— **Rapid Communication** —

Consumption of Coffee Polyphenols Increases Fat Utilization in Humans

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Long-term ingestion of coffee polyphenols (CPP) reduces body fat in humans. The aim of the present study was to investigate the effect of daily consumption of CPP on energy metabolism in humans. Seven healthy male subjects, with a mean (± SEM) age of 34.7 ± 2.0 y and a body mass index (kg/m^2) of 21.8 ± 0.6, participated in a placebo-controlled, double-blind, crossover intervention study with two different test beverages. The subjects consumed 185 g of a test beverage with or without CPP (359 mg) daily for 1 week. Energy metabolism was evaluated by indirect calorimetry before and after the test period after fasting and up to 3.5 hr postprandially, and during cycle ergometry. Indirect calorimetry showed that, compared to 1-week ingestion of the control beverage, 1-week ingestion of the CPP beverage led to significantly higher oxygen consumption in the sedentary period and during the cycle ergometry. CPP beverage consumption led to a higher fat utilization in the sedentary period and a higher anaerobic threshold during exercise compared with control beverage consumption. In conclusion, daily consumption of CPP increases postprandial fat utilization in healthy humans.

Key words —— fat utilization, human, indirect calorimetry, oxygen consumption

INTRODUCTION

Coffee and tea are the most popular beverages in the world and have been consumed for thousands of years for their attractive flavors and health benefits. Many studies have demonstrated a relationship between coffee and tea consumption and their potential disease prevention properties, which might be due to their polyphenol contents.[1,2] Polyphenols are secondary metabolites contained in plants, especially in the seeds and leaves, that protect them from oxidative damage via their antioxidant activity.[3] Polyphenols comprise approximately 5000 species, which are classified into flavonoids (*e.g.*, catechins in tea; isoflavones in beans; apigenin, quercetin, and lutein in vegetables; and anthocyanins in fruit) and nonflavonoids (chlorogenic acids in coffee). Caffeic acid and its derivative chlorogenic acid (a caffeic acid ester of quinic acid) are the most abundant polyphenols in coffee. A single cup of coffee contains 70–350 mg of chlorogenic acid.[4]

Oxidative stress is a key risk factor for human disease, and some foods and beverages rich in polyphenols are reported to possibly contribute to reduce several disease risks.[5] Coffee, rich in chlorogenic acids, is one of the best-documented foods with epidemiologic study results. The risk of type 2 diabetes,[6–8] liver cirrhosis,[9,10] liver and colorectal cancer,[11–13] and death attributed to inflammatory and cardiovascular diseases[14] are reduced by coffee consumption in some people.

Recently, Nagao *et al*. reported that continuous consumption of coffee polyphenols (CPP) reduces body fat, particularly abdominal fat, including visceral fat, in humans.[15] Accumulating evidence indicates that dietary supplementation with green tea polyphenols reduces body fat and improves physical performance,[16–18] which might be attributable to increased fat catabolism in the liver and skeletal muscle.[19–25] Like green tea polyphenols (flavonoids), daily ingestion of nonflavonoid CPP might also mediate fat catabolism. To date, however, the relationship between CPP ingestion and energy consumption in humans has gone largely unexplored.

The aim of the present study was to clarify the

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effect of daily ingestion of CPP on energy consumption in humans. We examined the effects of 1-week ingestion of a beverage containing CPP on energy consumption in healthy human subjects.

MATERIALS AND METHODS

Subjects —— Informed written consent was obtained from 7 healthy male volunteers after approval of the protocol by the Ethics Committee of the Kao Corporation and following the tenets of the Declaration of Helsinki. The subjects (age: 34.7 ± 2.0 y, body weight: 67.1 ± 2.4 kg, body mass index: 21.8 ± 0.6 kg/m^2) had no abnormalities on physical examination. None of the subjects had a family history of diabetes. All subjects abstained from coffee and green tea for 4 weeks and alcohol for 2 days before the study period.

Test Beverage —— The coffee-flavored test beverages, the CPP and control beverages, were prepared to be indistinguishable based on appearance and flavor, and were canned (185 g).[15] We prepared the CPP beverage using roasted coffee bean extract as a source of CPP. To prepare the control beverage, we removed CPP from roasted coffee bean extract using activated charcoal, which specifically adsorbs chlorogenic acids. The chlorogenic acid (5-caffeoyl; 3-caffeoyl; 4-caffeoyl; 3,4-dicaffeoyl; 3,5-dicaffeoyl; 4,5-dicaffeoyl; 3-ferulyl; 4-ferulyl; and 5-ferulyl quinic acid) content was 359 mg/185 g in the CPP beverage and undetectable in the control beverage. The energy content was equivalent between both beverages (13 kcal/100 g, Table 1).

Study Design —— The study had a double-blind, placebo-controlled, randomized cross-over design. The study design consisted of two 1-week intervention periods separated by a 1-week washout period.

Table 1. Composition of CPP in a Test Beverage

		CPP beverage	Control beverage
Chlorogenic acids	(mg/can)	359	0
Caffeine	(mg/can)	82	78
Nutritional facts			
Energy	(kcal/100 g)	13	13
Protein	(g/100 g)	0.6	0.5
Fat	(g/100 g)	0.4	0.3
Carbohydrate	(g/100 g)	1.8	2.0
Total volume	(g/can)	185	185

During the intervention period, the subjects consumed a test beverage either with or without CPP daily. Energy metabolism was evaluated by indirect calorimetry before (on day 1) and after (on day 8) the intervention period after fasting and up to 3.5 hr postprandially, and during cycle ergometry. Throughout the study period, the subjects refrained from drinking coffee and green or black tea.

Indirect Calorimetry —— From 2 days before the indirect calorimetric analysis, subjects consumed specified meals for breakfast, lunch, and dinner (total calories: 2509 kcal/day; protein : fat : carbohydrate ratio = 12 : 22 : 66). During these 2 days, alcohol consumption was not allowed, and the subjects were instructed to refrain from eating between meals. After dinner on the day before the indirect calorimetric analysis, intake of food or beverage other than water was prohibited for at least 12 hr.

At 8:30 AM, the subjects were adapted to a room maintained at 25°C for 15 min. Respiratory metabolic performance in the sedentary condition was measured using an open circuit breath-by-breath gas exchange measurement system (ARCO2000, ARCO SYSTEM, Chiba, Japan) 8 times (before the meal [−15–0 min] and at 30–45, 60–75, 90–105, 120–135, 150–165, 180–195, and 210–225 min after the meal). Subjects ingested a meal containing 76 g carbohydrates, 16 g fat, and 23 g protein (total calories: 540 kcal) with one of the test beverages. Subjects remained in a sedentary position throughout the study hours. For baseline data, an equilibrium period of 5 min was allowed; data from the last 10 min were averaged for calculation of the respiratory exchange ratio (RER).

After indirect calorimetry in the sedentary condition, the subjects were seated on an electromagnetically braked cycle ergometer (AerobikeTM 75XL; Combi Co., Tokyo, Japan) with a heart rate monitor, and performed a warm-up exercise at 20 W for 3 min and a graded exercise according to the following protocol: the subjects started cycling at 20 W, and the work rate was increased 15 W every minute up to 60% the maximal heart rate (HRmax) according to the conventional equation (HRmax = 220 − age).[26] The calorimetric data were acquired from 2 min after the beginning of the warm-up session (1 min before the beginning of the graded exercise session). The RER and substrate utilization were calculated from the measured values of oxygen consumption (VO_2) and carbon dioxide production (VCO_2) using the following equation:[27]

$RER = VCO_2/VO_2$

Carbohydrate utilization (mg/min)

$= 4.113 \times VCO_2 - 2.907 \times VO_2$

Fat utilization (mg/min)

$= 1.689 \times (VO_2 - VCO_2)$

Anaerobic Threshold (AT) —— AT was determined by a single blinded expert reader based on the V-slope analysis of the VO_2 and VCO_2.[28]

Statistical Analysis —— Numerical data are expressed as the mean ± SEM. Paired *t*-tests were used to compare values between the groups. Differences were considered significant when the error probability was less than 0.05.

RESULTS

Metabolic Response in the Sedentary Condition after CPP Ingestion for 1 Week

VO_2 was similar between the CPP and control conditions before the intervention period (on day 1). After the 1-week intervention period (on day 8), the average VO_2 was higher before and after meal ingestion when the subjects ingested the CPP beverage compared to the control beverage (Fig. 1). Postprandial VO_2 in the CPP condition was significantly higher compared to the control condition at 30 and 60 min after the meal. Area under the curve (AUC) of VO_2 at 60, 90, and 120 min was significantly higher, and that at 30, 150, 180, and 210 min tended to be higher in the CPP condition than in the control condition (Table 2). Average VO_2 at 60, 90, 120, and 150 min was significantly higher, and that at 180 and 210 min tended to be higher in the CPP condition than in the control condition (Table 3). The RER before and after meal ingestion was similar between the CPP and the control condition before and after the intervention period (data not shown).

On day 8, average fat utilization during the experimental period (210 min) was higher in the CPP condition than in the control condition. Fat utilization at 90 min after the meal was significantly higher in the CPP condition compared to the control condition (Fig. 2). AUC of fat utilization at 30, 60, 90, 120, 150, 180, or 210 min was significantly higher in the CPP condition than in the control condition (Table 2). Average fat utilization at 90 and 120 min was significantly higher, and that at 60, 150, 180, and 210 min tended to be higher in the CPP condition than in the control condition (Table 3). Carbohydrate utilization was similar between the CPP and control conditions (data not shown).

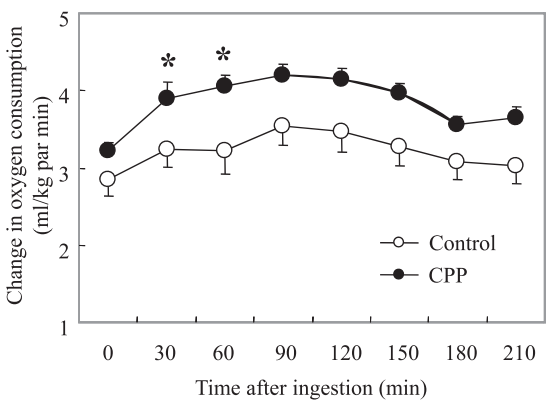

Fig. 1. Oxygen Consumption (VO_2) before and for up to 210 min after Meal Consumption, after 1 Week Ingestion of the Test Beverage with (Filled Circles and Bar) or without (Open Circles and Bar) CPP in Healthy Male Subjects

Data are expressed as means ± SEM; $n = 7$ in each group. Statistical analysis was conducted using a paired *t*-test. *: $p < 0.05$.

Table 2. AUC of Oxygen Consumption and Fat Utilization in the Sedentary Period

Time (min)	AUC of Oxygen Consumption (ml/kg)			AUC of Fat Utilization (mg/kg)		
	Control	CPP	P	Control	CPP	P
0– 30	91 ± 6	107 ± 4	0.062	21.3 ± 2.5	27.6 ± 3.1	0.038
0– 60	188 ± 13	226 ± 9	0.033	41.7 ± 4.5	52.7 ± 5.6	0.022
0– 90	289 ± 21	350 ± 13	0.034	62.0 ± 6.1	79.4 ± 7.7	0.017
0–120	394 ± 29	475 ± 16	0.040	81.3 ± 7.5	106.5 ± 10.3	0.026
0–150	496 ± 36	591 ± 21	0.052	102.2 ± 8.5	130.8 ± 13.4	0.042
0–180	591 ± 43	710 ± 22	0.053	122.6 ± 10.3	155.8 ± 15.6	0.046
0–210	683 ± 50	818 ± 26	0.055	144.8 ± 13.3	185.2 ± 18.4	0.049

Means ± SEM ($n = 7$). AUC was calculated using the trapezoid rule. Statistical analysis was conducted using a paired *t*-test.

Table 3. Average Oxygen Consumption and Fat Utilization in the Sedentary Period

Time (min)	Average Oxygen Consumption (ml/kg par min)			Average Fat Utilization (mg/kg par min)		
	Control	CPP	P	Control	CPP	P
30– 60	3.23 ± 0.26	3.98 ± 0.16	0.026	0.681 ± 0.076	0.837 ± 0.093	0.066
30– 90	3.33 ± 0.26	4.05 ± 0.15	0.031	0.665 ± 0.068	0.880 ± 0.083	0.021
30–120	3.36 ± 0.26	4.07 ± 0.14	0.043	0.662 ± 0.063	0.870 ± 0.088	0.048
30–150	3.35 ± 0.26	4.06 ± 0.13	0.049	0.677 ± 0.055	0.851 ± 0.092	0.066
30–180	3.30 ± 0.25	3.97 ± 0.12	0.055	0.668 ± 0.063	0.858 ± 0.084	0.053
30–210	3.26 ± 0.24	3.93 ± 0.12	0.055	0.695 ± 0.068	0.888 ± 0.092	0.060

Means ± SEM (n = 7). Statistical analysis was conducted using a paired t-test.

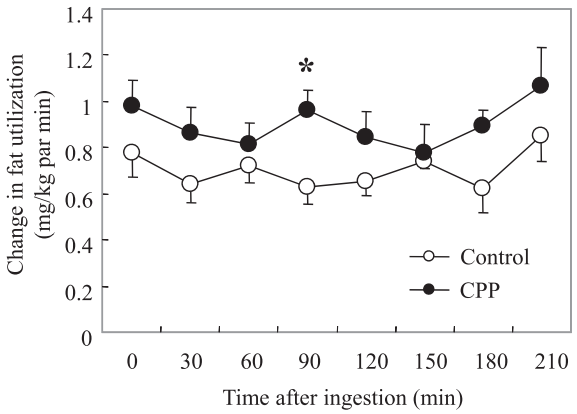

Fig. 2. Fat Utilization before and for up to 210 min after Meal Consumption, after 1 Week Ingestion of the Test Beverage with (Filled Circles and Bar) or without (Open Circles and Bar) CPP in Healthy Male Subjects

Data are expressed as means ± SEM; n = 7 in each group. Statistical analysis was conducted using a paired t-test. *: $p < 0.05$.

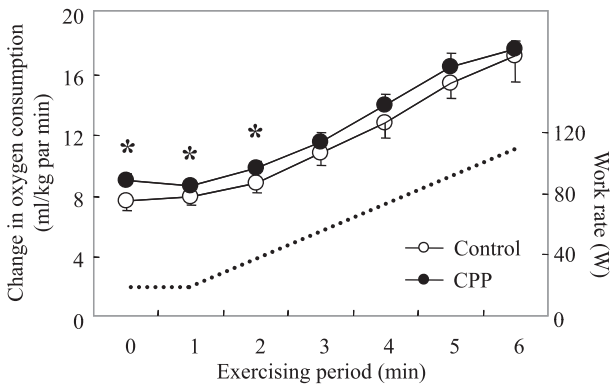

Fig. 3. Oxygen Consumption (VO_2) during the Graded Cycle Ergometry after 1 Week Ingestion of the Test Beverage with (Filled Circles) or without (Open Circles) CPP in Healthy Male Subjects

The calorimetric data were acquired from 2 min after the beginning of the warm-up session (1 min before the beginning of the graded exercise session). "0 min" indicates oxygen consumption in the warm-up session (20 W). The dotted line shows the work rate (W) in the cycle ergometry. Data are expressed as means ± SEM; n = 7 in each group. Statistical analysis was conducted using a paired t-test. *: $p < 0.05$.

Metabolic Response during Exercise after CPP Ingestion for 1 Week

VO_2 and RER during the cycle ergometry were similar between the CPP and the control conditions on day 1. On day 8, the average VO_2 during the exercise was higher after daily ingestion of the CPP beverage for 1 week compared to the control beverage. VO_2 in the CPP condition was significantly higher compared to the control condition in the warming-up session (20 W for 3 min) and up to 2 min of the graded exercise session (50 W, Fig. 3). The RER did not differ between the CPP and the control conditions during the exercise period (data not shown). Fat utilization during the exercise tended to be higher in the CPP condition than in the control condition, but the difference was not statistically significant. Carbohydrate utilization was similar between the CPP and control conditions (data not shown).

AT was similar between the CPP and control conditions on day 1. After the 1 week intervention period (on day 8), AT was significantly higher when the subjects ingested the CPP containing compared to the control beverage (Fig. 4).

DISCUSSION

This study demonstrated that daily intake of CPP in a beverage for 1 week increased postprandial fat utilization compared to the placebo beverage. Moreover, there was an increase in oxygen consumption during exercise and anaerobic threshold after intake of the CPP beverage compared to the control beverage in this study.

The significant increase in fat utilization after 1-week ingestion of the CPP beverage was not driven by disparate responses amongst subjects, as 6 of

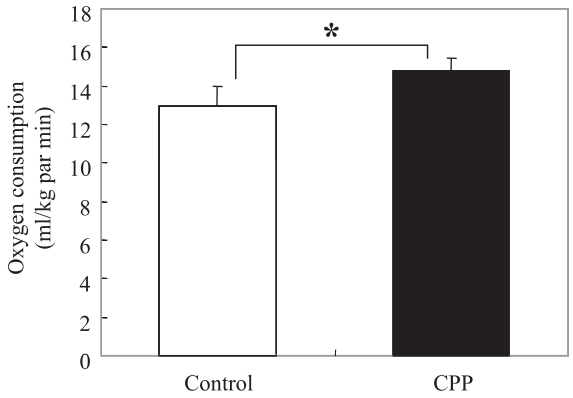

Fig. 4. AT after 1 Week Ingestion of the Test Beverage with (Filled Bar) or without (Open Bar) CPP in Healthy Male Subjects

Data are expressed as means ± SEM; $n = 7$ in each group. Statistical analysis was conducted using the paired t-test. *: $p < 0.05$.

the 7 subjects showed a greater fat utilization in response to CPP, relative to the control beverage consumption. Supplementation of a beverage with CPP increased postprandial energy consumption and fat utilization by approximately 21 and 32%, respectively. In addition, the increase in oxygen consumption during cycle exercise was observed in 6 of the 7 subjects studied with the CPP beverage. Energy expenditure and fat utilization during the exercise were increased after ingestion of the CPP beverage by more than 9.5 and 22%, respectively, compared to the control beverage. These results are consistent with the results of Nagao *et al.*, showing that continuous consumption of coffee chlorogenic acids reduces visceral fat in obese subjects.[15)]

Due to limitations of the present study, we cannot explain the underlying mechanism of increased fat utilization after CPP ingestion. The effect of CPP on energy metabolism in humans has not been sufficiently investigated. Several studies in animals, however, have suggested how the ingestion of CPP increases fat utilization. Shimoda *et al.* demonstrated that green coffee bean extract reduces visceral fat content and body weight in mice.[29)] For the mechanism, they reported that green coffee bean extract and phenolic compounds, such as neochlorogenic acid and feruloylquinic acid mixture, significantly enhanced hepatic carnitine palmitoyltransferase activity, which is a pivotal component in fuel homeostasis.[30)] More recently, Cho *et al*. reported that CPP significantly decreases high-fat diet-induced obesity in mice, which may be attributed to decreased lipogenic enzyme activities and increased fatty acid beta-oxidation activity in the liver.[31)] Chlorogenic acid seems to be more potent for body weight reduction and the regulation of lipid metabolism than caffeic acid. In this study, oxygen consumption was not affected in the latter period of the sedentary condition, whereas the CPP beverage increased VO_2 at the beginning of the exercise session compared to the control beverage. The increased VO_2 during exercise after CPP consumption seems likely to be due to stimulated energy catabolism in the skeletal muscle. Furthermore, increased AT, which is the aerobic to anaerobic metabolism transition point,[32)] may suggest that daily consumption of CPP increased endurance capacity and stimulated fatty acid oxidation in the skeletal muscle.[33)] Additional studies in animals and *in vitro* are in progress to clarify the underlying mechanisms of increased fat utilization induced by CPP ingestion, with a focus on the liver and skeletal muscle.

In conclusion, this study is the first to identify that daily consumption of CPP in a beverage significantly increase postprandial fat oxidation, oxygen consumption during exercise, and anaerobic exercise threshold in healthy individuals. These findings might provide clues to understanding the effects of CPP on energy metabolism in the control of obesity. Further, the magnitude of the increase in fat oxidation indicates that this effect is biologically relevant and could be important for preventing fat accumulation in the long term by influencing the total fat balance under conditions of chronic CPP-consumption.

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