Effect of a Thermogenic Beverage on 24-Hour Energy Metabolism in Humans

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Abstract

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Objective: To test whether consumption of a beverage containing active ingredients will increase 24-hour energy metabolism in healthy, young, lean individuals.

Research Method and Procedures: Thirty-one male and female subjects consumed 3 × 250-mL servings of a beverage containing green tea catechins, caffeine, and calcium for 3 days in a single-center, double-blind, placebo-controlled, cross-over design study. On the 3rd day, 23-hour energy metabolism, extrapolated to 24-hour, was measured in a calorimeter chamber. Blood pressure and heart rate were measured, and total day and night urines were analyzed for urea and catecholamine excretion.

Results: Twenty-four-hour energy expenditure (EE) and 24-hour fat oxidation were lower in women than in men ($p < 0.0001$ and $p < 0.015$, respectively). Although there were no treatment or treatment/gender effects on substrate oxidation, treatment increased 24-hour EE by 106 ± 31 kcal/24 hours ($p = 0.002$), equivalent to 4.7 ± 1.6 kcal/h (day; $p = 0.005$) and 3.3 ± 1.5 kcal/h (night; $p = 0.04$). No significant differences were observed in hemodynamic parameters.

Discussion: The present study provides evidence that consumption of a beverage containing green tea catechins, caffeine, and calcium increases 24-hour EE by 4.6%, but the contribution of the individual ingredients cannot be distinguished. Although this increase is modest, the results are discussed in relation to proposed public health goals, indicating that such modifications are sufficient to prevent weight gain. When consumed regularly as part of a healthy diet and exercise regime, such a beverage may provide benefits for weight control.

Key words: 24-hour energy expenditure, fat oxidation, green tea, caffeine, epigallocatechin gallate

Introduction

Obesity is pandemic and continues to increase in developed, developing, and even some strata of society in underdeveloped nations. Although the pharmaceutical industry has developed and continues to develop drugs to control obesity, they have so far met with limited success, with at present only two drugs for body weight control recognized by the Food and Drug Administration, both of which are often used in combination with a reduced energy dietary regime: Orlistat (Xenical), an intestinal lipase inhibitor, which decreases the digestibility of dietary fat and increases fat excretion (1); and Sibutramine, a serotonin and noradrenaline uptake inhibitor, which reduces appetite and increases energy expenditure (EE).[1] These drugs, however, can also have cardiovascular side effects such as palpitations and hypertension (1). Consequently, dietary concepts and formulations, with or without physical activity, will always play a principal role in any weight control program.

More recently, select micronutrients and phytochemicals have been proposed for body weight management and prevention of obesity (2,3). Research in this area is expanding, with particular emphasis in the area of lipid mobilization (4,5) and oxidation (6,7). However, to date, very few, if any, ingredients that specifically stimulate fat oxidation have been identified.

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[1] Nonstandard abbreviations: EE, energy expenditure; BMR, basal metabolic rate; EGCG, epigallocatechin gallate.

An exception to this trend has been the limited but increasing number of investigations using methylxanthines, tea catechins, and calcium. Caffeine and tea catechins, such as epigallocatechin gallate, have been postulated to play a role in weight management largely through their modulation of fatty acid oxidation by interaction with the sympathetic nervous system (6–8). An adequate supply of calcium vs. calcium deficiency has also been proposed to favor weight loss and fat loss during energy restriction (4,5), but the mechanism of action has not been clearly demonstrated in properly designed and controlled clinical trials.

The aim of the present study was to investigate the effect of consuming three servings per day of a beverage containing a mixture of green tea extract, caffeine, and calcium, ingredients that have individually been demonstrated to increase EE (2,8–11) and lipid oxidation (2,8,9,11,12) and decrease fat mass (13–17) in human volunteers, on 24-hour EE, substrate use, and markers of sympathetic nervous stimulation in a group of young, healthy, normal-weight men and women.

Research Methods and Procedures

The present study was a double-blind, placebo-controlled, single-center, randomized cross-over clinical trial, the experimental protocol of which was reviewed and approved by the ethical committee of Lausanne University School of Medicine. The study was fully monitored and conducted according to Good Clinical Practice guidelines (18).

Subjects

Male and female subjects were recruited by advertisement posted on the Medical School notice boards. Interested individuals visited the Physiology Department, University of Lausanne, where they received a detailed oral explanation and a written synopsis of the study. After several days of reflection and providing their signed consent, potential volunteers were given a medical check-up (brief medical history and physical examination including measurements of blood pressure and heart rate). Thirty-two non-smoking, moderately active, healthy, young subjects between 18 and 35 years, with a BMI between 20 and 25 kg/m^2, consuming $<$5 cups of coffee or tea per day, were selected to participate in the study.

Experimental Design

Each subject was studied on three occasions.

Period 1. The first occasion was to collect patient anthropometric data and assess basal metabolic rate (BMR) and body composition. Subjects presented at the Physiology Department in the morning, after an overnight fast. After voiding, his/her body weight and height were measured and recorded, and skinfold thickness measurements were taken at four sites, biceps, triceps, subscapular, and suprailiac, to assess body composition (19). The subject's BMR was then measured using a ventilated-hood, open-circuit, indirect calorimeter (Deltatrac Metabolic Monitor II; Datex, Helsinki, Finland) while the subject was comfortably installed in a semisupine position in bed. Continuous respiratory exchange measurements were made for 60 minutes, of which the last 30 minutes were averaged and used to calculate the subject's 24-hour BMR. Twenty-four-hour BMR was then used to calculate each individual's 24-hour energy requirements. Participants were then randomized to the two possible sequences of beverage intake, A-B or B-A (Periods 2 and 3), with sex used as a stratification factor.

Periods 2 and 3. Each period lasted 3 days, during which the subject's energy requirements, calculated from measured BMR, were provided by the Physiology Department's dietitian. The subjects maintained a low, sedentary physical activity and did not take any medication in this period. During the first 2 days, the subject was free-living and consumed 1.6 $\times$ 24-hour BMR energy. He/she was instructed on how to prepare the easy-to-prepare meals and to consume only the diet provided (food and test beverages and water ad libitum). In the eventuality that less food than provided was eaten, the subjects were requested to note the food and quantity that was not eaten. On the 3rd day, the subject was confined to an indirect calorimeter chamber, where his/her energy metabolism was measured continuously for 23 hours, and his/her diet (energy equivalent to 1.4 $\times$ 24-hour BMR) was provided. The diets were prepared to provide energy with a composition of $\sim$55% carbohydrates, $\sim$35% fat, and $\sim$15% protein. The energy content of the beverage formula A or B (Table 1) was not taken into account when calculating 24-hour energy intake. The menus and meals consumed during Period 2 were repeated exactly, meal for meal and day for day, during Period 3 with the exception that the beverage was changed. Periods 2 and 3 were separated by at least 21 days so that women could be studied in the follicular phase of their cycle.

Beverage Composition

The test beverage and placebo were blinded at the production site and were distinguishable to the investigators and subjects only by the label Formula A or Formula B. The ingredients used in the two beverages are presented in Table 1. The green tea extract was cold water soluble and was prepared from a green tea powdered extract (Choladi TCTG; Nestlé Co., Choladi, India) containing catechins and caffeine naturally in levels similar to a standard tea profile (20). After batch analysis, chemically synthesized caffeine was added to bring the dose to 100 mg caffeine/serving. Calcium was added because the lactate salt and Fibersol-2 (Matsutani Chemical Industry Co., Itami City, Japan) provided the soluble fiber. The placebo beverage contained 3

Table 1. Energy content and major ingredients in the treatment and placebo beverages

	Treatment		Placebo	
	Per day	**Per serving**	**Per day**	**Per serving**
Energy* (kcal)	57	19	49†	16†
Carbohydrates (g)	0	0	0	0
Fiber (g)	9	3	9	3
Green tea extract‡ (mg)	2100	700	0	0
Total catechins§ (mg)	540	180	0	0
EGCG¶ (mg)	282	94	0	0
Caffeine§ (mg)	300	100	0	0
Calcium (mg)	633	211	0	0

* Using energy value of 3.8 kcal/g Fibersol-2.
† Energy difference from fiber content due to energy values of minor constituents and flavor compounds.
‡ Choladi TCTG.
§ According to product analysis.
¶ Epigallocatechin gallate.

grams of fibersol-2 and natural colorants to obtain visual aspects similar to the test beverage. The beverages were served cold (~6 °C) and were consumed within 20 min at 9:30 AM, 3 PM, and 8 PM each day.

Metabolic Measurements

The subject arrived at the Physiology Institute at 7:30 AM, and an investigator confirmed that the subject had followed instructions and filled out the compliance questionnaire. After voiding and recording body weight, the subject was equipped with a sphygmomanometer (-2430 Ambulatory Blood Pressure Monitoring System; A&D Company, Ltd., Tokyo, Japan) for automatic blood pressure and heart rate measurement during the 23 hours in the chamber (every 15 minutes during the day and every 2 hours during the night).

The subject entered the metabolic chamber at 8 AM and remained in the chamber until 7 AM the next morning. While in the chamber, the subject was occupied with sedentary activities such as watching television, listening to music, reading, etc. However, on two occasions, from 11 AM to 11:30 AM and from 4:30 PM to 5 PM, light exercise (50 watts for 30 minutes) was performed on a bicycle ergometer. Lights were turned off at 11 PM, and the subject was allowed to sleep until just before 7 AM, when he/she exited the chamber. Continuous respiratory exchange measurements were made for 23 hours, as previously described (21), with values being printed and electronically stored every 15 minutes.

Total urine was collected as two-timed collections from ~8 AM to ~11 PM and from ~11 PM to ~7 AM for measurement of urinary urea nitrogen and catecholamine concentrations. Aliquots of the urine samples were taken, of which some were frozen at −20 °C for urea analysis (Beckman Urea analyzer; Beckman Coulter, Fullerton, CA), while others were acidified with 6 N HCl (0.1 mL/10 mL) and stored at −20 °C until catecholamine analysis using high-performance liquid chromatography with electrochemical detection (22).

Data Management and Analysis

Raw data from each subject's case report form was entered into a Clintrial database (Clintrial 4.3; Phase Forward, Waltham, MA) with double entry. Electronic data from the 23-hour respiratory exchange and blood pressure recordings, made in the calorimeter chamber, were extracted from Microsoft Excel worksheets (Microsoft, Redmond, WA), extrapolated to 24 hours, and entered into the Clintrial database for calculations and data reporting.

Calculations

Protein oxidation was calculated from urinary urea nitrogen excretion measured in the two-timed urine collections, assuming that urea nitrogen contributes 90% of total nitrogen excretion, after which EE and substrate use were calculated from the respiratory exchange data using standard equations (23).

Statistical Analysis

The beverage codes were broken after the protocol and intention-to-treat data sets had been defined and the primary outcome had been analyzed. The codes were: A, placebo; and B, treatment.

Table 2. Physical characteristics of the subjects ($n = 31$; mean ± SD)

	Number	Age (years)	Weight (kg)	Height (cm)	BMI (kg/m^2)	Body fat (%)	Body fat (kg)	Lean body mass (kg)
Men	15	22.0 ± 2.0	70.0 ± 7.0	179.0 ± 5.8	21.8 ± 1.3	13.5 ± 3.4	9.3 ± 2.9	60.7 ± 5.3
Women	16	22.7 ± 2.5	61.0 ± 7.8	167.0 ± 5.9	21.9 ± 2.2	17.8 ± 3.2	11.0 ± 3.2	50.0 ± 5.5
Total	31	22.4 ± 2.3	65.3 ± 1.5	172.8 ± 1.5	21.8 ± 1.8	15.9 ± 3.9	10.2 ± 3.1	55.2 ± 1.4

Statistical Methods

Thirty-two subjects were recruited; however, one subject took nonprescribed medication before the first 3-day test period. Consequently, only 31 subjects were studied in the metabolic chamber, and the protocol results are presented.

All parameters were analyzed using Student's paired *t* test to assess the effect of the treatment vs. placebo beverage. SAS software (version 8.02; SAS Institute Inc., Cary, NC) was used. Values are expressed as mean ± SE, unless stated otherwise, and p values < 0.05 were considered significant.

Results

The physical characteristics of the 31 subjects who completed the trial are presented in Table 2. Although there was a global effect of gender on 24-hour EE ($p < 0.0001$) and 24-hour fat oxidation ($p < 0.015$), with the men in general expending more energy (2540 ± 49 kcal/24 hours) and oxidizing more fat (102 ± 5 g/24 hours) than the women (2161 ± 30 kcal/24 hours and 87 ± 4 g/24 hours, respectively), there were no gender/treatment interactions for these parameters (24-hour EE, $p = 0.16$; 24-hour fat oxidation, $p = 0.449$).

Results calculated from the respiratory exchange data are summarized in Figure 1. The total column represents 24-hour EE, which is divided into the energy contributions from fat, carbohydrate, and protein oxidized during that period.

The primary outcome, 24-hour fat oxidation, was 908 ± 33 kcal (96.0 ± 3.5 grams) with the treatment beverage and 878 ± 50 kcal (92.8 ± 5.3 grams) during the placebo test. The difference in fat oxidized, 30 ± 57 kcal (3.2 ± 6.0 grams), was not significantly different.

Carbohydrate oxidation was also slightly, but not significantly, greater with treatment, 1294 ± 41 kcal/24 hours (309.5 ± 9.8 g/24 hours), than with the placebo beverage, 1210 ± 041 kcal/24 hours (289.5 ± 9.8 g/24 hours).

Total EE was greater with treatment (2398 ± 55 kcal/24 hours) than with placebo (2291 ± 49 kcal/24 hours, $p < 0.002$), but the energy contributions of fat, carbohydrate, and protein were not significantly different.

Figure 2 illustrates the frequency distribution of the subjects and their percentage change in 24-hour EE with treatment. It can be seen that of the 31 subjects, 25 increased and six decreased 24-hour EE with the treatment.

When EE was considered separately during the day and the night, it was also significantly greater, by 4.7 ± 1.6 ($p = 0.005$) and 3.3 ± 1.5 ($p = 0.04$) kcal/h, respectively, with the treatment beverage than with the placebo. Although the energy expended during the two exercise periods tended to be greater with treatment, 4.3 ± 5.0 kcal/h, it was not significantly different from that measured during the exercise periods while consuming the placebo.

Sympathetic Nervous Activity

Blood pressure, heart rate, and urinary catecholamine excretion were used as markers of sympathetic nervous activity; however, no differences were observed between treatments over the measurement period. Systolic and diastolic blood pressures were 117 ± 1.4 and 116 ± 1.5 mm Hg and 69 ± 1 and 68 ± 1 mm Hg, respectively, and heart rate was 67 ± 2 and 68 ± 2 beats/min with treatment and placebo, respectively.

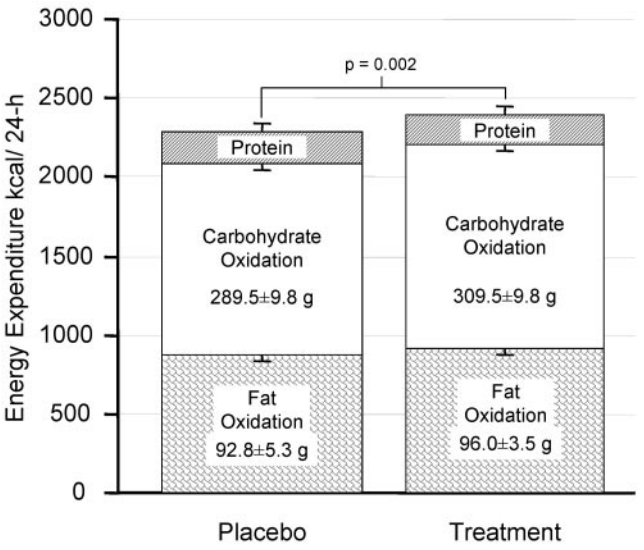

Figure 1: Total 24-hour EE (whole column) and the energy contributions from fat, carbohydrate, and protein oxidized when consuming the placebo and treatment beverages. ($n = 31$; mean ± SE).

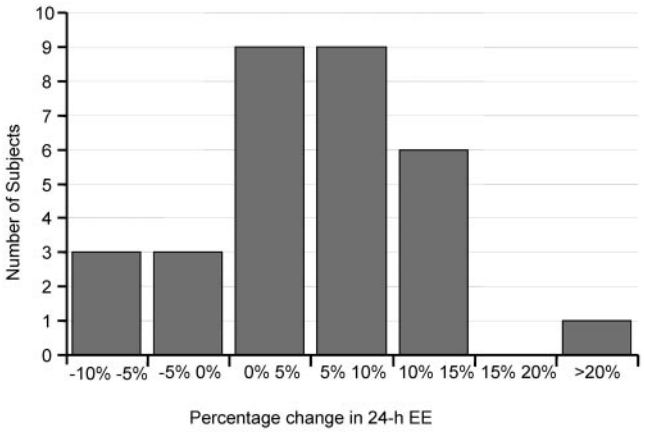

Figure 2: Frequency distribution of percentage change in 24-hour EE.

Urinary Catecholamines

Urinary norepinephrine excretion was 202.4 ± 2.1 and 218.7 ± 18.2 nmol/24 hours and that of epinephrine was 64.3 ± 6.0 and 61.5 ± 6.9 nmol/24 hours with the treatment and placebo beverages, respectively. No correlations were observed between changes in 24-hour EE or 24-hour fat oxidation and changes in urinary catecholamines with treatment for the group as a whole or when considered by gender.

Compliance

All of the empty beverage bottles were returned to the investigators and accounted for. Those taken during the metabolic measurements were consumed at the scheduled times under supervision of the investigator(s).

Discussion

The present study was carried out to investigate whether a number of food ingredients that have been demonstrated individually to increase acute fat oxidation (2,8,9,11,12) or promote weight loss and fat loss in longer studies (13,14,16) might have thermogenic effects when combined in a beverage that was consumed as part of the daily diet. The concentrations of the different ingredients included in the beverage (Table 1) were based on data available in the scientific literature (8,10,13,24–26) and a consideration of potential consumer safety and regulatory issues, essentially concerning daily caffeine intake. The treatment beverage, containing green tea extract, caffeine, calcium, and fiber, or a placebo, containing fiber alone, was consumed three times a day for 3 days, the last of which was spent in a metabolic chamber where continuous respiratory exchange measurements were made, and total urine excretion was collected for 23 hours, and from which EE and substrate oxidation rates were calculated.

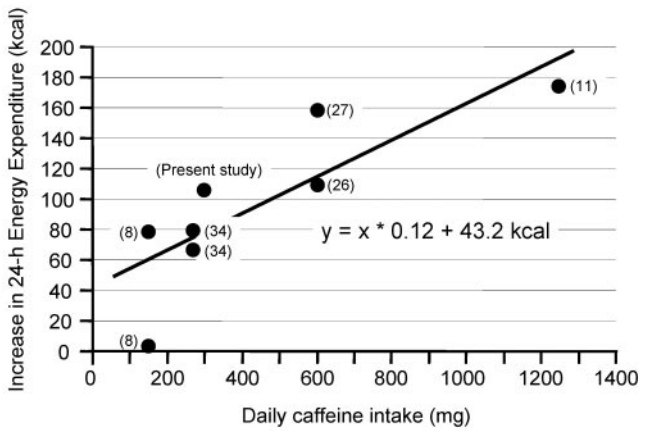

Figure 3: Relationship between daily caffeine intake and 24-hour EE. Values taken from the literature with references are indicated in parentheses.

Although the primary objective, to demonstrate that the mixture of ingredients would increase 24-hour fat oxidation, was not achieved, the nonsignificant increments in EE produced by oxidation of the individual substrates combined were sufficient to cause a significant increase in total 24-hour EE (106 kcal) and EE during the day and the night. The 106 kcal/24 hours increase represents 4.6% of 24-hour EE of the group as a whole and was similar to that (4%) observed by Dulloo et al. (8), whose subjects consumed a similar amount of epigallocatechin gallate (EGCG) and one-half the amount of caffeine as those in the present study. When the caffeine dose was double that given in the present study, 600 mg of caffeine, given as 3 × 200 mg caffeine/d, with varying amounts of EGCG, 24-hour EE increased almost proportionally, to 8% (~179 kcal) greater ($p < 0.005$) than after placebo (27). Although there was a mild dose response increase in 24-hour EE with EGCG, the differences were not significant.

Some of the physiological effects of caffeine (increased heart rate and blood pressure) have been proposed to act by its sympathomimetic activity (28); however, the amount (300 mg/d) provided by the test beverage was not sufficient to cause an observable effect in the surrogate markers of sympathetic nervous activity used in this study. However, with twice this dose, small increases in systolic (7 mm Hg; not significant) and diastolic (5 mm Hg; $p < 0.005$) blood pressure have been observed (27), which one might consider of little importance for individuals with normal blood pressure but of more concern for those with hypertension.

Unlike Dulloo et al. (8), we and others (27) did not demonstrate that these ingredients increased 24-hour fat oxidation. Although Bérubé-Parent et al. (27) propose that lipid oxidation appeared to increase at their lowest dose of EGCG (i.e., 3 × 90 mg/d), the present study does not support this.

Caffeine has been extensively studied since the beginning of the last century because of its physiological and pharmacological effects, and it is well accepted that caffeine stim-

ulates thermogenesis (Figure 3) (2, 9–11, 26, 29–32) and fat oxidation (2,9,11). However, there is less evidence that teas, tea extracts, and calcium might have similar effects on energy and fat metabolism. Dulloo et al. (8) were among the first to demonstrate that a green tea extract, which also contained caffeine, could increase 24-hour EE. Because a quantity of caffeine similar to that contained in the green tea extract had little or no effect alone on 24-hour EE, it was concluded that the observed effect was due either to the green tea polyphenols or a combination of green tea polyphenols and caffeine. Since then, oolong tea, which also contains caffeine, has also been shown to increase EE (33,34) and 24-hour fat oxidation (34). Calcium has also been proposed, by Zemel et al. (25), to play a role in energy metabolism. Although their hypothesis principally concerns the effect of dietary calcium on adipocyte lipolysis, they did observe increases in core body temperatures of their transgenic agouti mice placed on high-calcium diets, which they interpreted as an increase in thermogenesis. A similar effect of dietary calcium on 24-hour EE was not confirmed in human studies (12,35); however, acute calcium intake was associated with 24-hour fat oxidation in one study (12) although not in the other (35).

There is evidence to suggest that the principal active component is caffeine. Results from studies of caffeine alone and of tea containing caffeine on 24-hour EE are presented in Figure 3, which illustrates the relationship between daily caffeine intake and EE. Linear regression analysis indicates that a dose of 300 mg of caffeine/d will increase EE by ~79 kcal/d, accounting for 75% of the response observed in the present study, with the remaining 27 kcal/d being provided by the other ingredients and/or synergies between them. If one performs a similar relationship for EGCG in the presence of 600 mg caffeine/d, using the results of Bérubé et al. (27), EE increases of 4 to 5 kcal/24 hours for every 100 mg increase in EGCG/d can be observed.

Whether the major effect responsible for the increase in 24-hour EE is due to EGCG per se, green tea per se, caffeine per se, or their combination, the results suggest that by using the ingredients investigated in the present study, one might expect an increase in 24-hour EE of ~100 kcal/d. Although a number of studies have indicated that such an increase is statistically significant, with 95% confidence or more, the physiological significance of such an increase would seemingly be small. However, from epidemiological studies, Hill et al. (36) estimated that the average weight gain of the American population is slightly less than 1 kg/yr, which represents a median excess energy of 15 kcal/d, and that 90% of the population gain only 50 kcal/d or less. They argue that because energy is stored with ~50% efficiency, a negative energy balance of 100 kcal/d would be sufficient to prevent weight gain in most of the U.S. population, and they believe that it is a realistic public health goal for the American population that can be achieved without making drastic changes in their present day lifestyles. The present study provides evidence indicating that this type of beverage, when consumed regularly as part of a healthy diet and exercise regime, may be helpful in weight control. However, more long-term studies would be necessary to confirm these short-term observations.

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