Effect of a Thermogenic Supplementation on Post Aerobic Exercise Hemodynamic Responses in Healthy Young Men

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ABSTRACT
Introduction: The use of food supplements with esthetic or performance-enhancing goals has been largely investigated. Thermogenics are supplements that increase energy expenditure through thermogenesis and are widely consumed by individuals seeking to improve body composition and exercise performance. Objective: To evaluate the effects of a commercially available thermogenic supplement on post-exercise blood pressure responses. Materials and Methods: Twenty-seven healthy young men participated in the study. Nine volunteers were assigned in the control group (21.67 ± 1.87 years), nine in the thermogenic group (24.00 ± 4.18 years), and nine in the placebo group (23.67 ± 3.04 years). The volunteers performed a treadmill aerobic exercise session for 60 minutes at 60 to 85% HRmax after the treatment protocol. The hemodynamic variables were measured at rest and during 60 minutes in the post-exercise recovery. The normality of the data was evaluated using the Shapiro-Wilk test. Baseline momentum and post-exercise recovery were analyzed using the two-way Anova test (group versus time factors), with Bonferroni post-hoc test. The level of statistical significance was set at p <0.05. Results: The thermogenic supplement did not significantly compromise post-exercise hypotension when compared to the other groups. However, thermogenic supplementation increased the blood pressure in >5 mmHg, which reportedly plays an important role in cardiovascular diseases. Conclusion: The use of the thermogenic Lipo 6 Black Ultra Concentrate Nutrex® did not alter PEH in healthy youngsters. However, since an increase in the blood pressure was observed, this supplementation must be administered with caution.

Keywords: Thermogenic. Running. Post-exercise hypotension.

RESUMO
Introdução: O uso de suplementos alimentares com objetivos estéticos ou de melhoria no desempenho tem sido amplamente investigado. Termogênicos são suplementos que aumentam o gasto de energia através da termogênese e são comumente consumidos por indivíduos que buscam melhorar a composição corporal e o desempenho no exercício. Objetivo: Avaliar os efeitos de um suplemento termogênico comercialmente disponível nas respostas da pressão arterial pós-exercício. Materiais e Métodos: Vinte e sete jovens voluntários participaram do estudo. Nove voluntários foram designados no grupo controle (21,67 ± 1,87 anos), nove no grupo termogênico (24,00 ± 4,18 anos) e nove no grupo placebo (23,67 ± 3,04 anos). Os voluntários realizaram uma sessão de exercício aeróbio na esteira por 60 minutos em 60-85% da FCmax após o protocolo de tratamento. As variáveis hemodinâmicas foram avaliadas em repouso e durante 60 minutos após recuperação do exercício. A normalidade dos dados foi avaliada pelo teste de Shapiro-Wilk. O nível de significância estatística foi estabelecido em p <0,05. Resultados: O suplemento termogênico não comprometeu significativamente a hipotensão pós-exercício quando comparado aos outros grupos. No entanto, o suplemento termogênico aumentou a pressão arterial em >5 mmHg, o que reportadamente pode desempenhar um papel importante em doenças cardiovasculares. Conclusão: O uso do termogênico Lipo 6 Black Ultra Concentrate Nutrex® não alterou a HPE em homens jovens saudáveis. No entanto, como foi observado um aumento na pressão sanguínea, essa suplementação deve ser administrada com cautela.

Palavras-chave: Termogênico. Corrida. Hipotensão Pós-Exercício.
INTRODUCTION

The use of dietary supplementation by physical activity practitioners has been widely employed to improve sports performance or for aesthetic purposes. Dietary supplements are concentrated sources of nutrients (vitamins, minerals, carbohydrates, fats, proteins, or plant extracts) intended to correct nutritional deficiencies or support specific physiological functions (CRIVELIN et al., 2018). It is estimated that approximately 20% of the American population consumes supplements for physical-enhancing purposes (DICKINSON et al., 2014).

A popular subset of these supplements, termed thermogenic, purportedly increases thermogenesis, promotes fat oxidation and improves physical performance (TINSLEY et al., 2017). Thermogenic supplements are ergogenic resources containing a combination of ingredients such as caffeine, green tea, rauwolscine, plant extracts, and fruits. They are used by many physical activity practitioners in order to keep the metabolism accelerated due to its thermogenic action. The increase in metabolism provided by this action promotes higher energy expenditure through fat oxidation (OUTLAW et al., 2014).

The sympathomimetic substances present in thermogenic compounds have been regarded as regulatory agents of adrenergic receptors (β1, 2, and 3 or α1). In general, blood pressure increases through the activation of α1-adrenergic receptors. Similarly, β1-adrenergic receptors increase heart rate. Additionally, ghrelin secretion in the stomach can alter appetite. β2 adrenergic receptors binding produces smooth muscle relaxation and is associated with bronchodilation, and the activation of β3 adrenergic receptors is associated with fatty acids oxidation and energy production (MUND; FRISHMAN, 2013).

A commercial thermogenic supplement that has been widely marketed is called Nutrex Lipo-6 Black Ultra Concentrated® (Nutrex Research, Inc., Oviedo, Fla.). It consists of caffeine, yohimbine and diiodine that act synergistically with synephrine. Although the mechanisms of this thermogenic supplement are understood, its effects on exercise-induced hemodynamics responses, such as post-exercise hypotension (PEH), have never been investigated. It has been reported that this supplement interacts with the central nervous system by stimulating vasoconstriction and elevating blood pressure, but its physiological role is not fully described (CAMPBELL et al., 2016). Recent studies with healthy individuals have shown that the use of thermogenic supplements could be associated with brain damage, gastrointestinal problems, and cardiovascular diseases (GOMES et al., 2014). In spite of the expressive adverse effects, there is no guarantee that thermogenic supplements were causative since they were reported in case studies.

It is well known that a single exercise session can promote a decrease in blood pressure levels immediately after it is over, and this effect remains for many hours. This clinical phenomenon is called post-exercise hypotension, in which the blood pressure values can be even smaller than those before the exercise session (RODRIGUES-JUNIOR et al., 2017). The mechanisms that affect post-exercise blood pressure are related to hemodynamic, humoral, and neural factors (ANUNCIAÇÃO; POLITO, 2011). Hemodynamic factors reduce cardiac output and peripheral vascular resistance, while neuro-humoral affect the afferent system, renin-angiotensin-aldosterone mechanism, and the antidiuretic hormone (BRUM et al., 2004). Efferent action of the autonomic sympathetic and parasympathetic nervous systems also contributes to this phenomenon (ADER et al., 2005).

Although several effects related to the use of thermogenic supplements have been reported, there are few studies regarding the influence of the use of these substances on PEH, which is an important non-drug tool for blood pressure lowering and control. Therefore, the present study aims to investigate the effect of an aerobic exercise session in the post-exercise blood pressure response in thermogenic supplement users.

MATERIALS AND METHOD

Search Type

This single-blind, placebo-controlled investigation was carried out with twenty-seven volunteers divided into three groups: Thermogenic + Exercise (TE) (n=9, 24.0 ± 4.18 years); Placebo + Exercise (PE) (n = 9, 23.67 ± 3.04 years), and Control + Exercise (CE) (n = 9, 21.67 ± 1.87 years). Volunteers participated in this study when the following inclusion criterion was fulfilled: subjects were athletes or recreational practitioners of strength or aerobic training (at least five times a week, 30 minutes per session). Subjects with any known chronic-degenerative disease, smokers, and users of any anti-hypertension medicines or nutritional supplements were excluded from this investigation. A previous study about PEH and cardiac autonomic modulation was considered to calculate the minimum sample size (TEIXEIRA et al., 2011). Using a
statistical power of 0.90 and an α error of 0.05, a sample size of at least fifteen participants was found to be required for this study. The volunteers were recruited through electronic and printed advertisements on notice boards at a local university.

All volunteers were considered active according to the Ipaq test. Participants who had difficulties performing the aerobic exercise session were not used in this research. During the study, subjects were instructed to refrain from any other supplement. They were also asked to maintain their regular diet and training program. This study was approved by the ethics committee of the Universidade Federal do Piauí (Ufpi), Teresina, PI, Brazil under protocol 57089516.3.0000.5214. All participants signed the consent form according to resolution 196/96 of the National Health Council.

Subjects completed the experimental trial at the same time (8-11 am). During the first stage, the volunteers were given the supplements. At the next stage, individuals were anthropometrically evaluated. Before aerobic exercise, volunteers remained at rest for 10 minutes when heart rate and blood pressure baseline measurements were assessed. Blood pressure measurements were taken before and during a post-exercise 60 min period of recovery, at intervals of 20 min between each measurement.

EXPERIMENTAL PROCEDURES

Anthropometric measurements

Body mass was assessed using a digital scale (Welmy, model W300, Brazil) with an accuracy of 0.02 grams and a capacity of 150 kg. Height was measured using a portable stadiometer attached to the scale. Sample characterization is presented in Table 1 with values of mean and standard deviation of the volunteers’ body characteristics.

Table 1 – Anthropometric variables of the participants

|                | Control       | Thermogenic   | Placebo       |
|----------------|---------------|---------------|---------------|
| Age (years)    | 21.67 ± 1.87  | 24.00 ± 4.17  | 23.67 ± 3.14  |
| Weight (kg)    | 74.54 ± 13.48 | 76.80 ± 5.95  | 70.17 ± 10.57 |
| Height (cm)    | 176.45 ± 5.24 | 172.68 ± 4.99 | 173.33 ± 7.60 |
| BMI (kg/m²)    | 24.25 ± 3.41  | 25.76 ± 2.22  | 23.31 ± 2.84  |

SD, standard deviation; BMI, body mass index; n=9 each group. Source: Research data.

Supplementation

TE and PE volunteers ingested identical capsules with different content. Capsules intake started 20 hours before exercise, one capsule being ingested every 10 hours, totalizing at the end 3 capsules per volunteer. The last capsule was ingested 1 hour before aerobic exercise. PE group ingested capsules composed...
of 12mg starch and TE group ingested capsules with Lipo 6 Black Ultra Concentre Nutrex. The capsules were identical in taste, smell, and color. The dosage of the termogenic supplementation was determined according to the manufacturer’s recommendation. CE group did not intake any capsule.

Figure 2 – Thermogenic Supplement Label (Lipo 6 Black Ultra Concentre Nutrex®)

Source: Lipo 6 Black Ultra Concentre Nutrex® label.

Physical exercise intervention

The experimental aerobic exercise session was performed on a treadmill (ProAction BH fitness, Puerto del Carmen, Spain). Firstly, the subjects were instructed and submitted to a warm-up session on the treadmill for three minutes at low intensity (<60% of age-predicted HRmax (220 – age in years)). Immediately thereafter, they started a gradual increase in speed every minute, during the first 5 min until they reached the prescribed intensity, determined through the equation (HRmax – HRresting) x % intensity) + HRresting, described by Karvonen, Kentala e Mustala (1957). They remained in this intensity range until the end of the workout (60 minutes).

Hemodynamic variables

Heart rate (HR) values were measured with the heart rate monitor V800 (Polar® Electro Oy, Kempele, Finland) before, at 0, 20, 40, and 60 minutes during the 60-minute post-exercise recovery period. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured according to the recommendations of the Brazilian Guidelines on Hypertension (2010) using a BR A100 Plus oscillometric device (MICROLE BR3BTO-A/BR), previously validated by Cukson et al. (2002). During this period, the volunteers were asked to remain seated for at least 20 min in a quiet environment with a temperature between 24°C and 27°C.

Statistical analysis

The data are presented as mean ± standard deviation of the mean. The normality of the data was evaluated using the Shapiro-Wilk test. The groups and moments (before and at 0, 20, 40, and 60 min post-exercise) were compared using the two-way Anova test, and post hoc tests with the Bonferroni correction were performed to analyse the interaction between the factors (group versus time). The significance level was set at p <0.05. Cohen’s d effect size (ES) was used to estimate the magnitude of the difference (COHEN, 1988). Values of 0–0.19, 0.20–0.49, 0.50–0.79, and >0.80 were considered trivial, small, moderate, and large, respectively (LAKENS, 2013). The entire analysis was performed using SigmaPlot 11.0 software.

RESULTS

The participants were statistically similar in age, height, body mass and BMI. Hemodynamic behavior at rest did not show significant differences between groups (Table 2). No adverse events occurred as a result of supplementation. Most hemodynamic and safety variables were unaltered after the supplementation.
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Table 2 – Hemodynamic responses before and during the 60 min of post-exercise recovery

|                | Before  | 0     | 20    | 40     | 60     |
|----------------|---------|-------|-------|--------|--------|
| **HR (bpm)**   |         |       |       |        |        |
| Control        | 70.44±6.73 | 125.67±13.04* & | 93.89±6.90# & | 87.78±9.35# & | 85.78±9.67# & |
| Placebo        | 67.11±8.33 | 132.44±10.65* & | 84.11±11.76# & | 78.56±11.86# & | 74.78±13.18# & |
| Thermogenics   | 73.67±10.00 | 121.44±9.15* & | 98.00±6.48# & | 89.33±10.91# & | 88.22±12.40# & |
| **SBP (mmHg)** |         |       |       |        |        |
| Control        | 120.78±12.09 | 130.00±14.80β | 115.44±12.02# & | 110.89±10.03# & | 112.44±9.23β & |
| Placebo        | 128.00±13.03 | 144.78±16.55β | 121.44±13.52# | 119.56±11.38# | 117.22±9.99β & |
| Thermogenics   | 126.67±12.39 | 130.33±15.07β | 121.56±14.90# | 119.78±15.87# | 118.22±10.76β & |
| **DBP (mmHg)** |         |       |       |        |        |
| Control        | 72.89±12.19 | 75.33±17.13β | 74.00±12.09# | 69.89±9.28# | 69.67±11.54β & |
| Placebo        | 69.89±6.68 | 79.11±10.66β | 71.56±10.22# | 68.67±11.18# | 71.00±8.92β & |
| Thermogenics   | 73.22±5.24 | 80.00±11.08β | 72.22±8.06# | 71.56±6.71# | 70.00±7.23β & |
| **MBP (mmHg)** |         |       |       |        |        |
| Control        | 88.85±11.61 | 93.56±15.00 | 87.81±10.97 | 83.56±8.38 | 83.93±9.91 |
| Placebo        | 89.26±9.28 | 101.00±10.88β | 88.07±9.77# | 85.63±10.46# | 86.41±8.20# |
| Thermogenics   | 91.04±7.10 | 96.78±8.62 | 88.67±8.49# | 87.63±7.41# | 86.07±7.17# |

Source: Research data.

HR * significant difference at 0 min compared to resting in placebo, control, and thermogenic groups (p < 0.05); # significant differences at 20-min post-exercise intervals (20, 40, and 60 min) compared to 0 min in all groups (p < 0.05). & significant difference for 0 min and 20-min post-exercise intervals (20, 40, and 60 min) compared to rest. There was no group x time interaction for the SBP and DBP variables. However, there was a moment interaction. DBP β, SBP β - significant difference at 0 min and 60 min compared to resting. & significant difference between 20 min post exercise intervals (20, 40, and 60 min) compared to 0 min. MBP * significant difference for 0 min compared to resting in placebo; # significant differences at 20 min post exercise intervals (20, 40, and 60 min) compared to 0 min in placebo and thermogenic groups.

Figure 3 – Behavior of the heart rate during the 60 min of post-exercise recovery. Data presented as means and standard deviation of the means

Source: Research data.

HR * significant difference between 0 min and resting in placebo, control, and thermogenic groups (p < 0.05); # significant differences at 20-min post-exercise intervals (20, 40, and 60 min) compared to 0 min in all groups (p < 0.05). & significant difference between 0 min and at 20-min post-exercise intervals (20, 40, and 60 min) compared to rest.

Thermogenic supplementation did not abolish PEH compared to PE and CE groups. However, it was observed that the supplement suppresses SBP reduction. There was no interaction between the factors group x time in the SBP analysis (p = 0.16, ᵃ = 0.22). There was also no effect for the group factor (p = 0.24, ᵃ = 0.12), but there was an effect for the moment factor (p <0.01, ᵃ = 1.00) in which the means of the groups (125.14 ± 2.10) was significantly lower at 0 min (135.03 ± 2.10, p <0.01, ᵃ = 4.71), and higher at 20 min (119.37 ± 2.10, p < 0.01, ᵃ = 2.75), 40 min (116.79 ± 2.43, p < 0.01, ᵃ = 3.68), and 60 min (115.96 ± 2.10, p <0.01, ᵃ = 4.37).

Figure 4 – Behavior of the systolic blood pressure before and during the 60 min of post exercise recovery. Data presented as means and standard deviation of the means

Source: Research data.

* ᵃ significant difference to 0 min and moment post exercise at 60-min intervals compared to resting. & significant difference to moment post exercise at 20-min intervals (20, 40, and 60 min) compared to immediately post exercise.

There was no interaction between the factors (group vs. moment) in the DBP analysis (p = 0.84, ᵃ = 0.29). There was also no effect for the group factor (p = 0.97, ᵃ = 0.10), but there was an effect for the moment factor (p <0.01, ᵃ = 0.98) in which the means of the groups (72.00 ± 1.44) was significantly lower at 0 min (78.14 ± 1.44, p <0.01, ᵃ = 4.26), and higher at 20 min (72.59 ± 1.44, p <0.01, ᵃ = 0.41), 40 min (75.40 ± 15.92, p < 0.01, ᵃ = 0.39), and 60 min (70.22 ± 1.44, p <0.01, ᵃ = 1.24).
single dose of the Nutrex Lipo-6 Black® in young sub-
taining cellulose (500mg), after 60 minutes of inges-
trients. The placebo group ingested a capsule con-
mogenic supplement containing anhydrous caffeine
maining mainly synephrine (20 mg), yohimbine (4 mg),
s of the thermogenic supplement based on caffeine,
theobromine, p-synephrine, yohimbine HCL, and
auwolscine was not able to significantly alter the 1-
hour PEH in healthy young men. However, therrno-
gen supplementation increased the blood pressure
in >5 mmHg compared to the placebo and control
groups. The reduction of >5 mmHg is reportedly asso-
ated with >34% less stroke risk and >21% less coro-
nary heart diseases (MACMAHON et al., 1990).
Magalhães (2013) investigated the effect of a
single dose of the Nutrex Lipo-6 Black® in young sub-
jects in a 30-minute resting state, immediately after
an aerobic exercise session and 30 min post-exercise.
There were no significant differences between supple-
mented and placebo groups in resting measures and
after 30 minutes of a 40-minute moderate aerobic
session. This result is presumably due to the low do-
sage of the supplement ingested: two capsules con-
taining mainly synephrine (20 mg), yohimbine (4 mg),
caffeine (200 mg), phenylethylamine (120 mg), diiodo-
thyronine (100 mcg), and other substances. The main
differences compared to our study was the dosage (3
capsules) used and the time of supplement adminis-
tration (24h).

Moreover, Jitomir et al. (2008) analyzed the ef-
ef of a thermogenic containing the same active in-
gredients as ours. They compared 3 capsules of a ther-
mogenic supplement containing anhydrous caffeine
(317 mg), mate herb extract, synephrine HCL (20 mg),
yohimbine and yohimbine HCL (9 mg), and other in-
gredients. The placebo group ingested a capsule con-
taining cellulose (500mg), after 60 minutes of inges-
tion and 60 minutes after an aerobic exercise session
using an incremental protocol. Similar, they reported
no significant differences in HR, SBP, and DBP at mo-
ments before, during, and after the exercise for the
supplement and placebo groups.

However, Haller et al. (2008) reported an in-
crease in DBP after a 30-minutes cycle ergometer ses-
ion at 75-80% HRmax after the use of a thermogenic
supplement containing synephrine (21mg) and caffei-
ne (304mg) in adults. It is possible that the moderate
duration and the type of exercise (cycle ergometer)
did not significantly alter the absorption of synephrine
and caffeine, causing this increase in DBP differently
from our long-duration exercise study.

The effects of synephrine, an ingredient present
in several thermogenic supplements, is controver-
sial. When investigated in combination with caffeine,
some studies show that it causes an increase in HR and
PA (BENT; PADULA; NEUHAUS, 2004; PENZAK et al.,
2001). However, when we investigated supplements
containing synephrine, caffeine, and other ingredients,
no increase in HR and PA was observed (HALLER; BE-
NOWITZ; JACOB, 2005), which reinforces our findings.

It has been reported that supplements con-
taining yohimbine, another thermogenic component
used in our study, is related to adverse effects such as
increased SBP, DBP, and HR after supplementation at
rest (SWANN et al., 2013), as well as increased panic
symptoms respectively (VASA et al., 2009). They re-
ported changes in hemodynamic variables in healthy
youngsters after 0.4 mg/kg dosages. Moreover, Hof-
man et al. (2009) observed a significant increase in
HR and SBP, but no change in DBP. On the other hand,
Wilborn et al. (2009) and Jitomir et al. (2008) stated
that the supplementation containing yohimbine did
not cause an increase in HR and BP.

A study observed blood pressure elevation
caused by caffeine in subjects prone to hyperten-
sion (NOORDZIJ et al., 2005). This effect is corrobo-
rated by studies that evaluated PEH after caffeine use
in the respective populations, in which caffeine had
adverse effects on hemodynamic variables (SOUZA et al.,
2016). However, similarly to our investigation,
the same result was not found in a study with healthy
youngsters when they underwent the ingestion of caf-
feine (FERNÁNDEZ-ELÍAS et al., 2015).

Mitchell et al. (2011) found that the consump-
tion of theobromine, also present in the Lipo-6 Black
Ultra Concentre Nutrex®, in combination with caffeine
increased SBP, DBP, and HR at rest when compared to
the group that ingested only the caffeine. This effect is
presumably due to its vasodilatory properties, which
theoretically would explain the control of HR and BP, and probably the non-attenuation of SBP immediately after exercise. Rauwolscine, also known as α-yohimbine, is an alkaloid found in the same plant from which yohimbine is extracted, and it acts as an adrenergic blocking agent (LUCAS; NEAL-KABABICK; ZWEIGENBAUM, 2015). To the best of our knowledge, there are no studies in the literature evaluating the effects of this ingredient alone or with other ingredients in hemodynamic variables. Only one study with dogs found a vasodilator effect and an adrenergic blockade, but no significant changes in HR were found (LEVY; KOELLE, 1958).

The effects of acute thermogenic supplementation on PEH are controversial. Tinsley et al. (2017) compared the chronic effects of two supplements over six weeks, in combination with a resistance training program. One group ingested a thermogenic containing Green Tea, Anhydrous Caffeine, Ginseng, N-Acetyl-L-Tyrosine, 4: 1 Maca (Lepidium meyenii) Root Extract, Alpha Lipoic Acid and other ingredients. The other group ingested a maltodextrin-containing placebo. There were no differences in resting HR and BP between both groups.

The main limitation of our study is that we investigated only the acute effect of thermogenic supplementation. Thus, we were unable to detect significant changes in the PEH during the exercise session. Moreover, the sample consisted of healthy volunteers only, and therefore, the results cannot be extended to people with health problems. Further investigation, with longitudinal and crossover designs, should assess the effect of the long-term use of thermogenics on the post-exercise hemodynamic response, as well as in other populations.

CONCLUSION

This study aimed to verify the effects of thermogenic supplements on post aerobic exercise session hemodynamic responses. We demonstrated that there was an increase of >5mmHg on post-exercise blood pressure after 3 dosages of thermogenic supplements ingestion, which can increase the risk of cardiovascular diseases, such as hypertension and stroke. Based on the results of the present investigation, the intake of thermogenic supplements may abolish the PEH response in healthy young people. Our results reinforce the need for further studies on a larger population and with chronic administration of thermogenic supplements in order to better clarify the hemodynamic effects of this supplement.

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