2022, Volume 5 (Issue 1): 1 OPEN ACCESS

Effects of a Single Dose of BURN-XT™ on Resting Metabolic Rate, Substrate Oxidation, and Various Indices of Affect

Original Research

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Open Access

Published: January 5, 2022

Journal of Exercise and Nutrition: *2022, Volume 5 (Issue 1): 1*

ISSN: 2640-2572

Abstract

Introduction: Many consumers use dietary supplements in the hopes of increasing energy and burning more calories, which if sustained over time may help accelerate weight loss. The purpose of this clinical trial was to investigate the effects of an over-the-counter thermogenic supplement called Burn-XT™ (BXT) on metabolic rate, substrate oxidation, and various psychometric indices of affect that impact weight management.

Methods: Using a double-blind, placebo-controlled, cross-over design, 16 women and 10 men (29.3 ± 7.3 yr, 169.4 ± 8.6 cm, 75.5 ± 14.3 kg) underwent two testing sessions: placebo (PL) and BXT. Seated metabolic rate and substrate oxidation, vital signs, and anchored visual analogue scale (VAS) assessments of energy, mood, motivation, focus, fatigue, concentration, and appetite were made before supplementation and hourly for three hours post-ingestion. Two-factor (2x4) factorial ANOVAs and paired sample t-tests (corrected for multiple comparisons) were used for analyses.

Results: Significant increases in metabolic rate (oxygen consumption) were noted at 60 minutes in BXT (+11.9 mL O2/min) vs. PL (-2.5 mL O2/min), $p = 0.004$, $d = -0.74$. Only BXT increased metabolic rate compared to baseline at 60 minutes (+11.9 mL O2/min, $p = 0.021$, $d = -0.53$) and 120 minutes (+12.1 mL O2/min, $p = 0.019$, $d = -0.54$). The AUC for resting energy expenditure increased more in BXT vs. PL ($p = 0.007$, $d = -0.57$). VAS detected significant improvements in energy, mood, focus, and concentration for BXT vs. PL at 120 and 180 minutes (all $p < 0.05$, $d = -0.58$ to -0.68). In all cases, within-group changes from baseline for these VAS parameters were significant (all $p < 0.05$, $d = -0.76$ to -1.38) in BXT but not in PL. No within or between group differences in appetite, substrate oxidation, or heart rate were noted. Small (~3-4 mm Hg), but statistically significant ($p < 0.05$, $d = -0.51$ to -0.69) increases in diastolic blood pressure were noted in BXT at 60, 120, and 180 min vs. PL; and in systolic blood pressure at 60 min vs. PL. In all cases, values remained within normal clinical hemodynamic ranges.

Conclusions: A single dose of BXT safely increased metabolic rate, energy, mood, focus, and concentration. Given that these factors are known to favorably impact weight management, future studies should determine whether daily supplementation with BXT reduces body weight and improves body composition.

Key Words: thermogenic, metabolism, resting energy expenditure

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Introduction

Dietary supplements designed to stimulate thermogenesis and enhance energy, mood, focus, and concentration are popular in today's society. However, relatively few of these products are supported by competent and reliable scientific evidence to support their label claims[1]. Since weight loss is known to be affected by a myriad of factors (e.g., appetite, energy expenditure, thermic effect of food, stress, mood, etc.), many thermogenic products designed to promote weight loss have multiple ingredients that attempt to address this enigma. The multi-ingredient approach has become popular among active people and thermogenic products have the potential to help dieters achieve weight loss through greater energy expenditure[2].

The two most commonly studied ingredients in terms of their ability to increase energy expenditure are caffeine and green tea[3]. Caffeine is commonly used in many 'fat-burning' products because it can stimulate the SNS thereby increasing energy expenditure and fat oxidation while suppressing hunger[1,4]. Caffeine can exert its thermogenic effects through multiple routes (first as a competitive inhibitor of the enzyme phosphodiesterase in vascular smooth muscle cells which attenuates the breakdown of cAMP and, in turn, increases the AMP/ATP ratio and second by binding to and inhibiting adenosine A1 and A2a receptors thus activating adenylate cyclase with a resulting increase in cAMP and protein kinase A activity associated with stimulating the CNS)[5,6]. Overall caffeine's physiological impact results in increased energy metabolism, a greater stimulatory effect on the heart due to a greater catecholamine release, relaxation of smooth muscle, and increased blood pressure[6]. However, adding compounds to caffeine in a multi-ingredient approach may provide additional metabolic benefits.

Caffeine with green tea extract has shown to increase resting energy expenditure (REE) by 2.8% and decrease respiratory exchange ratio (RER) over a 24-hour period compared to caffeine alone[7]. In addition, Belza et al.[8] noted increases in RMR over a 4-hour post-ingestion period at baseline and after 8 weeks of chronic use with a supplement containing caffeine, green tea, and capsaicin compared to a placebo. On the other hand, a recent meta-analysis[9] reported inconclusive evidence for acute and chronic green tea extract as some studies reported increases, decreases, or no change in energy expenditure and RER. Nonetheless green tea extract may exert its thermogenic effects by inhibiting the enzyme catechol-O-methyltransferase (COMT) which slows the breakdown of catecholamines (i.e., epinephrine and norepinephrine) in the synaptic cleft, thereby stimulating the SNS[6].

Similarly, L-Carnitine has been shown to increase fat oxidation and lower respiratory quotient by facilitating long chain fatty acid transport into the mitochondria for ß-oxidation[1,10]. L-Carnitine may also activate regulators of lipid breakdown (hormone sensitive lipase, carnitine palmitoyltransferase I-A, and acyl-coenzyme A oxidase) and inhibit regulators of adipogenesis (peroxisome proliferator-activated receptor and adipose-specific fatty acid-binding protein)[11] while having a potential for inducing satiety[12].

Meanwhile capsaicinoids, usually ingested as chili, cayenne pepper, or red pepper, have been shown to reduce body weight and improve body composition over a 12-week supplementation period[13] . Capsaicinoids may stimulate the release of catecholamines, activate transient receptor potential vanilloid 1 receptors, which may aid in the lipolytic action on adipocytes, and have vasodilatory responses that increase blood pressure and heart rate in order to stimulate its thermogenic effects[6]. Our lab has previously demonstrated that the same capsaicinoid-rich preparation, when utilized as part of a multi-ingredient product that also contained caffeine and piperine from black pepper led to improvements in body composition, perceived energy levels, craving for fatty foods and serum adipokine profile[14].

The purpose of this clinical trial was to investigate the effects of a single dose of the over-the-counter multi-ingredient thermogenic supplement Burn-XT™ (BXT), on metabolic rate, substrate oxidation, and various indices of affect that impact weight management. Based on previous research with similar active ingredients, we hypothesized that BXT would increase resting energy expenditure (REE) and oxygen consumption compared to placebo.

Scientific Methods

This study was a randomized, double-blind, placebo-controlled, cross-over consisting of three study visits. During the initial screening visit each participant's medical history and routine blood work (CBC, CMP, and Lipid Panel) were collected, and baseline diet was assessed. During the next two visits subjects underwent a body weight measurement, followed by baseline measurements of vitals (blood pressure and heart rate), visual analog scales (VAS) for appetite, energy, mood, concentration, focus, motivation, and fatigue, and resting metabolic rate (RMR). Following the baseline measurement (i.e., 0 min) each participant ingested one of two test products before undergoing vitals, VAS, and

metabolic rate testing at 60 min, 120 min, and 180 min post ingestion. After a minimum 3-day washout period, subjects repeated all testing procedures but ingested the opposite supplement. See Figure 1.

Comprehensive side effect profile/adverse event monitoring took place throughout the study duration. The study was conducted following ICH-GCP guidelines to ensure subject safety and scientific integrity of the data and was approved by Advarra Institutional Review Board on March 15, 2021 (Pro00050238).

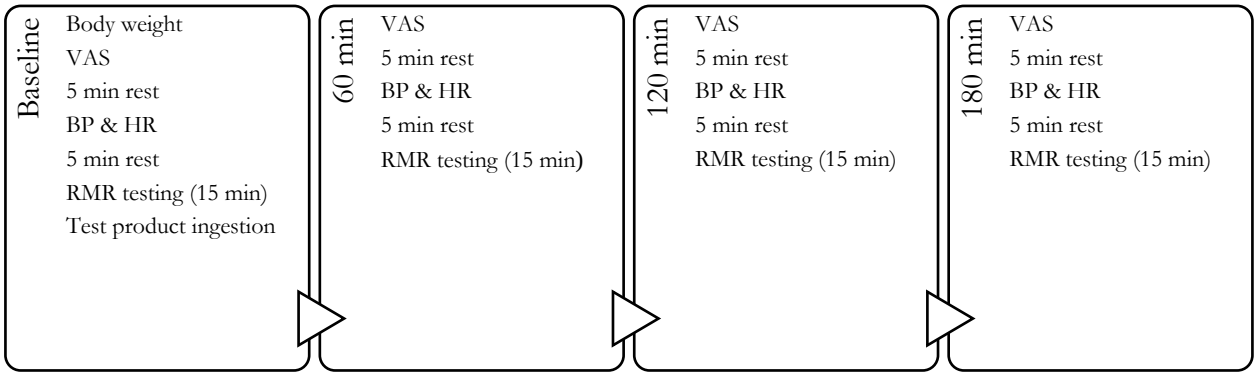

Figure 1. Experimental flow diagram of Resting Metabolic Rate (RMR) testing.

Participants

26 volunteers (10 men and 16 women) participated in this study (see Table 1). All subjects were pre-screened using health history questionnaires, vital signs, and routine blood work (CBC, CMP, and a lipid panel).

Participants were recruited using the same inclusion and exclusion criteria. Consequently, all participants were in good health as determined by physical examination, medical history, and routine blood work, and were between the ages of 20 and 44 years and had a body mass index (BMI) of 18.5-34.9 $kg \bullet m^{-2}$. Prior to participation, all participants indicated their willingness to comply with all aspects of the experimental and supplement protocol by signing an informed consent. Participants were excluded if they: (a) had a history of any metabolic disorder including known electrolyte abnormalities, diabetes, thyroid disease, hypogonadism, or other endocrine disorder; (b) had a history of malignancy in the previous 5 years except for non-melanoma skin cancer (basal cell cancer or squamous cell cancer of the skin); (c) had prior gastrointestinal bypass surgery; (d) known gastrointestinal or metabolic diseases that might impact nutrient absorption or metabolism (e.g. short bowel syndrome, diarrheal illnesses, history of colon resection, gastro paresis, Inborn-Errors-of-Metabolism); (e) had any chronic inflammatory condition or disease; (f) had a known allergy to any of the ingredients in the supplement or the placebo; (g) had currently been participating in another research study with an investigational product or have been in another research study in the past 30 days; (h) had a caffeine intake of three or more cups of coffee or equivalent (>400 mg) per day; (i) had a history of cardiovascular or cardiorespiratory disease; (j) had smoked or had quit smoking within the past 6 months; (k) had migraine headaches; (l) females who were pregnant or were planning to become pregnant during the study; (m) had a history of hepato-renal, musculoskeletal, autoimmune, or neurologic disease; (n) had taken weight loss supplements or drugs within 30 days prior to the start of the study; (o) had gained or lost more than 10 pounds within the past 30 days; (p) had any other diseases or conditions that, in the opinion of the medical staff, could confound the primary endpoint or place the participant at increased risk of harm if they were to participate; or (q) did not demonstrate a verbal understanding of the informed consent document.

Participants were instructed to follow their normal diet and activity patterns. Participants were required to complete a 24-hour diet record prior to arriving at the laboratory for their first initial screening visit. Participants were given a copy of this dietary record and instructed to duplicate all food and fluid intake 24 hours prior to each of their laboratory visits. In addition to replicating food and fluid intake for 24 hours prior to their subsequent testing session, study participants were also asked to refrain from heavy exercise 24 hours prior, abstain from caffeine 12 hours prior, and arrive at least 4 hours fasted to all testing sessions. Prior to metabolic rate testing, participants were asked to confirm their adherence to these procedures.

Table 1. Subject demographics (10 men and 16 women)

	M ± SD
Age (yr)	29.3 ± 7.3
Height (cm)	169.4 ± 8.6
Weight (kg)	75.5 ± 14.3
BMI ($kg \cdot m^{-2}$)	26.1 ± 3.4
SBP (mmHg)	116 ± 13
DBP (mmHg)	74 ± 8
HR (bpm)	66 ± 11

SBP = Systolic blood pressure; DBP = Diastolic blood pressure; HR = Heart rate

Metabolic Measures-Resting Energy Expenditure (REE) and Substrate Oxidation

All gas exchange data were measured using an indirect calorimeter (TrueOne 2400, ParvoMedics, Salt Lake City, UT). Participants were fitted with a facemask attached to a one-way valve to measure O_2 consumption and CO_2 production. The metabolic gas analyzer was calibrated with gases of known concentration (16% O_2, 5% CO_2, and N_2 bal) every four hours and calibrated for airflow with a 3 L syringe as per the manufacturer's instruction manual before each measurement. Participants sat quietly for 5 min before getting their blood pressure and heart rate measured. Then participants remained seated in a reclined position for an additional 5 min prior to the baseline REE measurement. The metabolic measurement was collected for 15 minutes (the first 5 minutes were discarded) at each assessment time point (i.e., baseline, 60 min, 120 min, and 180 min post product ingestion). Respiratory exchange ratio (RER) was calculated as the product of VCO_2/VO_2. REE was continuously monitored by indirect calorimetry and reported as kilocalories per day (kcal/day). Gas exchange measurements were collected and subsequently analyzed as 30 second averages. Participants remained awake and seated in a reclined position inside a naturally lit room (indirect sunlight) and instructed not to talk or fidget during each measurement. Previous reliability measurements from our lab reported a test-retest correlation with a range of 0.550-0.747 and a mean ICC of 0.893[15].

Supplement Protocol

Throughout the study protocol, all supplements were prepared in capsule form for oral ingestion and packaged in coded generic containers for administration. Participants orally ingested one capsule of either placebo (rice flour) or BURN-XT™ (BXT) containing, per one capsule: acetyl L-carnitine (350 mg), green tea leaf extract (225 mg standardized for 98% polyphenols, 75% catechins, 45% EGCG), caffeine anhydrous (135 mg), Capsimax® cayenne pepper fruit extract (25 mg), and Bioperine black pepper fruit extract (2.5 mg). The identity and potency of each ingredient was confirmed prior to starting the study via third-party analysis. Each treatment was administered after the baseline resting metabolic rate measurement during the two testing visits in a double-blinded fashion using a Latin Square approach to minimize order effects. All trials were conducted at the research center under the supervision of a study team member.

Anthropometric and Other Resting Measures

Standing height was determined using a wall-mounted stadiometer and body weight was measured using a Seca 767TM Medical Scale. Resting heart rate and blood pressure were measured using an automated blood pressure cuff (Omron HEM-780) before, 60, 120, and 180 minutes after ingestion of each assigned supplement.

Visual-Analog Scales

10-cm anchored VAS were completed before, 60, 120, and 180 minutes after ingestion of each assigned supplement. VAS were anchored with "Lowest Possible" and "Highest Possible" and assessed subjective ratings of appetite, energy, mood, concentration, focus, motivation, and fatigue.

Statistical Analysis

Separate 2-way full factorial analyses of variance (group × time) were used with t-tests (corrected for multiple comparisons) to analyze REE, VO_2, RER, VCO_2, HR, SBP, DBP, and VAS measures (Appetite, Energy, Fatigue, Mood, Concentration, Motivation, and Focus). When the sphericity assumption was violated, Greenhouse-Geisser corrections were applied. A paired samples t-test was used to compare differences in the area under the curve (AUC) for REE. Gas exchange data were examined for outliers and removed for any value outside of ±3.0 SD. Alpha level

was set a priori at < 0.05 for statistical significance and ≤ 0.10 for trends. Effect sizes are expressed as Cohen's d with 95% confidence intervals and interpreted as ≥ 0.2 for a small effect, ≥ 0.5 for a moderate effect, and ≥ 0.8 for a large effect. All analyses were completed with GraphPad Prism version 9.2.0 (GraphPad Software, San Diego, CA, USA).

Results

Metabolic Measures

RER

There was no condition x time interaction for RER (p = 0.243). See Figure 2.

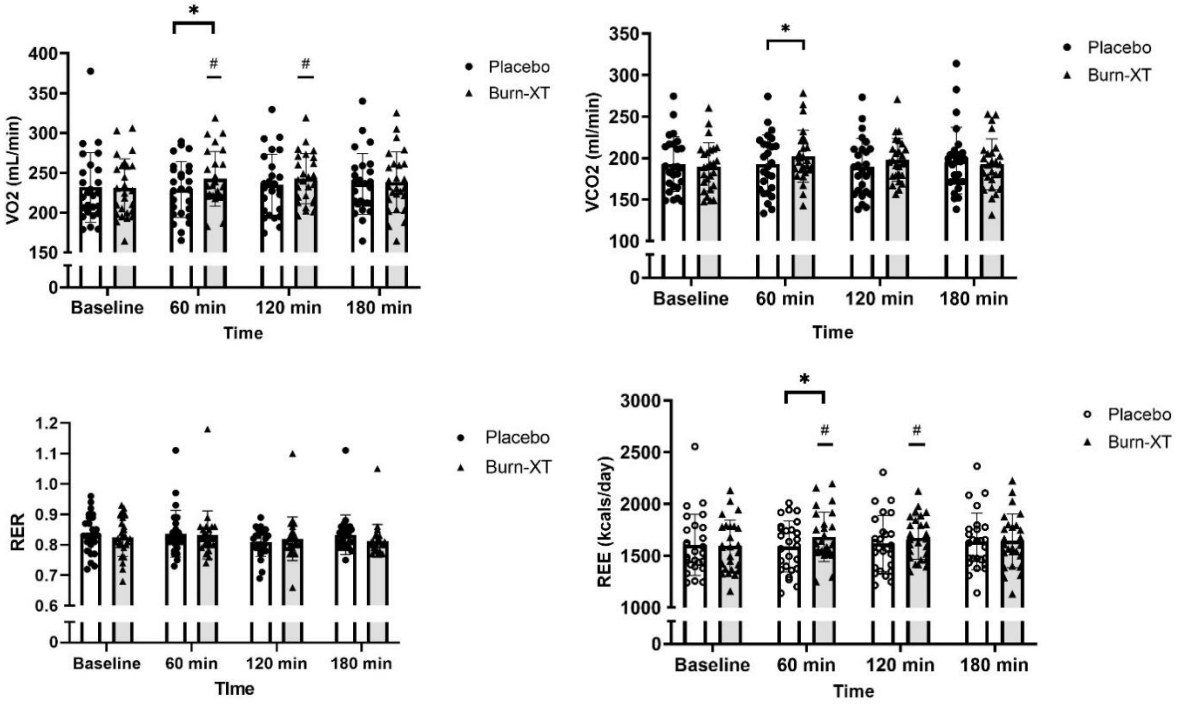

Figure 2. Individual (circles and triangles) and mean (bars) ± SD changes in metabolic measures between trials at each time point. *Significant difference between trials p ≤ 0.05. #Significantly different from Baseline p ≤ 0.05.

REE

There was a condition x time interaction trend for REE (p = 0.100) and a significant main effect of group for REE (p = 0.038). Post hoc analysis revealed a significantly higher REE from baseline at 60 min (mean difference = 87.3 kcals/day, CI: 11.3 to 163.3 kcals/day, p = 0.020, d = -0.53) and 120 min (mean difference = 78.8 kcals/day, CI: 2.8 to 154.9 kcals/day, p = 0.040, d = -0.48) for BXT while no differences were noted over time in PL. Also, BXT was significantly higher than PL at 60 min (1684 ± 238 vs. 1591 ± 246 kcals/day, p = 0.005, d = -0.72, CI: -1.1 to -0.3). See Figure 2. BXT had a significantly greater AUC for REE compared with PL (4979 ± 648 vs. 4831 ± 743 au, p = 0.007, d = -0.57, CI: -1.0 to -0.2). See Figure 3.

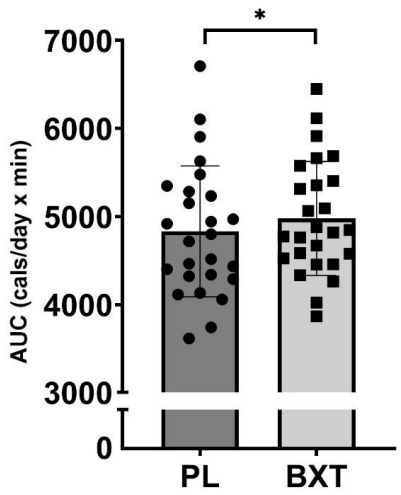

Figure 3. Comparison of 3-hour REE AUC between BXT and PL. *Significant difference $p \leq 0.05$.

VO_2

There was no condition x time interactions for VO_2 ($p = 0.102$). There was a significant main effect of group for VO_2 ($p = 0.030$). Post hoc analysis revealed a significantly higher VO_2 from baseline at 60 min (mean difference = 11.9 ml/min, CI: 1.5 to 22.3 ml/min, $p = 0.021$, $d = -0.53$) and 120 min (mean difference = 12.1 ml/min, CI: 1.7 to 22.5 ml/min, $p = 0.019$, $d = -0.54$) for BXT while no differences were noted over time in PL. Also, BXT had a significantly higher VO_2 than PL at 60 min (242.5 ± 34.3 vs. 229.1 ± 35.0 ml/min, $p = 0.004$, $d = -0.74$, CI: -1.2 to -0.3). See Figure 2.

VCO_2

There was a trend for a condition x time interaction within VCO_2 ($p = 0.094$). Post hoc analysis revealed BXT was significantly higher than PL at 60 min (202.2 ± 31.4 vs. 192.2 ± 35.5 ml/min, $p = 0.018$, $d = -0.5$, CI: -0.9 to -0.1). See Figure 2.

Vitals (Blood pressure and heart rate)

SBP

There was no condition x time interaction for SBP . However, there was a significant main effect of time and group for SBP. Post hoc analysis revealed a significantly higher SBP from baseline at 120 min (mean difference = 4.2 mmHg, CI: 1.1 to 7.3 mmHg, $p = 0.005$, $d = -0.56$) and 180 min (mean difference = 3.4 mmHg, CI: 0.3 to 6.5 mmHg, $p = 0.026$, $d = -0.46$) in BXT. Also, BXT was significantly greater than PL at 60 min ($d = -0.55$, CI: -1.0 to -0.1). See Table 2.

DBP

There was a significant condition x time interaction, main effect of group, and main effect of time in DBP. Post hoc analysis revealed a significantly higher DBP from baseline at 60 min (mean difference = 3.4 mmHg, CI: 1.0 to 5.8 mmHg, $p = 0.035$, $d = -0.58$), 120 min (mean difference = 3.5 mmHg, CI: 1.0 to 5.9 mmHg, $p = 0.003$, $d = -0.60$), and 180 min (mean difference = 4.0 mmHg, CI: 1.6 to 6.4 mmHg, $p = 0.001$, $d = -0.69$) in BXT. Also, BXT was significantly greater than PL at 60 min ($d = -0.62$, CI: -1.0 to -0.2), 120 min ($d = -0.69$, CI: -1.1 to -0.3), and 180 min ($d = -0.51$, CI: -0.9 to -0.1). See Table 2.

HR

There was no condition x time interaction, but there was a significant main effect of time for HR. Post hoc analysis showed that baseline was significantly higher than all other time points for PL (60 min: mean difference -4.7 bpm, CI: -7.4 to -2.0 bpm, $p < 0.001$, $d = 0.77$; 120 min: mean difference -3.7 bpm, CI: -6.3 to -1.0 bpm, $p = 0.005$, $d = 0.59$; 180 min: mean difference -3.7 bpm, CI: -7.3 to -1.9 bpm, $p < 0.001$, $d = 0.75$) and BXT (60 min: mean difference -7.7 bpm, CI: -10.3 to -5.0 bpm, $p < 0.001$, $d = 1.23$; 120 min: mean difference -4.3 bpm, CI: -7.0 to -1.6

bpm, p = 0.001, d = 0.69; 180 min: mean difference -5.5 bpm, CI: -8.2 to -2.8 bpm, p < 0.001, d = 0.89). See Table 2.

Visual-Analog Scales

Appetite
There was no condition x time interaction, but there was a main effect of time for appetite. Post hoc analysis showed that baseline was significantly less than all other time points for PL (60 min: mean difference 1.0 cm, CI: 0.5 to 1.5 cm, p < 0.001, d = -0.73; 120 min: mean difference 1.7 cm, CI: 1.2 to 2.2 cm, p < 0.001, d = -1.22; 180 min: mean difference 2.1 cm, CI: 1.6 to 2.6 cm, p < 0.001, d = -1.48) and BXT (60 min: mean difference 0.7 cm, CI: 0.2 to 1.2 cm, p = 0.006, d = -0.41; 120 min: mean difference 1.3 cm, CI: 0.8 to 1.8 cm, p < 0.001, d = -0.79; 180 min: mean difference 1.7 cm, CI: 1.2 to 2.2 cm, p < 0.001, d = -1.03). See Table 2.

Fatigue
There was no condition x time interaction for fatigue. See Table 2.

Concentration
There was a significant condition x time interaction, main effect for group, and main effect for time for concentration. Post hoc analyses revealed that baseline was significantly less than 120 min (mean difference = 1.0 cm, CI: 0.4 to 1.5 cm, p < 0.001, d = -0.81) and 180 min (mean difference = 1.2 cm, CI: 0.7 to 1.8 cm, p < 0.001, d = -1.03) for BXT and that BXT was significantly greater than PL at 120 min (d = -0.58, CI: -1.0 to -0.2) and 180 min (d = -0.63, CI: -1.1 to -0.2) with a trend in favor of BXT at 60 min (d = -0.45, CI: -0.9 to -0.0). See Table 2.

Energy
There was a significant condition x time interaction, main effect for group, and main effect for time for energy. Post hoc analyses revealed that baseline was significantly less than 60 min (mean difference = 1.0 cm, CI: 0.4 to 1.6 cm, p = 0.001, d = -0.67), 120 min (mean difference = 1.7 cm, CI: 1.1 to 2.3 cm, p < 0.001, d = -1.18), and 180 min (mean difference = 2.0 cm, CI: 1.4 to 2.6 cm, p < 0.001, d = -1.38) for BXT while PL had a trend for greater energy at 180 min (mean difference = 0.6 cm, CI: -0.05 to 1.2 cm, p = 0.079, d = -0.40). Also, BXT was significantly greater than PL at 120 min (d = -0.68, CI: -1.1 to -0.3) and 180 min (d = -0.51, CI: -0.9 to -0.1). See Table 2.

Focus
There was a significant condition x time interaction and main effect for time with a trend for group effect for focus. Post hoc analyses revealed that baseline was significantly less than 120 min (mean difference = 1.1 cm, CI: 0.6 to 1.6 cm, p < 0.001, d = -0.92) and 180 min (mean difference = 1.3 cm, CI: 0.8 to 1.8 cm, p < 0.001, -1.11) with a trend suggesting greater focus at 60 min (mean difference = 0.5 cm, CI: 0.0 to 1.0 cm, p = 0.063, d = -0.42) for BXT while no time differences were noted within PL. In addition, BXT was significantly greater than PL at 120 min (d = -0.61, CI: -0.8 to -0.2) and 180 min (d = -0.6, CI: -1.0 to -0.2). See Table 2.

Mood
There was a significant condition x time interaction, main effect for group, and a trend for time for mood. Post hoc analyses revealed that baseline was significantly less than 180 min (mean difference = 1.1 cm, CI: 0.5 to 1.6 cm, p < 0.001, d = -0.76) with a trend suggesting a more positive mood at 120 min (mean difference = 0.7 cm, CI: 0.2 to 1.3 cm, p = 0.087, d = -0.52) for BXT while no time differences were noted within PL. In addition, BXT was significantly greater than PL at 120 min (d = -0.61, CI: -0.8 to -0.3) and 180 min (d = -0.63, CI: -0.9 to -0.4) with a trend favoring BXT at 60 min (d = -0.44, CI: -0.8 to 0.0). See Table 2.

Motivation
There was a significant condition x time interaction) and a main effect for time for motivation. Post hoc analyses revealed that baseline was significantly less than 60 min (mean difference = 0.6 cm, CI: 0.1 to 1.1 cm, p = 0.019, d = -0.48), 120 min (mean difference = 1.1 cm, CI: 0.6 to 1.6 cm, p < 0.001, d = -0.86), and 180 min (mean difference = 1.5 cm, CI: 0.9 to 2.0 cm, p < 0.001, d = -1.15) for BXT while no time differences were noted within PL. In addition, BXT was significantly greater than PL at 180 min (d = -0.57, CI: -1.0 to -0.2) with a trend favoring BXT at 120 min (d = -0.44, CI: -0.8 to 0.0). See Table 2.

Table 2. Vitals and indices of affect data. Data presented as M ± SD.

	Time	PL	BXT	Significance	
SBP (mmHg)	Baseline	109 ± 12	110 ± 11	Group	p = 0.013
	60 min	108 ± 15	112 ± 13*	Time	p = 0.005
	120 min	111 ± 15	114 ± 13↓	G x T	p = 0.520
	180 min	111 ± 13	113 ± 12↓		
DBP (mmHg)	Baseline	75 ± 8	74 ± 8	Group	p = 0.004
	60 min	74 ± 9	78 ± 6↓*	Time	p = 0.031
	120 min	75 ± 9	78 ± 9↓*	G x T	p = 0.032
	180 min	75 ± 8	78 ± 7↓*		
HR (bpm)	Baseline	65 ± 12	67 ± 12	Group	p = 0.652
	60 min	61 ± 11↓	59 ± 10↓	Time	p < 0.001
	120 min	62 ± 10↓	63 ± 11↓	G x T	p = 0.291
	180 min	61 ± 10↓	61 ± 11↓		
Appetite (cm)	Baseline	5.3 ± 2.0	5.3 ± 2.1	Group	p = 0.196
	60 min	6.3 ± 1.6↓	6.0 ± 2.1↓	Time	p < 0.001
	120 min	7.0 ± 1.6↓	6.6 ± 1.9↓	G x T	p = 0.394
	180 min	7.4 ± 1.8↓	7.0 ± 2.0↓		
Energy (cm)	Baseline	5.0 ± 1.5	4.6 ± 1.7	Group	p = 0.027
	60 min	5.2 ± 1.2	5.6 ± 1.2↓	Time	p < 0.001
	120 min	5.4 ± 1.6	6.4 ± 1.2↓*	G x T	p < 0.001
	180 min	5.6 ± 1.9#	6.7 ± 1.6↓*		
Mood (cm)	Baseline	6.3 ± 1.5	5.8 ± 1.7	Group	p = 0.042
	60 min	5.7 ± 1.6	6.2 ± 1.4^	Time	p = 0.056
	120 min	6.0 ± 1.5	6.5 ± 1.4#*	G x T	p = 0.005
	180 min	6.0 ± 1.7	6.9 ± 1.7↓*		
Concentration (cm)	Baseline	6.1 ± 1.5	5.7 ± 1.5	Group	p = 0.020
	60 min	5.7 ± 1.5	6.2 ± 1.6^	Time	p < 0.001
	120 min	6.1 ± 1.7	6.7 ± 1.1↓*	G x T	p = 0.001
	180 min	6.1 ± 1.8	7.0 ± 1.3↓*		
Focus (cm)	Baseline	6.0 ± 1.7	5.5 ± 1.6	Group	p = 0.060
	60 min	5.6 ± 1.6	6.0 ± 1.6#	Time	p < 0.001
	120 min	6.0 ± 1.7	6.6 ± 1.1↓*	G x T	p = 0.003
	180 min	6.1 ± 1.9	6.9 ± 1.4↓*		
Motivation (cm)	Baseline	5.6 ± 1.8	5.2 ± 1.8	Group	p = 0.133
	60 min	5.5 ± 1.6	5.8 ± 1.4↓	Time	p < 0.001
	120 min	5.8 ± 1.5	6.3 ± 1.4↓^	G x T	p < 0.001
	180 min	5.8 ± 1.7	6.7 ± 1.6↓*		
Fatigue (cm)	Baseline	4.4 ± 1.7	4.5 ± 1.9	Group	p = 0.142
	60 min	4.8 ± 1.3	4.1 ± 1.4	Time	p = 0.233
	120 min	4.8 ± 1.7	3.9 ± 1.8	G x T	p = 0.179
	180 min	4.2 ± 1.4	3.8 ± 1.9		

Note: Data are Means ± SD. *Significantly different from PL ($p \leq 0.05$); ^Trend from PL ($p \leq 0.1$); ⸸Significantly different from Baseline ($p \leq 0.05$); #Trend from Baseline ($p \leq 0.1$). SBP = Systolic blood pressure; DBP = Diastolic blood pressure; HR = Heart rate.

Discussion

This investigation aimed to examine changes in resting energy expenditure, substrate oxidation, various indices of affect that impact weight maintenance, and the safety and tolerability of the putative thermogenic product BURN-XT™. In this sample of men and women, a single capsule of BXT increased metabolic rate, concentration, energy, focus, mood, and motivation compared to PL. Small increases in systolic (at 60 min) and diastolic blood pressure (at 60, 120, and 180 min) were noted in BXT compared to PL; in all cases, values remained within normal clinical hemodynamic ranges (<120/80 mm Hg). Finally, all study participants responded positively to each treatment and did not report any negative health consequences, adverse events, or side effects.

The primary outcome for this study was REE which was significantly elevated above baseline over the first 2 hours (+5.5% at 60 min and +4.9% at 120 min) within the BXT trial while also being significantly greater than PL (+5.5% vs. -0.9%) after the first hour post-ingestion. In conjunction, BXT had a significantly greater (+3.1%) REE AUC than PL over the three-hour post ingestion window. This could be explained by the observed changes in respiratory gases where BXT had an increase in VO_2 (+5.2%) and VCO_2 (+4.3%) while PL had a reduction in VO_2 (-1.1%) and VCO_2 (-0.1%) at 60 min. However, there were no changes in substrate oxidation between trials. Similar investigations of a thermogenic supplement have reported increases in REE over 3- and 4-hours post ingestion without changes in RER[16-18]. Conversely, two of those investigations[17,18] tested products with more than twice the caffeine content utilized in the current investigation as well as different doses of green tea and/or catechin content within green tea. Dulloo et al.[7] found a synergistic effect of green tea extract (i.e., standardized for EGCG) and caffeine on 24 hour energy expenditure that was 2.8% greater than caffeine alone. It has also been observed that elevations in REE have been accompanied with elevations in free fatty acids over a 3-hour period in a caffeine and green tea thermogenic drink[16]. Likewise, capsaicinoids, such as the one in the investigational product, have shown to increase REE, lipolysis, fatty acid oxidation[19,20], reduce fat mass and improve body composition over 12 weeks of supplementation[13]. Additionally, L-Carnitine plays a role in fat metabolism by facilitating the transport of long chain fatty acids across the mitochondrial inner membrane, aiding in β-oxidation, and therefore may be useful for weight loss[21], however the current investigation did not observe changes in substrate oxidation via RER nor did it measure plasma free fatty acid levels. Caffeine has also been shown to elevate metabolic rate through respiratory alteration (i.e., hyperventilation and lower RER), stimulation of the SNS, and mobilizing free fatty acids via lipolysis[4,22]. A recent review by Rondanelli et al.[9] shows equivocal evidence for green tea's effect on REE whether taken chronically or acutely, however slightly more favorable results were shown for RER (i.e., significantly lower fasting value suggesting greater fat oxidation) when green tea extract is consumed chronically. Future studies should analyze circulating free fatty acids and glycerol as biomarkers of fatty acid oxidation and determine whether the observed elevation in REE translate to significant weight loss with chronic consumption of BXT. Notably, our lab published data on a multi-ingredient thermogenic dietary supplement that contained caffeine, capsicum and black pepper extract amongst other bioactives, standardized for capsaicinoids and piperine that demonstrated significant improvements over placebo in body composition, waist and hip girth, and cravings over an 8-week period in conjunction with exercise and a hypocaloric diet[14].

In addition to the observed effects on metabolic parameters, BXT significantly elevated multiple indices of affect that impact weight management. Concentration, energy, mood, and focus were positively influenced by BXT compared with PL at 120 and 180 min. Given the noted trends, this positive effect from BXT may have also occurred earlier (at 60 min) for concentration and mood. Motivation was also positively influenced by BXT compared with PL at 180 min and possibly earlier given the trend at 120 min. Caffeine has been shown to positively enhance mood state, energy, creative problem-solving, and motivation[23,24]. Caffeine and capsaicinoids may both suppress appetite through neurotransmitter and catecholamine release (i.e., increased dopamine, norepinephrine, and serotonin levels)[25,26] and inhibition of appetite stimulating signals (i.e., ghrelin)[27]; however, this investigation observed appetite suppression in both groups similarly. Alternatively, no changes were observed in fatigue within or between groups. It has been noted that successful performance in any weight loss regimen must begin and be anchored by positive thinking, mood, and greater energy[28,29]. Thus, these observed effects from BXT are notable.

Lastly, BXT did significantly elevate blood pressure compared with PL, but always stayed within normal clinical ranges (<120/80 mm Hg). SBP was significantly greater at 60 min while DBP was significantly greater for BXT at all time points post-ingestion (i.e., 60, 120, and 180 min) compared to PL. There were no differences in HR between groups.

Brown et al.[30] found that EGCG significantly reduced diastolic blood pressure; however, the dose was more than twice that of the current investigational product. In contrast, caffeine can increase blood pressure by increasing vascular resistance[31] and thus has been observed in other thermogenic supplements over an acute 3-hour post ingestion window[32]. Therefore, the interaction between the combination of EGCG and caffeine may attenuate the increase in blood pressure. According to one review, caffeine may be expected to increase blood pressure by approximately +2-4 mm Hg, but there was no mention of a specific dose to provide context[33]. In a more recent review, Higdon and Frei[34] noted that caffeine doses greater than 200 mg could cause blood pressure elevation in some normotensive individuals, and that this elevation may be problematic for individuals with existing hypertension since a 2-mm Hg reduction could drop stroke mortality by 10% and lower mortality by CHD by 7%. That said, during this clinical trial BXT was well tolerated without any reported adverse events by the subjects.

Conclusions

We conclude that a single dose of BURN-XT™ was able to safely increase resting energy expenditure, energy, mood, focus, concentration, and motivation. Given that these factors are known to favorably impact weight management, future studies should determine whether daily supplementation with BXT reduces body weight, alters plasma metabolomics, myokine secretion and/or improves body composition. Given the known response with many of the ingredients in BXT, future studies should also examine the effect of higher doses on the changes in REE, RER, and substrate oxidation.

Media-Friendly Summary

This study demonstrated that a single dose of an over-the-counter thermogenic supplement (BURN-XT™) increased metabolic rate, energy, mood, focus, and concentration compared to a placebo. These findings in healthy men and women are notable since it is known that metabolic rate and the aforementioned indices of affect have beneficial effects on weight loss and weight management. Aside from small, transient increases in systolic (at 60 min) and diastolic (at 60, 120, 180 min) supplementation was well tolerated with no side effects being reported by the subjects. Future studies should ascertain if daily dosing with BURN-XT™ over an extended period of time results in weight loss and/or beneficial changes in body composition.

Author Contributions

ML carried out participant recruitment, data collection, coordination of the study and compliance, data analysis, interpretation, and prepared the manuscript. TZ and HL carried out the study design, interpretation, and prepared the manuscript. All authors read and approved the final manuscript.

Funding

This study was funded in part by a research grant from NutraHoldings, Inc.

Acknowledgements

The authors would like to thank all the study participants who completed the study protocol. Publication of these results should not be considered as an endorsement of any product used in this study by the Center for Applied Health Sciences.

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