

Effects of Dietary Supplementation with a Compound Composed of Caffeine, Capsaicin, Sesamine, L-Carnitine, Banaba and Lotus on Human Autonomic Nervous System Activity and Lipid Oxidation

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Abstract

This study was conducted to determine if supplementation with a compound composed of caffeine (50 mg), capsaicin (75 mg), sesamine (30 mg), L-carnitine (300 mg), banaba (50 mg) and lotus (10 mg) enhanced human autonomic nervous activities (ANS) associated with thermogenic sympathetic activity and fat utilization. Ten healthy college males (21.2 ± 1.0 yr) volunteered for this experiment. Autonomic nervous activities associated with energy metabolism were examined at 30 min intervals for a total of 120-min while at rest and every 5-min during exercise at 50% of the ventilation threshold before and after intake of the compound or placebo with 100 ml of water for 10 days. In addition, heart rate variability power spectral analysis was used to assess human autonomic nervous activities. The results indicated that there were no significant differences in heart rate during rest and exercise among trials. Furthermore, the autonomic nervous activity tended to increase after 10-days of consumption of the test compounds during the experimental period, but the differences did not reach statistical significance. However, before and after the compound test trial there was a significantly higher respiratory gas exchange ratio (rest 0: 0.83 ± 0.01 vs. rest 3: 0.89 ± 0.02 , $p < 0.05$), carbohydrate oxidation (CHO) rate (rest 0: 44.57 ± 5.83 vs. rest 2: $63.86 \pm 5.91\%$, $p < 0.05$) and a lower fat oxidation rate (rest 0: 55.43 ± 5.83 vs. rest 2: $36.14 \pm 5.91\%$, $p < 0.05$). In conclusion, the results of the present study suggested that the compound composed of caffeine, capsaicin, sesamine, L-carnitine, banaba and lotus components that was evaluated in this study did not induce a significant increase in human autonomic nervous activities or lipolysis, even though the individual components have been reported to induce increased fat oxidation.

Key words: autonomic nervous system, heart rate variability power spectrum analysis, thermogenic sympathetic activity, fat oxidation, compound supplementation

INTRODUCTION

Various food components such as caffeine, capsaicin, sesamine and L-carnitine have been reported to influence autonomic nervous activity and lipid activation (1-3). In addition, banaba, which is the leaf of the tropical plant *Lagerstroemia speciosa* L., has long been used as a folk medicine for the treatment of diabetes and kidney diseases (4). The extract from banaba was found to lead to a significant reduction in blood glucose and insulin levels in type II KK-Ay diabetic mice (4). Additionally, it was recently reported that banaba extract induced an anti adipogenic activity by effectively reducing weight gain and parametrial adipose tissue in female diabetic mice (5). Furthermore, lotus has traditionally been used in Oriental medicine as an anti-inflammatory agent in Taiwan (6), and it has been reported that lotus seed has antioxidant properties and effectively protects against

DNA damage in human lymphocytes (7). Although it has been reported that each of these components increases dietary substrate oxidation, especially fat oxidation and anti inflammation, the combined effects of caffeine, capsaicin, sesamine, L-carnitine, banaba and lotus components on fat oxidation have not been studied to date. Furthermore, there is currently no data describing changes in cardiac autonomic nervous system (ANS) activity in response to thermogenic sympathetic nervous activity associated with modulators of energy metabolism available. Therefore, it is important to evaluate the effects of treatment with a combination of the aforementioned compounds on cardiac ANS activity associated with energy metabolism to determine if such treatment can lead to fat oxidation.

Cardiac ANS activity plays an important role in the maintenance of homeostasis under diverse physiological and psychological environments. The sympathetic nerv-

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ous system (SNS) and adrenal medulla combine to form the sympathoadrenal system, which is an important regulator of a number of physiological processes. Since the coordination of energy homeostasis is particularly dependent on normal functioning of the sympatho-adrenal system (8), alterations in the SNS activity are widely believed to contribute to the pathophysiology of obesity. However, no other consensus has been made among investigators with respect to the predominant sympathetic abnormality (increase or decrease) (9,10). This may be partially due to difficulties in adequately assessing the sympathetic function that modulates energy metabolism in humans.

The electrocardiogram (ECG) R-R interval or inter-beat interval of the heart rate is determined by the net effect of sympathetic and parasympathetic input. Heart rate variability (HRV) power spectral analysis has been shown to be a reliable non-invasive method and has provided a comprehensive quantitative and qualitative evaluation of neuroautonomic function under various physiological conditions (11-13). In general, high-frequencies (>0.15 Hz) of the HRV are associated almost entirely with vagal nerve activity, while low-frequencies (<0.15 Hz) of the HRV may be mediated by both vagal and SNS activities (14-16). Frequencies much lower than 0.1 Hz are believed to reflect thermoregulatory fluctuations in vasomotor tone (17,18). We recently demonstrated that very low frequency (VLF) components (0.007~0.03 Hz) are increased selectively against thermogenic perturbation such as acute cold exposure and mixed-food ingestion (19). This finding suggests that is possible to evaluate SNS activities associated with energy metabolic regulation by HRV spectral analysis in humans.

Therefore, in this study, HRV power spectral analysis was used to evaluate energy metabolism and ANS activity, particularly thermogenic-sympathetic function in response to treatment with tablets that contained of a combination of components that could be taken as a convenient nutritional supplement.

MATERIALS AND METHODS

Subjects

Ten healthy male [mean (SE) 21.2 (1.0) yr, 172.8 (2.4) cm, 62.2 (2.0) kg and % fat 14.6 (1.0) (estimated by bio-impedance method)] students from K University volunteered for this experiment. All experimental procedures were explained in detail to each subject, who then signed a statement of informed consent. The physical characteristics of the subjects are shown in Table 1.

Experimental Procedures.

Subjects came to the laboratory at 9:00 am after eating a traditional Japanese breakfast that consisted of 70% carbohydrates, 20% protein and 10% fat at least 2 hr before arriving at the laboratory on four different occasions. The ANS activity and energy metabolism were measured as baseline data prior to ingestion of the compound which consisted of caffeine (50 mg), capsaicin (75 mg), sesamine (30 mg), L-carnitine (300 mg), banaba (50 mg) and lotus (10 mg), or placebo. In addition, the ANS and energy metabolism were measured for 5-min at 30 min intervals for a total of 120-min while at rest and every 5-min during exercise at 50% of ventilation threshold 1 hr after the intake of the compound or placebo with 100 mL of water. After consumption of the compound or placebo for 10 days, the cardiac ANS activity and energy metabolism of the subjects were measured. The experimental protocols are shown in Table 2.

Our R-R interval power spectral analysis procedures have been fully described elsewhere. Briefly, the analog output of the ECG monitor (Life Scope, Nihon Kohden, Japan) was digitized using a 13-bit analog-to-digital converter (Trans Era HTB 420) at a sampling rate of 1000 Hz. The digitized ECG signal was then differentiated, and the resultant QRS spikes and intervals of the impulses (R-R intervals) were stored sequentially on a hard disk for later analyses.

Subjects were requested to avoid any medication for one week prior to the study, but to follow their usual

Table 1. Physical characteristics of the subjects

Subject (N)	Age (yr)	Height (cm)	Weight (kg)	BMI (kg/m ²)	Body fat (%)
10	21.2 (1.0)	172.8 (2.4)	62.2 (2.0)	20.8 (0.7)	14.6 (1.0)

Values represent the means \pm SE. BMI: body mass index.

Table 2. Experimental protocol

▼Rest 0	Placebo or test tablets before and after 10 days	▼Rest 1 30 min	▼Rest 2 60 min	▼Rest 3 90 min	▼Rest 4 120 min	▼EXE 5~10 min
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▼: ANS activity and energy metabolism measurement, Rest: rest period, EXE: exercise period.

diet. Each subject was instructed to avoid any food or beverages containing alcohol, caffeine or capsaicin after 9:00 pm on the night preceding the study. The room in which the measurements took place was temperature controlled (23~24°C), quiet and contained minimal arousal stimuli. The subjects rested for at least 30 min before the start of the experiment.

To evaluate the ANS activity, we analyzed the VLF, LF, HI, and total power by integrating the spectra of each respective bandwidth. The mean heart rate of each 256-s segment was also calculated with the standard error.

To calculate the respiratory quotient (RQ), carbohydrate (CHO) and fat oxidation (FAT) from expired gas data, we used the table developed by Lusk (20).

RQ was determined from VO_2 (L/min) and VCO_2 (L/min) using the following equations:

$$\% \text{CHO} = 100 \times [(R - 0.707) / 0.293]$$

$$\% \text{Fat} = 100 \times [(1.0 - R) / 0.293]$$

where 0.707 is the RQ when only fat is oxidized and 0.293 is the difference between the CHO and FAT.

The baseline values of each trial were standardized as 100%, and the relative values of the combined test tablets were then compared to the baseline data because the integrated values of the basal spectrum differed greatly among individuals.

Statistical analyses

All statistical analyses were conducted using a commercial software package (SPSS version 11.5 for Windows, SPSS Inc., Illinois, USA). Statistical differences between treatments were assessed using two-way analysis of variance (ANOVA) with repeated measurements for time, treatment and time \times treatment as well as one-way ANOVA to evaluate the effects of the test tablet after 10 days. P values < 0.05 were considered to be statistically significant. All data are expressed as the mean \pm SE.

RESULTS

Power spectral changes

Fig. 1~3 represent the results of cardiac ANS activity among trials. The ECG R-R interval power spectral results did not differ among trials in terms of the spectral total power, representation of the over-all ANS activity, VLF power associated with the SNS thermogenic component and the LF power containing the sympatho-vagal component. Fig. 1 shows the changes in total power of the ANS after consumption of the test tablets at rest for 120-min and 5-min during exercise as determined using heart rate variability power spectral analysis in healthy

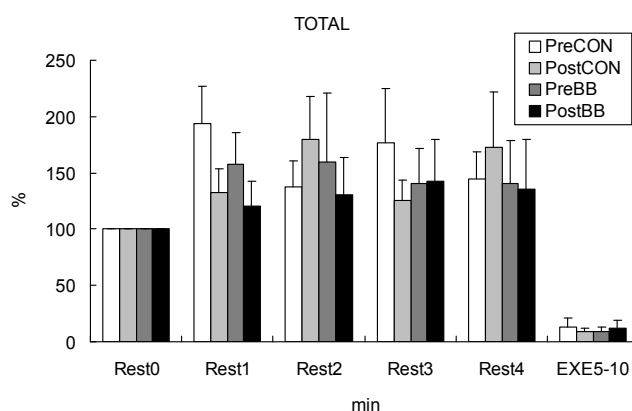


Fig. 1. Changes in the total power of ANS in healthy males after consumption of the test tablets at rest for a total of 120-min and for 5-min during exercise as determined by heart rate variability power spectral analysis. There were no significant differences among test trials. All values shown represent the means \pm SE.

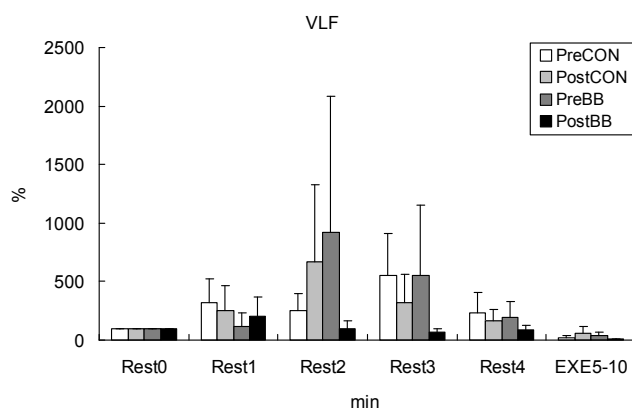


Fig. 2. Changes in VLF of ANS in healthy males after consumption of the test tablets at rest for a total of 120-min and for 5-min during exercise as determined using heart rate variability power spectral analysis. There were no significant differences among test trials. Values represent the means \pm SE.

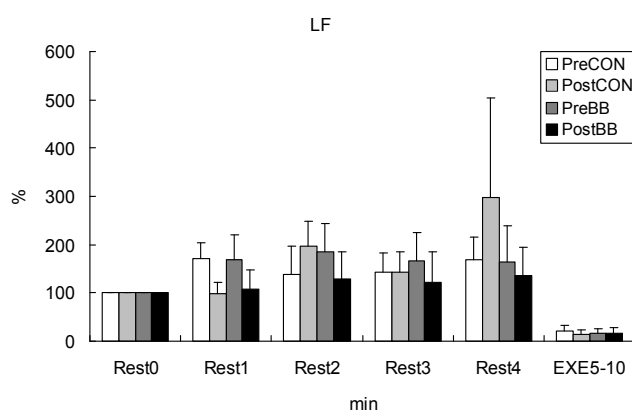


Fig. 3. Changes in the LF of ANS in healthy males after consumption of test tablets at rest for 120-min and for 5-min during exercise as determined using heart rate variability power spectral analysis. There were no significant differences among test trials. Values represent the means \pm SE.

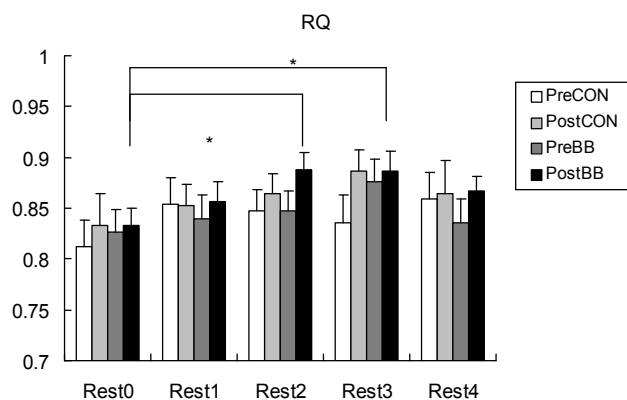


Fig. 4. Changes in the respiratory gas exchange ratio (RQ) after ingestion of test tablets at rest and during exercise in healthy young men. The RQ values increased significantly before and after consumption of the compound (BB) [rest 0, 0.83 (0.38) vs. rest 2, 0.88 (0.38); rest 0, 0.83 (0.38) vs. rest 3, 0.88 (0.43), $p < 0.05$]. Values represent the means \pm SE, * $p < 0.05$.

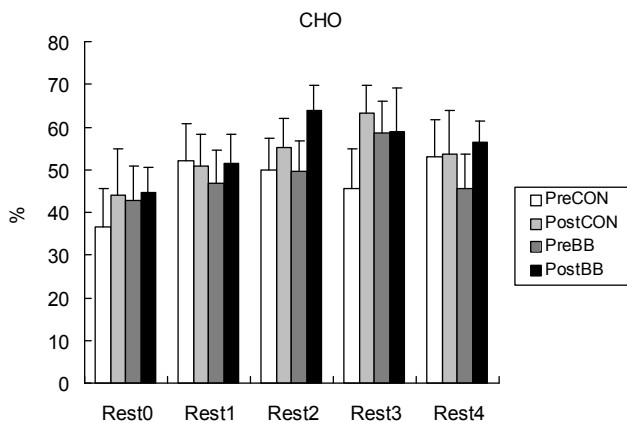


Fig. 5. Changes in carbohydrate oxidation (CHO, %) after ingestion of test tablets at rest and during exercise in healthy young men. Values represent the means \pm SE. There were no significant differences in the metabolic responses among test trials.

males. There were no significant differences among test trials. Fig. 2~3 show the changes in the LF and VLF of the ANS after consumption of test tablets at rest for 120-min and 5-min during exercise as determined using heart rate variability power spectral analysis. There were no significant differences in LF and VLF among test trials.

Metabolic responses

Fig. 4~6 show the alterations in energy metabolism among trials. Fig. 4 shows the changes in RQ before and after ingestion of the test tablets at rest and during exercise in healthy young men. The results indicate that the RQ values increased significantly before and after consumption of the compound [rest 0, 0.83 (0.38) vs. rest 2, 0.88 (0.38); rest 0, 0.83 (0.38) vs. rest 3, 0.88 (0.43), $p < 0.05$]. Fig. 5 shows the changes in CHO (%)

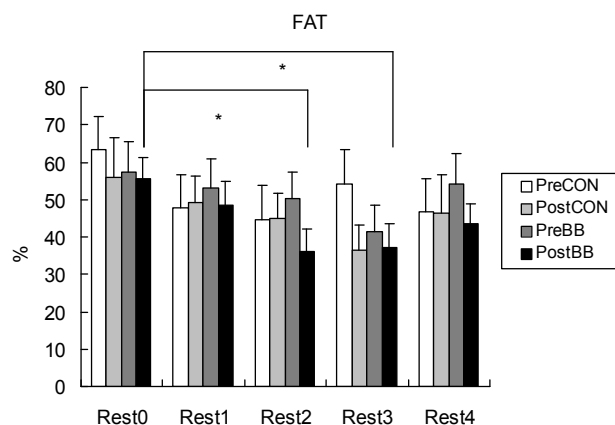


Fig. 6. Changes in fat oxidation (FAT, %) after ingestion of test tablets at rest and during exercise in healthy young men. Fat oxidation (FAT) yielded significant decreases after BB consumption [rest 0, 55.43 (13.04) vs. rest 2, 36.88 (13.04); rest 0, 55.43 (13.04) vs. rest 3, 37.18 (14.41), $p < 0.05$]. Values represent the means \pm SE, * $p < 0.05$.

after ingestion of test tablets at rest and during exercise in healthy young men. There were no significant differences in metabolic responses among test trials. Fig. 6 shows the alterations in the FAT (%) after ingestion of test tablets at rest and during exercise in healthy young men. Fat oxidation (%) decreased significantly after BB consumption [rest 0, 55.43 (13.04) vs. rest 2, 36.88 (13.04); rest 0, 55.43 (13.04) vs. rest 3, 37.18 (14.41), $p < 0.05$]. No significant differences were observed among test trials. Taken together, these results indicate that the tablets composed of caffeine, capsaicin, sesamine, L-carnitine, banaba and lotus had no effect on lipolysis activation.

DISCUSSION

In this study, we evaluated the effects of a combination of caffeine, capsaicin, sesamine, L-carnitine, banaba and lotus components on ANS activity and energy metabolism in healthy males during resting and exercise periods. Specifically, we evaluated the effects of test tablets containing the aforementioned compounds to determine if they induced an increase in cardiac ANS activity associated with energy metabolism that led to fat oxidation. However, no significant differences in ANS activities were observed among treatment groups. This lack of significant differences among trials may have resulted from the following: the HRV power values may have had a wide inter-individual variation; the mixture of the test components may have had an adverse effect on cardiac ANS activity, even though the individual food components have been reported to improve the effects of ANS activity. Furthermore, we did not consider the

genotype of the subjects evaluated in the present study; however, such differences may impact energy metabolism.

In previous studies, capsaicin, which has long been used as an ingredient of spices, preservatives and medicines, was found to have the greatest impact on metabolism in various capsicum containing fruits such as hot chili peppers (21). Watanabe et al. (22) investigated the neurophysiological functions of capsaicin and found that it increases energy metabolism via catecholamine secretion from the adrenal medulla through sympathetic activation via the central nervous system. Sesamine, which is one of the most abundant lignans present in sesame seeds and oil, has been reported to act as an antioxidant (23) and an anticarcinogen (24), as well as to have a blood pressure lowering (25) and serum lipid lowering (26) effect in animals and humans. In addition, dietary sesamine is known to reduce the hepatic concentrations of triacylglycerol (27), although it causes a temporary increase in phospholipid levels accompanying liver hypertrophy (27,28). L-carnitine is essential for the transport of long chain fatty acids across the mitochondrial membrane for subsequent fat degradation and energy production (29). It has been suggested that L-carnitine supplementation influences lipid metabolism and can effect body composition (30). In addition, it is well known that the physiological effects of caffeine ingestion improves performance during exercise prolonged to exhaustion (31,32), and that this effect occurs due to an increase in the circulation of free fatty acids (33). Finally, observation of endogenous catecholamine release (34-36) confirmed that caffeine ingestion enhances the activity of the sympathetic nervous system in humans at rest and during exercise.

However, the test tablets administered in the present study did not enhance the RQ and substrate oxidation. Although each individual component of the test tablets has been reported to induce an increase in dietary fat oxidation, the results of the present study showed that tablets containing a mixture of these compounds had no effect on metabolism. Further research should be conducted to provide a more in-depth comprehension of this mechanism.

It is important to note that the results of this study were derived from a small number of subjects using non-invasive measures; therefore, interpretation of the results must be carefully considered until a larger scale study confirms the present findings. Nevertheless, to the best of our knowledge no studies have been conducted to date to evaluate the effects of compound administered to subjects in the present study in humans. Therefore, this study provides useful results, even though there were

no significant differences observed in the cardiac ANS activity and substrate oxidation among groups.

In conclusion, we demonstrated that oral administration of the compound for 10-days did not induce any changes in the ANS activity and lipolysis activation in human subjects. It should be considered the consumption of the compound dietary supplementations for weight control and/or energy homeostasis.

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