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A caffeine containing weight loss supplement augments hemodynamic responses after exercise

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ABSTRACT

Background: Since the effects of supplements can be potentially harmful and/or ineffective to obtain desired positive benefits, there is a need to investigate supplementation to understand the responses of physiological systems, to educate consumers, and to provide feedback for businesses creating these supplements. The purpose of the current study was to test hemodynamic responses of a weight loss supplement and determine its effects on hemodynamic variables.
Methods: 31 participants underwent a randomized, double-blind, crossover study design and received a placebo or supplement on two separate days. Baseline measures of all variables were assessed prior to exercise. During exercise, each participant performed treadmill running at 80% VO_{2PEAK} until volitional fatigue. Immediately post-exercise, hemodynamic measures were recorded at multiple time points.
Results: There was a significant condition * time interaction with the supplement having a higher PWV for the carotid to femoral segment ($p = 0.004$). There were also significant condition * time interactions for heart rate ($p = 0.001$). Large arterial elasticity was significantly lower for the supplement ($p = 0.005$). Systolic blood pressure was conditionally higher ($p = 0.001$), as was diastolic blood pressure ($p = 0.003$) and mean arterial pressure ($p = 0.003$). Vascular resistance was conditionally higher for the supplement ($p = 0.044$).
Conclusions: Ingredients in the supplement caused multiple negative effects within hemodynamics and were ineffective at increasing running time.

1. Introduction

The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) estimates that over 1 billion people worldwide have hypertension [1] and the World Health Organization estimates 9.4 million deaths per year are caused by it, along with other issues of cerebrovascular disease and ischemic heart disease [2]. An approach to lowering blood pressure is through the loss of excess body weight in individuals who are obese [3] through a combination of diet, exercise, and/or nutritional supplements. In 2008, a survey showed 33.9% of Americans attempting to lose weight turned to dietary supplements, many of which contain caffeine as a primary ingredient, for help [4]. Of concern, approximately 2661 emergency department visits per year for tachycardia, heart palpitations, and chest pain, are attributed to weight-loss supplements in persons 20–34 years of age in the United States [5].

Previous research conducted on dietary supplements investigated the various effects of caffeine and supplements containing caffeine. Caffeine has been shown to have negative effects on hemodynamic variables during exercise and rest [6–11]. Negative effects include rises in systolic (SBP) and diastolic (DBP) blood pressure [8,12–14], augmentation of the exercise pressor response [15], and increased vascular resistance [10].

Other supplements demonstrate inverse hemodynamic responses relative to caffeine and may potentially offset negative effects. Garlic is one such ingredient and has been shown in a meta-analysis to lower blood pressure in hypertensive participants taking the supplement chronically [16]. Another study demonstrated garlic's effectiveness in lowering blood pressures over a 12-week period, but was dose dependent. Results demonstrated a dose response in the ability of garlic to attenuate blood pressures in participants with hypertension [17]. Turmeric, derived from the plant *Curcuma longa*, may also oppose caffeine's negative effects on hemodynamics. One of the few human studies observing turmeric's effects on arterial elasticity measured differences between four groups of postmenopausal women prescribed with turmeric and exercise, exercise only, turmeric only, or a control. The most positive increases in elasticity were observed in the exercise and turmeric group, but the turmeric only group was greater than the

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control and similar to the exercise only group in increasing arterial elasticity. Both turmeric groups also significantly lowered central and peripheral systolic blood pressure [18].

Lowering of blood pressure in hypertensive and normotensive populations through aerobic exercise has been well established [19]. At the onset of exercise, central command and neural feedback from muscles signal to increase both heart rate and vascular resistance through the exercise pressor reflex, thus increasing systolic blood pressure [20]. At exercise cessation, baroreceptors in the aorta and carotid arteries signal to bring pressure back to homeostatic levels. However, oftentimes blood pressure will drop below resting values, to a state known as post exercise hypotension (PEH) [21]. Attenuation of PEH may potentially reduce the benefits of aerobic exercise on blood pressure and has been previously demonstrated after acute aerobic bouts in young males and females [11]. Based on a longitudinal study in middle-aged men, elevation of SBP recovery within 2 min post-exercise increases the risk of acute myocardial infarction [22].

The current product studied contains ingredients that, when combined, have unknown consequences on important physiological systems post-exercise. Furthermore, research investigating claims other than those listed on product labels may help shed new light on the potential benefits or risks of taking dietary weight loss supplements. Therefore, the purpose of the current study was to test hemodynamic responses of a weight loss supplement and determine its effects on hemodynamic variables after aerobic exercise. It was hypothesized the presence of both garlic and turmeric would attenuate any negative effects from caffeine on the hemodynamic system. It was also hypothesized that caffeine's presence would extend time to volitional fatigue.

2. Methods

Approval for study design was granted by the University of Texas at Brownsville Institutional Review Board and conformed to the ethical guidelines set forth by the 1975 Declaration of Helsinki. Participants were recruited from the surrounding community and underwent testing in a double-blind, crossover design to investigate hemodynamic responses to a weight loss supplement designed for athletes. Thirty-one participants (15 males, 16 females) between the ages of 18–40 reported to the lab for three sessions with each session separated by at least 48 h. Females were required to be within the luteal phase of their menstrual cycle for testing.

Inclusion criteria consisted of the participant being normotensive or prehypertensive (BP < 140) and devoid of cardiovascular or metabolic disease, joint issues, or chronic pain. Participants were required to refrain from consumption of other ergogenic aids, with the exception of caffeine, for at least 30 days and were also required to abstain from caffeine for at least 12 h prior to testing.

The first day, participants completed the informed consent form and health status questionnaires. Anthropometric measures of height and weight were collected, followed by treadmill VO_{2PEAK} testing utilizing the Bruce Protocol [23]. During treadmill testing, gases were collected and analyzed with the MOXUS Modular VO2 System (AEI Technologies, Inc., Pittsburgh, PA, USA).

For the two experimental protocols, participants fasted for at least 8 h prior to testing. Sessions were randomized and either a placebo or Shred Matrix (MusclePharm Corp., Denver, CO, USA) were ingested on two separate days with at least 48 h between each session. The supplement was administered as one dose (3 capsules) comprised of a proprietary blend (2698 mg) with unknown quantities of caffeine, garlic, and turmeric. Other ingredients within the supplement claimed to affect appetite, mood, and other systems not of interest to this study. Upon arriving, participants were required to give a urine sample to measure urine specific gravity (USG) with a Clinical Urine Refractometer 300005 (SPER Scientific, Scottsdale, AZ, USA). If inadequately hydrated, participants ingested approximately one cup of water to rehydrate. Urine samples were continuously collected every 20 min, with continuing ingestion of water as needed, until participants were deemed hydrated (USG ≤ 0.010) according to standards established by the National Athletic Trainers Association (NATA) [24]. Lower USG values recommended by NATA were deemed more appropriate for this study as participants were required to exercise at higher intensities for prolonged periods.

After adequate hydration, participants rested in the supine position for 10 min in accordance with equipment manufacturer recommendations. Prior to the administration of the supplement or placebo, baseline measures of heart rate (HR), SBP and DBP, vascular resistance (VR), and large arterial elasticity (LAE) measures were recorded via the HDI/PulseWave CR-2000TM Research Cardio Vascular Profiling System (Hypertension Diagnostic, Inc., Eagan, Minnesota, USA). The HDI equipment, used extensively in the cardiovascular field [25–31] is a noninvasive technique used to calculate capacitive and oscillatory arterial compliance. It utilizes a modified Windkessel model to explain the heart's burden while pumping blood and the association between blood flow through the arteries and blood pressure [31]. Cohn et al. (1995) validated the use of the noninvasive technique against brachial artery cannulation with Statham transducer recordings of waveforms. Noninvasive techniques of pulse wave analysis involve the use of a pressure cuff placed on the left-upper arm and a piezoelectric-based sensor placed over the right radial artery near the wrist. Software models use blood pressure and sensor readings to quantify large and small arteries from the mathematical relationship between capacitive and oscillatory arterial compliance, and systemic vascular resistance [30].

Equations provided by the manufacturer give insight into the derivation of estimation values. VR = MAP/CO. SV = −6.6 + 0.25(ET-35)-0.62HR + 40.4BSA-0.51Age (ml). CO = (SV ∗ HR)/1000 (L/min). ET = ejection time in milliseconds measured from approximate beginning of systole to approximate beginning of diastole. BSA = body surface area ($0.007184 * WT^{0.425} * HT^{0.725}$). WT = weight in kilograms. HT = height in centimeters. Age = age of participant in years. Baseline pulse wave velocity (PWV) was also recorded prior to exercise via the SphygmoCor® CPV Pulse Wave Analyzer (AtCor Medical, Itasca, IL, USA).

After baseline measures, the three capsules were ingested and the participant continued to rest for another 30 min prior to the start of exercise. This time frame was chosen to allow for peak serum concentrations of caffeine to occur in the midst of exercise or during post-testing [32]. This was deemed more practical, as not all people taking supplements wait for extended periods to exercise after supplement ingestion. During exercise, each participant exercised until volitional fatigue on a treadmill at 80% VO_{2PEAK}. Treadmill speed was determined by the formula Speed = $(((VO2_{PEAK}-3.5)/0.2)/26.8) * 0.8)$. HR, BP, VR, and LAE was measured immediately post-exercise (IP) and again at 10 (Post 10, 20 (Post 20), and 40 (Post 40) minutes post-exercise. Pulse wave velocity was measured at 5 (Post 5), 15 (Post 15), 25 (Post 25), and 35 (Post 35) minutes post-exercise. Calibration of all the equipment was performed regularly according to instructions provided by manufacturers.

2.1. Statistical analysis

A 2-way analysis of variance (ANOVA) (CONDITION [Placebo vs. Supplement] × TIME [varied depending on the variables]) with repeated measures and pairwise Bonferroni-adjusted estimated marginal means was used to see if significant differences existed for analyzed variables. All repeated measures data was checked with Mauchly's Test of Sphericity. Significant interactions were analyzed post-hoc with one-way ANOVAs at each time point. Where significant condition main effects were revealed, the origin of effects was determined by paired *t*-tests. An alpha of 0.05 was used to determine statistical significance and data was analyzed using SPSS 22.0 (IBM Corporation, New York, NY, USA) and Microsoft Excel 2013 for Windows (Redmond, WA, USA).

3. Results

3.1. Participant characteristics

The average age, height, weight, VO_{2PEAK} of the cohort was 22.6 years (3.5), 168.16 cm (10.3), 69.87 kg (15.7), and 45.54 ml/kg/min (10.1), respectively. Fig. 1A and B shows effects of exercise with and without supplement on participants' HR and running times to volitional fatigue, respectively. Paired *t*-test analysis showed no significant difference in running time between the supplement and the placebo ($p = 0.12$). The placebo group ran until volitional fatigue for 26:07 (±13:02) minutes while the supplement group ran until volitional fatigue for 28:11 (±14:38) minutes. For heart rate, repeated measures ANOVA showed significant interactions for condition ∗ time ($p = 0.001$). Post-hoc analysis of simple effects with Bonferroni adjustments showed significantly higher supplement means at IP ($p = 0.02$), Post 10 ($p < 0.001$), Post 20 ($p = 0.03$), and Post 40 ($p = 0.01$).

3.2. Hemodynamic responses

Fig. 2A and B shows effects of exercise with and without supplement on participants' systolic and diastolic blood pressure, respectively. Repeated measures ANOVA showed significant condition ($p = 0.001$) and time ($p < 0.001$) main effects, but no significant interaction ($p = 0.08$). For condition, paired *t*-tests showed significantly higher supplement means at IP ($p = 0.026$), Post 10 ($p = 0.008$), Post 20 ($p = 0.002$), and Post 40 ($p < 0.001$).

For diastolic blood pressure, repeated measures ANOVA showed significant condition ($p = 0.003$) and time ($p < 0.001$) main effects, but no significant interaction ($p = 0.17$). For condition, paired *t*-tests showed significantly higher supplement means at IP ($p = 0.009$), Post 20 ($p = 0.048$), and Post 40 ($p = 0.001$).

Fig. 3A and B shows effects of exercise with and without supplement on participants' vascular resistance and mean arterial pressure. For