These results, combined with our results in mice and the fact that caffeine increases the metabolic rate in humans,29 suggest that the ingestion of TACC-supplemented tea may increase both total energy expenditure and the metabolic rate, even in subcutaneous fat in human subjects.

Abdominal visceral and subcutaneous fat areas showed no intragroup or intergroup differences after the intervention (Table 4). However, decreases in the abdominal fat in the TACC group were positively correlated with BMI although no such correlation was seen in the control group (Fig. 1). Therefore, it is possible that the ingestion of TACC-supplemented tea is more effective in obese subjects. In fact, decreases in the abdominal total and visceral fat areas were significantly greater in obese TACC group subjects than in obese control group subjects (Table 5). These results are consistent with the previous observation that the initial abundance of visceral fat, which is reported to correlate with BMI,30 is significantly related to a larger loss of visceral fat.31 It has been suggested that abdominal visceral obesity is a critical outcome of the insulin resistance syndrome.32,33 We have recently demonstrated that the intake of TACC is effective in reducing mesenteric adipose tissue and in decreasing plasma insulin levels in obese non-insulin dependent diabetic KK mice.40 Thus, a reduction in abdominal visceral fat brought about by TACC-supplemented tea may contribute to the improvement of obesity-related disorders.

In this study, serum TG levels kept higher levels in the control group during the intervention but not in the TACC group. One possible reason for the increases in serum TG levels in the control group is the TG-increasing effect of the control group’s powdered tea. However, there have been no reports, as far as we know, that show any TG-increasing effect caused by the ingredients of the control powdered tea. Moreover, the calorie content of the control group tea was negligible (Table 2) in terms of increasing serum TG levels, and there was no increase in calorie intake in the control group during the intervention period, as estimated using the 3-d diet diary and the brief daily record. Another possible reason for the TG increases in the control group was seasonal variation. Since seasonal variations in serum TG have been reported in several studies,17-19 it is possible that the serum TG was increased in the control group as a result of a seasonal variation, but such an increase in TG due to seasonal variation was suppressed by TACC, resulting in no increase in the TACC group during the intervention. Thus, we analyzed the TG data in the TACC group after compensating for seasonal variation. After correction of the TG values in the TACC group by use of the mean control group value at the corresponding time point, the normalized TG values in the TACC group in the intervention and non-intervention periods were compared. This procedure clearly yielded a significantly lower value for serum TG during the intervention of TACC-supplemented tea (Table 7). In obese KK mice under calorie intake restriction, only a partial decrease in the plasma TG
level was achieved by treatment with TACC,\(^{10}\) while young women instructed not to change their usual dietary habits significantly decreased their serum TG level by intervention with TACC-supplemented tea (unpublished data). Though the study protocols were different, TACC may demonstrate a lowering action on circulating TG more prominently in humans than in mice. However, further investigations are needed to clarify the mechanism of TG reduction of TACC.

In conclusion, we have shown that the ingestion of TACC-supplemented tea reduced percent body fat, triceps skinfold thickness, and serum TG levels in healthy subjects with high percent body fat. Moreover, TACC ingestion was also effective in reducing visceral fat in obese subjects. Our results imply that TACC is beneficial for the mitigation of obesity.

References


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