Effects of ingesting a pre-workout dietary supplement with and without synephrine for 8 weeks on training adaptations in resistance-trained males

Y. Peter Jung, Conrad P. Earnest, Majid Koozehchian, Minye Cho, Nick Barringer, Dillon Walker, Christopher Rasmussen, Mike Greenwood, Peter S. Murano, and Richard B. Kreider

Abstract

Background: The purpose of this study was to examine whether ingesting a pre-workout dietary supplement (PWS) with or without synephrine (S) during training affects training responses in resistance-trained males.

Methods: Resistance-trained males (N = 80) were randomly assigned to supplement their diet in a double-blind manner with either a flavored placebo (PLA); a PWS containing beta-alanine (3 g), creatine nitrate as a salt (2 g), arginine alpha-ketoglutarate (2 g), N-Acetyl-L-Tyrosine (300 mg), caffeine (284 mg), Mucuna pruriens extract standardized for 15% L-Dopa (15 mg), Vitamin C as Ascorbic Acid (500 mg), niacin (60 mg), folate as folic acid (50 mg), and Vitamin B12 as Methylcobalamin (70 mg); or, the PWS supplement with Citrus aurantium extract containing 20 mg of synephrine (PWS + S) once per day for 8-weeks during training. Participants donated a fasting blood sample and had body composition (DXA), resting heart rate and blood pressure, cognitive function (Stroop Test), readiness to perform, bench and leg press 1 RM, and Wingate anaerobic capacity assessments determined at 0, 4, and 8-weeks of standardized training. Data were analyzed by MANOVA with repeated measures. Performance and cognitive function data were analyzed using baseline values as covariates as well as mean changes from baseline with 95% confidence intervals (CI). Blood chemistry data were also analyzed using Chi-square analysis.

Results: Although significant time effects were seen, no statistically significant overall MANOVA Wilks’ Lambda interactions were observed among groups for body composition, resting heart and blood pressure, readiness to perform questions, 1RM strength, anaerobic sprint capacity, or blood chemistry panels. MANOVA univariate analysis and analysis of changes from baseline with 95% CI revealed some evidence that cognitive function and 1RM strength were increased to a greater degree in the PWS and/or PWS + S groups after 4- and/or 8-weeks compared to PLA responses. However, there was no evidence that PWS + S promoted greater overall training adaptations compared to the PWS group. Dietary supplementation of PWS and PWS + S did not increase the incidence of reported side effects or significantly affect the number of blood values above clinical norms compared to PLA.

Conclusion: Results provide some evidence that 4-weeks of PWS and/or PWS + S supplementation can improve some indices of cognitive function and exercise performance during resistance-training without significant side effects in apparently health males. However, these effects were similar to PLA responses after 8-weeks of supplementation and inclusion of synephrine did not promote additive benefits.

(Continued on next page)
Background
Research has shown that ingestion of some nutrients and/or caffeenated beverages prior to exercise can improve mental focus and/or exercise capacity [1]. For this reason, a number of energy drinks and pre-workout supplements (PWS) have been developed and marketed to athletes. The primary ergogenic properties in most of these supplements appear to be water, carbohydrate, and caffeine [1]. However, more recently PWSs have been developed that not only contain nutrients that may affect acute exercise performance (e.g., carbohydrate, caffeine, nitrates, etc.), but also nutrients that can increase energy expenditure, reduce catabolism, and promote protein synthesis thereby enhancing training adaptations when taken regularly during training (e.g., amino acids, creatine, β-alanine, etc.) [1–3]. Consequently, there has been increased interest in examining the acute and chronic safety and efficacy of PWSs marketed to active individuals [4] as well as whether adding potentially ergogenic nutrients may promote additive benefits [1].

This study examined the safety and efficacy of daily ingestion of a market leading PWS on ratings of perception of readiness to perform, cognitive function, resting energy expenditure and metabolism, exercise performance, and markers of safety. The PWS studied contained several nutrients reported to have ergogenic properties including caffeine [5], beta-alanine [6], creatine [7], nitrate [8–11], arginine alpha-ketoglutarate [12] as well as other nutrients purported to affect cognitive function like tyrosine [13, 14] and Mucuna pruriens containing L-Dopa [15, 16]. It is well established that consuming caffeine prior to exercise (e.g., 3–6 mg/kg) can improve exercise performance, cognitive function, and vigilance [5]. A number of studies also indicate that ingestion of nitrate prior to exercise (e.g., 300 mg) can improve exercise capacity [9, 11, 17–20]. Theoretically, ingesting these nutrients at effective doses prior to exercise may improve cognitive function and vigilance leading to better workout performance. If so, regular use of these types of PWSs may affect quality of training and/or training adaptations particularly if they contain nutrients that have been reported to enhance training adaptations like beta-alanine [6, 21–27] and/or creatine [7, 28].

Citrus aurantium is found in the peel of bitter orange and contains p-synephrine. Citrus aurantium (generally containing 20–100 mg of synephrine) has been purported to suppress appetite [29], increase resting energy expenditure and/or carbohydrate and fat oxidation rates [30–33] and promote weight loss [34–36] with no negative effects on the cardiovascular system [37–39]. There is also evidence that Citrus aurantium ingestion can affect memory [40, 41] and resistance-exercise performance [31]. Theoretically, adding Citrus aurantium to a PWS may promote greater resting energy expenditure, cognitive function, and/or exercise capacity during an exercise bout.

In an initial companion study that has been submitted separately upon editor request [42–44], we reported that acute ingestion of this PWS and PWS + S promoted greater changes in resting energy expenditure, perceptions of vigor and energy, and cognitive function scores compared to PLA. Therefore, the purpose of this study was to examine the effects of ingesting a market leading PWS with and without synephrine during 8-weeks of resistance-training on ratings of perception of readiness to perform, cognitive function, resting energy expenditure and metabolism, exercise performance, and markers of safety.

Methods
This study was conducted as a prospective, randomized, double-blind, and placebo controlled cohort study. The study was conducted at the Exercise & Sport Nutrition Laboratory (ESNL) at Texas A&M University after obtaining approval from the university’s Human Participant Internal Review Board.

Participant recruitment and familiarization
Apparently healthy, resistance-trained males were recruited to participate from local advertisements. Inclusion criteria required that each participant have at least 6 months of resistance training immediately prior to entering the study inclusive of performing bench press and leg press or squat. Participants were excluded if they presented with a history of treatment for metabolic disease, hypertension, thyroid disease, arrhythmias, and/or cardiovascular disease; and/or were currently using any prescription medication. Further exclusion criteria included an intolerance to caffeine and/or other natural stimulants; a history of smoking; and, excessive alcohol consumption (>12 drinks/week).
A total of 213 individuals responded to advertisements to participate in this study. Participants who met initial study entry criteria via phone interview or online questionnaire screening were invited to a familiarization session where the details of the study were explained, informed consent was obtained, medical history was assessed, a fasting blood sample was obtained, and a general medical exam was performed by a registered nurse to determine eligibility to participate in the study. A total of 122 individuals were cleared to participate in the study and participated in a familiarization session. This included explanation of the protocol, instructions for completing the food record forms and training program logs, and practicing the strength and anaerobic capacity tests that were used in the study. Participants were then matched for age, body mass, and fat free mass (FFM) and randomized into one of three dietary supplement intervention arms in a randomized manner. A total of 80 males (22 ± 4 y, 178 ± 6 cm, 80.9 ± 13.9 kg, 15.2 ± 0.7% fat, 25.6 ± 4.0 kg/m²) completed the study.

**Strength training program**

All participants were required to follow the same resistance training routine. The resistance training program consisted of training 4-days per week split into two upper and two lower body workouts per week primarily consisting of free-weight exercises for a total of 8-weeks. The 8-week training protocol was periodized in 2–3 week segments and consisted of selection from a list of 2–4 exercises for the following muscle groups: chest (two exercises for a total of six sets), back (two exercises for a total of three sets), triceps (one exercise for a total of three sets), abdominals (one exercise for a total of three sets), quadriceps (two exercises for a total of six sets), hamstrings (two exercises for a total of six sets), and calves (one exercise for three sets). Each exercise consisted of three sets of ten repetitions (week 1–3), eight repetitions (week 4–6), or six repetitions (week 7–8) performed with as much weight as the participant could perform per set. The participants recorded the amount of weight lifted during each set of exercise on training log. A training partner or fitness instructor provided signed verification that the work out was completed as recorded. Prior research from our lab has shown that this program is effective in promoting significant strength and fat free mass gains in resistance-trained athletes without nutritional intervention [45].

**Supplementation protocol**

Participants were matched for age, body mass, and FFM and randomly assigned to ingest in a double-blind manner either: (1) a flavored dextrose placebo (PLA); (2) a PWS containing beta-alanine (3 g), creatine nitrate as a salt (2 g), arginine alpha-ketoglutarate (2 g), N-Acetyl-L-Tyrosine (300 mg), caffeine (284 mg), Mucuna pruriens extract standardized for 15% L-Dopa (15 mg), Vitamin C as Ascorbic Acid (500 mg), niacin (60 mg), folic acid (50 mg), and 70 mg of Vitamin B12 as Methylcobalamin (Cellucor C4 Pre-Workout, Nutrabolt, Bryan, TX); or, 3.) the PWS with Citrus aurantium (PWS + S) extract standardized for 30% synephrine (20 mg) (Nutratech Inc., Caldwell, NJ). Supplements were independently packaged by a third party into coded single foil packets for double-blind administration following Good Manufacturing Practices and certified to contain the aforementioned ingredients by VMI Nutrition (Salt Lake City, UT). All supplements had similar color and powdered texture. Participants were instructed to ingest one foil packet per day approximately 15–30 min prior to exercise on training days and in the morning with breakfast on non-training days. Supplement compliance was verified by weekly compliance verification and collecting and counting empty packets.

**Testing sequence**

Figure 1 shows the timeline of tests performed. Participants were instructed to refrain from exercise, caffeine, and supplements containing stimulants for 48-h prior to testing. Participants presented to the lab after a 12-h fast and were required to provide a 4-days food-log that recorded their consumption of food and energy containing...
fluids. Participants training logs were assessed by a trained exercise physiologist to ensure compliance and they submitted weekly side-effect questionnaires. Participants then donated ~ 20 ml of blood via venipuncture. Following blood sampling, we administered a series of tests. This included determination of body weight, total body water using bioelectrical impedance (BIA), body composition using dual-energy x-ray absorptiometry (DXA), resting heart rate and blood pressure, cognitive function (Stroop Word - Color test), perceptions of readiness to perform via use of a visual analogue scale (VAS), one repetition maximum (1 RM) bench press, 1 RM leg press, and a 30s Wingate anaerobic capacity test on a cycle ergometer. Subjects rested 5-min between bench press, leg press, and Wingate tests as well as 2-min between sets on the bench press and leg press. Participants completed these assessments at 0, 4, and 8-weeks of training.

**Procedures**

**Training assessment**

Total lifting volume was calculated based on information recorded on the training logs. This included multiplying the amount weight lifted per set times the number repetitions completed for each exercise performed during training sessions throughout the course of the study. Total lifting volume for upper and lower extremity lifts determined how well participants tolerated supplementation protocol; and, if participants experienced any symptoms during the supplementation period. Subjects were asked to rank the frequency and severity of their symptoms for dizziness, headache, fast or racing heart rate, heart skipping or palpitations, shortness of breath, nervousness, blurred vision, and unusual or adverse effects. Additionally, participants ranked the frequency of symptoms with 0 (none), 1 (minimal: 1–2/week), 2 (slight: 3–4/week), 3 (occasional: 5–6/week), 4 (frequent: 7–8/week), or 5 (severe: 9 or more/week) as well as severity of symptoms with 0 (none), 1 (minimal), 2 (slight), 3 (moderate), 4 (severe), or 5 (very severe).

**Body composition**

Body mass and height were determined according to standard procedures using a Healthometer Professional 500KL (Pelstar LLC, Alsip, IL, USA) self-calibrating digital scale with an accuracy of ± 0.02 kg. Total body water (TBW) was measured using bioelectrical impedance analysis (ImpediMed DF50, San Diego, CA) using standard procedures. Whole body bone density and body composition measures (excluding cranium) were determined with a Hologic Discovery W Dual-Energy X-ray Absorptiometer (DEXA; Hologic Inc., Waltham, MA, USA) equipped with APEX Software (APEX Corporation Software, Pittsburg, PA, USA) by using procedures previously described [8, 50]. Mean test-retest reliability studies performed on male athletes in our lab over repeated days revealed mean coefficients of variation (CV) for total bone mineral content and total fat free/soft tissue mass of 0.31–0.45% with a mean intraclass correlation of 0.985 [51]. On the day of each test, the equipment was calibrated following the manufacturer's guidelines.

**Resting heart rate & blood pressure**

As soon as the DXA scan was completed (about 6-min), resting heart rate was determined in the supine position by palpitation of the radial artery using standard procedures [52]. Blood pressure was then assessed by auscultation of the brachial artery using a mercurial sphygmomanometer using standard clinical procedures [52].

**Cognitive function assessment**

Cognitive function was assessed using the Stroop Word-Color test standardized by Golden [53]. The test consists of three pages/tests with 100 items, presented in 5 columns of 20 items. Items on the first page (Word) are the color words RED, GREEN, and BLUE in black ink. On the second page (Color) the items are XXX’s colored in red, green, or blue ink. Items on the third page (Word-Color) are the words RED, GREEN, and BLUE printed in red, green, or blue ink with the limitation that word and ink could not match. Participants were given standardized instructions and asked to read aloud each word or color on each page as fast as they could for 45 s. The number of correct responses obtained on each test during the time period is used to assess cognitive function.

**Readiness to perform assessment**

Perceptions about readiness to perform were assessed using a visual analogue scale (VAS) using a 5-item
Strength testing
Strength tests were performed using an isotonic Olympic bench press (Nebula Fitness, Versailles, OH) according to standard procedures [45]. Participants followed a warm-up consisting of 10 repetitions using 50% of their estimated 1RM, 5 repetitions using 70% of their estimated 1RM, and 1 repetition using 90% of their estimated 1RM. Participants were given 2-min recovery between attempts and performed 1RM lifts until reaching a failure weight. After 5-min recovery, participants warmed-up in a similar fashion as described above and then performed 1RM lift attempts on a standard hip sled/leg press (Nebula Fitness, Versailles, OH) according to standard procedures [45]. Test to test reliability of performing these tests in our lab on resistance-trained participants have yielded low CV’s and high reliability for the bench press (1.9%, r = 0.94) and hip sled/leg press (0.7%, r = 0.91).

Anaerobic capacity testing
Prior to performing the anaerobic capacity test, participants warmed-up on a bicycle ergometer at a self-selected work rate. Wingate anaerobic capacity tests were performed using a Lode Excalibur Sport Ergometer (Lode BV, Groningen, The Netherlands) with work rate set at 7.5 J/kg/rev. Participants were asked to pedal as fast as possible prior to application of the workload and sprint at an all-out maximal capacity for 30s. This test measures absolute and relative peak and mean power and total work. Test-to-test variability in performing repeated Wingate anaerobic capacity tests in our laboratory yielded a CV of 15% with a test retest correlation of r = 0.98 for mean power [47]. Participants practiced the anaerobic capacity test during the familiarization session to minimize learning effects.

Blood chemistry
All blood samples were analyzed for standard blood chemistries inclusive of alkaline phosphatase (ALP), aspartate transaminase (AST), alanine transaminase (ALT), creatinine, blood urea nitrogen (BUN), creatine kinase (CK), lactate dehydrogenase (LDH), glucose, and blood lipids (total cholesterol, high density lipoprotein [HDL], low density lipoprotein [LDL], triglycerides [TG]) using a Cobas® c 111 (Roche Diagnostics, Basel, Switzerland). The internal quality control for the Cobas® c 111 was performed according to standard procedures [54] using two levels of control fluids purchased from the manufacturer to calibrate to acceptable SD’s and CV’s. Samples were re-run if the observed values were outside control values and/or clinical norms according to standard procedures. Test-to-test reliability assessment of assays evaluated in this study yielded mean CV’s < ±2.0% with r values > 0.99. We also assessed a complete blood count with platelet differential on whole blood (hemoglobin, hematocrit, red blood cell counts, mean corpuscle volume (MCV), mean corpuscle hemoglobin (MCH), mean corpuscle hemoglobin concentration (MCHC), red cell distribution width (RDW), white blood cell counts, lymphocytes, granulocytes, and mid-range absolute count (MID) using an Abbott Cell Dyn 1800 (Abbott Laboratories, Abbott Park, IL, USA) automated hematology analyzer. The internal quality control for Abbott Cell Dyn 1800 was performed using three levels of control fluids to calibrate to acceptable SD’s and CV’s. Test-to-test reliability assessment of assays evaluated in this study yielded mean CV’s < ±6.3% with r values > 0.9.

Statistical analysis
Baseline demographic and training volume data were analyzed by one-way analysis of variance (ANOVA). All data were analyzed using general linear models (GLM) multivariate analysis of variance (MANOVA) with repeated measures with Wilks’ Lambda and Greenhouse-Geisser adjustments. For performance and cognitive function data, baseline values were used as a covariate and run with MANOVA for repeated measures with differences between groups assessed using a Dunnet-Hsu post-hoc assessment.
vs. the PLA condition. These data were also graphed with means and 95% Confidence Interval (CI) to determine whether changes from baseline were significant [55]. We also analyzed the number of changes in blood chemistry values observed from normal to exceeding normal clinical limits from baseline to week 4, baseline to week 8 and week 4 to week 8 using a Chi-square analysis to examine whether any nutritional treatment promoted a significant increase in the number of participants with values exceeding normal. All data are presented as mean ± SD or mean change and 95% CI.

**Results**

**Participant demographics**

Table 1 presents participant demographics by group assignment. A total of 80 participants completed the study (PLA = 27, PWS = 27, PWS + S = 26). One-way ANOVA revealed no significant differences among groups in baseline age, height, body weight, or body mass index.

**Training volume and diet analysis**

Table 2 presents total training volume observed among groups for upper and lower extremity exercises. One-way ANOVA analysis revealed that there were no significant differences in lifting volumes among groups. Table 3 shows 4-day diet analysis data observed among groups at 0, 4, and 8 weeks of training. MANOVA analysis revealed that no significant group x time interactions were observed among groups in relative energy intake ($p = 0.19$), protein intake ($p = 0.72$), carbohydrate intake ($p = 0.55$) or fat intake ($p = 0.79$).

**Side effect analysis**

Reported frequency and severity of dizziness, headaches, racing heart rate, palpitations, shortness of breath, nervousness, blurred vision, and/or other symptom were so infrequent among participants that statistical analysis was not valid as the vast majority of participants (i.e., 90–98%) typically reported 0 ratings on each item throughout the study. No study participant required medical referral.

**Body composition**

Table 4 presents body composition data observed during the course of the study. MANOVA analysis revealed significant time effects in changes in body weight ($0.96 ± 2.6$ kg, $p = 0.003$) and FFM $0.67 ± 1.8$ kg, $p = 0.001$). However, no significant interactions were observed among groups in body weight ($p = 0.28$), fat mass ($p = 0.61$), FFM ($p = 0.28$), body fat percentage ($p = 0.36$), or percent total body water ($p = 0.37$).

**Resting heart rate & blood pressure**

MANOVA analysis revealed no significant differences among groups in hemodynamic responses during the

### Table 2 Total Training Volume Data

| Variable       | Group | Number | Total Volume      | p-value |
|----------------|-------|--------|-------------------|---------|
| Upper body (kg)| PLA   | 25     | 279,831 ± 132,101 | 0.33    |
|                | PWS   | 27     | 236,691 ± 87,062  |         |
|                | PWS + S | 23     | 269,928 ± 103,130 |         |
| Lower body (kg)| PLA   | 25     | 314,516 ± 136,966 | 0.66    |
|                | PWS   | 27     | 283,825 ± 100,541 |         |
|                | PWS + S | 23     | 305,906 ± 133,611 |         |

Values are means ± standard deviations. Total training volume was analyzed by one-way MANOVA. MANOVA analysis revealed overall Wilks’ Lambda group ($p = 0.69$). p-values reported are with between-subjects effects.

### Table 3 Dietary Analysis Data

| Variable               | Group | Number | Time (wk)      | p-value |
|------------------------|-------|--------|----------------|---------|
|                        |       |        | 0       | 4       | 8       |         |
| **Energy Intake (kcal/d/kg)** | PLA   | 26     | 27.06 ± 10.94 | 25.33 ± 9.31 | 24.72 ± 13.50 | Group 0.27 |
|                        | PWS   | 25     | 30.15 ± 8.76  | 25.72 ± 8.10 | 26.29 ± 10.99 | Time 0.29  |
|                        | PWS + S | 23     | 29.03 ± 9.73  | 29.35 ± 13.75 | 32.13 ± 16.48 | G x T 0.19 |
| **Protein (g/d/kg)**   | PLA   | 26     | 1.48 ± 0.57   | 1.46 ± 0.64  | 1.49 ± 0.79   | Group 0.18 |
|                        | PWS   | 25     | 1.54 ± 0.50   | 1.37 ± 0.47  | 1.51 ± 0.84   | Time 0.86  |
|                        | PWS + S | 23     | 1.74 ± 0.79   | 1.83 ± 1.13  | 1.77 ± 0.94   | G x T 0.72  |
| **Carbohydrate (g/d/kg)** | PLA   | 26     | 2.60 ± 1.11   | 2.56 ± 0.95  | 2.21 ± 1.10   | Group 0.91 |
|                        | PWS   | 25     | 2.87 ± 1.10   | 2.46 ± 1.02  | 2.30 ± 1.00   | Time 0.008 |
|                        | PWS + S | 23     | 2.61 ± 0.89   | 2.64 ± 1.43  | 2.42 ± 1.17   | G x T 0.55  |
| **Fat (g/d/kg)**       | PLA   | 26     | 1.05 ± 0.54   | 0.90 ± 0.41  | 0.98 ± 0.67   | Group 0.14 |
|                        | PWS   | 25     | 1.22 ± 0.41   | 1.05 ± 0.45  | 1.14 ± 0.52   | Time 0.30  |
|                        | PWS + S | 23     | 1.19 ± 0.51   | 1.19 ± 0.84  | 1.30 ± 0.71   | G x T 0.79  |

Values are means ± standard deviations. Total calories, Protein, Carbohydrate, and Fat intake were analyzed by MANOVA. MANOVA analysis revealed overall Wilks’ Lambda group ($p = 0.04$), time ($p = 0.03$), and group x time ($p = 0.35$). Greenhouse-Geisser time and group x time (G x T) interaction p-values are reported with univariate group p-values.
study (Wilks’ Lambda group \( p = 0.62 \), time \( p = 0.33 \), and group x time \( p = 0.87 \)). Univariate analysis revealed no indication that PWS or PWS + S supplementation increased resting heart rate (\( p = 0.26 \)), systolic blood pressure (\( p = 0.96 \)), or diastolic blood pressure (\( p = 0.54 \)) during training compared to the PLA group. All group means remained within ± 2 beats/min for heart rate and ± 2 mmHg for blood pressure from baseline values.

**Cognitive function assessment**

Table 5 shows the results for cognitive function testing. MANOVA analysis revealed Wilks’ Lambda overall time effects (\( p < 0.001 \)) with no significant interaction effects (\( p = 0.17 \)). MANOVA univariate analysis showed similar trends. However, univariate ANOVA analysis revealed an interaction trend (\( p = 0.087 \)) among groups in color responses and a significant quadratic effect among groups.

**Table 4 Body Composition Data**

| Variables                  | Group     | Number | Time (wk)       | p-value |
|----------------------------|-----------|--------|-----------------|---------|
|                            |           |        | 0               | 4       | 8       |
| Body Weight (kg)           | PLA       | 27     | 81.1 ± 13.4     | 81.8 ± 14.2 | 82.1 ± 14.0 | Group 0.98 |
|                            | PWS       | 27     | 81.8 ± 13.3     | 81.3 ± 11.3 | 82.2 ± 12.8 | Time 0.003 |
|                            | PWS + S   | 26     | 80.4 ± 16.1     | 81.3 ± 16.7 | 81.8 ± 17.3 | G x T 0.28 |
| Fat Mass (kg)              | PLA       | 27     | 113.3 ± 5.4     | 119.9 ± 5.5 | 119.9 ± 5.2 | Group 0.75 |
|                            | PWS       | 27     | 127.7 ± 7.6     | 130.0 ± 7.7 | 128.7 ± 7.4 | Time 0.10 |
|                            | PWS + S   | 26     | 113.3 ± 7.3     | 116.8 ± 8.3 | 115.8 ± 8.5 | G x T 0.61 |
| Fat-Free Mass (kg)         | PLA       | 27     | 630.0 ± 10.7    | 632.1 ± 11.2 | 634.1 ± 11.0 | Group 0.94 |
|                            | PWS       | 27     | 623.2 ± 7.2     | 622.2 ± 6.7 | 627.2 ± 6.6 | Time 0.001 |
|                            | PWS + S   | 26     | 624.2 ± 9.2     | 630.0 ± 9.0 | 636.9 ± 9.1 | G x T 0.28 |
| Body Fat (%)               | PLA       | 27     | 151.1 ± 6.2     | 157.5 ± 6.0 | 157.5 ± 5.6 | Group 0.55 |
|                            | PWS       | 27     | 161.1 ± 6.6     | 164.6 ± 6.7 | 162.6 ± 6.3 | Time 0.23 |
|                            | PWS + S   | 26     | 145.5 ± 5.8     | 145.6 ± 6.3 | 143.6 ± 6.1 | G x T 0.36 |
| Total Body Water (%)       | PLA       | 27     | 53.6 ± 6.4      | 53.0 ± 6.4  | 52.0 ± 5.5  | Group 0.40 |
|                            | PWS       | 27     | 50.5 ± 5.5      | 51.0 ± 5.7  | 51.7 ± 6.3  | Time 0.82  |
|                            | PWS + S   | 26     | 52.2 ± 5.7      | 51.4 ± 5.1  | 51.8 ± 5.9  | G x T 0.37 |

Values are means ± standard deviations. All variables were analyzed by MANOVA. MANOVA analysis revealed overall Wilks’ Lambda group (\( p = 0.40 \)), time (\( p = 0.003 \)), and group x time (\( p = 0.50 \)). Greenhouse-Geisser time and group x time (G x T) interaction p-values are reported with univariate group p-values.

**Table 5 Stroop Word-Color Cognitive Function Data**

| Variable       | Group     | Number | Time (wk)       | p-value |
|----------------|-----------|--------|-----------------|---------|
| Word (counts)  | PLA       | 27     | 109.8 ± 16.9    | 113.6 ± 17.2 | 116.2 ± 17.5 | Group 0.33 |
|                | PWS       | 27     | 107.7 ± 11.4    | 110.6 ± 11.3 | 113.6 ± 11.3 | Time <0.001 |
|                | PWS + S   | 26     | 102.3 ± 11.2    | 108.2 ± 11.2 | 112.4 ± 11.2 | G x T 0.45 |
| Color (counts) | PLA       | 27     | 80.8 ± 10.6c    | 83.2 ± 11.8c  | 85.7 ± 12.5c  | Group 0.35 |
|                | PWS       | 27     | 78.2 ± 9.4c     | 83.6 ± 9.6c   | 86.7 ± 10.1c  | Time <0.001 |
|                | PWS + S   | 26     | 77.0 ± 10.4bc   | 79.7 ± 9.8abc | 82.1 ± 10.8abc | G x T 0.087 |
| Word-Color (counts) | PLA | 27 | 54.1 ± 11.5c | 55.5 ± 11.5c | 58.5 ± 12.6c | Group 0.42 |
|                | PWS       | 27     | 53.1 ± 5.9c     | 56.7 ± 7.4c   | 59.1 ± 7.6c   | Time <0.001 |
|                | PWS + S   | 26     | 49.2 ± 11.1ab   | 55.0 ± 9.6bc  | 55.6 ± 10.2ab | G x T 0.044 |

Values are means ± standard deviations. Word, Color, and Word-Color counts were analyzed by MANOVA. MANOVA analysis revealed overall Wilks’ Lambda group (\( p = 0.83 \)), time (\( p < 0.001 \)), and group x time (\( p = 0.17 \)). Greenhouse-Geisser time and group x time (G x T) interaction p-values are reported with univariate group p-values. \( q \) represents quadratic effect and \( l \) represents linear p-value from univariate ANOVA. * represents \( p < 0.05 \) difference from baseline. ^ represents \( p < 0.05 \) difference from wk 4. ^ represents \( p < 0.05 \) from PLA. *represents \( p < 0.05 \) from PWS. ^ represents \( p < 0.05 \) from PWS + S.
mean changes in Color, Word, and Word-Color counts where generally increased to a greater degree with 95% CIs above baseline in the PWS and/or PWS + S groups compared to the PLA group values that were lower and had 95% CIs crossing baseline. After 8-weeks of intervention, all groups demonstrated significant increases in Color, Word, and Color-Word counts. More specifically, comparisons at week 4 demonstrated a significant increase in Word count for the PLA (3.92 counts, 95% CI 1.39, 7.45) and PWS + S (5.46 counts, 95% CI 2.09, 9.19) group, but not for PWS (3.21 counts, 95% CI −0.31, 6.72). By week 8, all groups increased their respective word counts: PLA (6.74 counts, 95% CI 3.32, 10.16), PWS (7.56 counts, 95% CI 4.15, 10.97) and PWS + S (9.93 counts, 95% CI 6.49, 13.73). For the Color assessment comparison, week 4 changes are: PLA (2.77 counts, 95% CI, 0.43, 5.09); PWS (5.05 counts, 95% CI, 2.72, 7.38); and, PWS + S (2.57 counts, 95% CI, 0.24, 4.88). For week 8, color assessment changes are: PLA (4.90 counts, 95% CI, 2.32, 7.46); PWS (8.33 counts, 95% CI, 5.76, 10.89); and, PWS + S (5.08 counts, 95% CI, 2.51, 7.63). Week 4 word-color changes were significant for the PWS (3.99 counts, 95% CI, 1.75, 6.23), and PWS + S (5.27 counts, 95% CI, 3.01, 7.52), but not the PLA (2.08 counts, 95% CI, −0.15, 4.31) group. By week 8, all groups demonstrated a significant increase in word-color counts: PLA (5.02 counts, 95% CI, 2.44, 7.59); PWS (5.84 counts, 95% CI, 3.27, 8.41); and, PWS + S (6.13 counts, 95% CI, 3.54, 8.72).

**Readiness to perform assessment**

Table 6 presents Readiness to Perform VAS data observed throughout the study. MANOVA revealed an overall time effect with no significant interactions among groups. Likewise, MANOVA using baseline values and age as a covariate and analysis of mean changes with 95% CI’s revealed no significant differences among groups.

**Performance assessment**

Performance testing outcomes are presented in Table 7. MANOVA revealed significant time effects for bench press and leg press 1RM performance. However, no significant univariate interactions were observed among groups. MANOVA analysis using baseline values as a covariate and assessment of mean change with 95% CI’s of 1RM strength data (Fig. 3) revealed that there were significant increases in bench press 1RM strength at week 4 for the PWS (8.17 kg; 95% CI 1.88, 14.47) and PWS + S (6.95 kg; 95% CI 0.62, 13.28), but not for the PLA (5.45 kg, 95% CI −0.82, 11.73). By week 8, all groups demonstrated a significant increase in BP 1 RM: PLA (7.18 kg, 95% CI 1.01, 13.36), PWS (14.36, 95% CI 8.13, 20.59) and PWS + S (13.84 kg, 95% CI 7.64, 20.04). No between group differences were noted at week 4 or week 8. A similar pattern for leg press 1 RM strength
Table 6 Readiness to Perform Visual Analogue Scale Data

| Variable                         | Group     | Number | Time (wk)        | p-value | p-value |
|----------------------------------|-----------|--------|------------------|---------|---------|
|                                  |           |        | 0    | 4       | 8       |
| I slept well last night          | PLA       | 27     | 3.46 ± 0.90      | 3.43 ± 0.92 | 3.53 ± 0.90 | Group 0.25 |
|                                 | PWS       | 27     | 3.77 ± 0.93*     | 3.75 ± 0.89 | 3.52 ± 1.17 | Time 0.83 |
|                                 | PWS + S   | 26     | 3.21 ± 1.09     | 3.26 ± 1.11 | 3.59 ± 0.91 | G x T 0.34 |
| I am looking forward to today’s  | PLA       | 27     | 3.93 ± 0.64      | 3.92 ± 0.61 | 3.63 ± 0.84 | Group 0.94 |
| workout                          | PWS       | 27     | 3.85 ± 0.90      | 4.01 ± 0.68 | 3.77 ± 0.86 | Time 0.22 |
|                                 | PWS + S   | 26     | 3.73 ± 0.66      | 3.92 ± 0.68 | 3.93 ± 0.82 | G x T 0.35 |
| I am optimistic about my future  | PLA       | 27     | 4.39 ± 0.49      | 4.16 ± 0.66 | 3.71 ± 0.95 | Group 0.25 |
| performance                      | PWS       | 27     | 4.50 ± 0.63      | 4.42 ± 0.63 | 4.05 ± 0.66 | Time <0.001 |
|                                 | PWS + S   | 26     | 4.21 ± 0.75      | 4.30 ± 0.67 | 3.88 ± 0.99 | G x T 0.51 |
| I feel vigorous and energetic    | PLA       | 27     | 3.56 ± 0.71      | 3.24 ± 0.75 | 3.21 ± 0.93 | Group 0.26 |
|                                 | PWS       | 27     | 3.46 ± 0.94      | 3.46 ± 0.84* | 3.55 ± 0.73 | Time 0.17 |
|                                 | PWS + S   | 26     | 3.21 ± 0.80      | 3.00 ± 0.93* | 3.38 ± 0.85 | G x T 0.17 |
| My appetite is great             | PLA       | 27     | 4.48 ± 0.64*     | 4.25 ± 0.81 | 4.17 ± 0.79 | Group 0.13 |
|                                 | PWS       | 27     | 4.03 ± 0.81*     | 4.03 ± 0.88 | 4.03 ± 0.79 | Time 0.12 |
|                                 | PWS + S   | 26     | 4.05 ± 0.92      | 3.96 ± 1.03 | 3.73 ± 1.11 | G x T 0.63 |
| I have little muscle soreness    | PLA       | 27     | 3.84 ± 0.43      | 3.84 ± 0.89 | 3.58 ± 1.04 | Group 0.66 |
|                                 | PWS       | 27     | 3.56 ± 1.15      | 3.67 ± 1.11 | 3.52 ± 1.00 | Time 0.93 |
|                                 | PWS + S   | 26     | 3.52 ± 1.17      | 3.52 ± 1.17 | 3.73 ± 1.11 | G x T 0.68 |

Values are means ± standard deviations. Six questions were analyzed by MANOVA. MANOVA analysis revealed overall Wilks’ Lambda group (p = 0.27), time (p < 0.001), and group x time (p = 0.66). Greenhouse-Geisser time and group x time (G x T) interaction p-values are reported with univariate group p-values.
* represents p < 0.05 difference from baseline. ^ represents p < 0.05 difference from wk 4. *represents p < 0.05 from PLA. ^represents p < 0.05 from PWS. ^represents p < 0.05 from PWS + S

Table 7 Performance Data

| Variable               | Group | Number | Time (wk)        | p-value |
|------------------------|-------|--------|------------------|---------|
|                       |       |        | 0    | 4       | 8       |
| Bench Press (kg)       | PLA   | 27     | 100.6 ± 20.8     | 102.9 ± 24.7 | 104.0 ± 23.3 | Group 0.56 |
|                        | PWS   | 27     | 96.7 ± 23.1      | 99.2 ± 21.3 | 102.7 ± 21.7 | Time <0.001 |
|                        | PWS + S | 26    | 102.0 ± 16.3    | 106.2 ± 16.7 | 108.6 ± 17.1 | G x T 0.33 |
| Leg Press (kg)         | PLA   | 27     | 472.8 ± 149.8    | 490.3 ± 134.2 | 491.1 ± 131.0 | Group 0.67 |
|                        | PWS   | 27     | 436.6 ± 96.6     | 466.0 ± 101.9 | 474.0 ± 96.3 | Time <0.001 |
|                        | PWS + S | 26    | 454.2 ± 79.4    | 474.4 ± 92.1 | 494.9 ± 100.9 | G x T 0.28 |
| Peak Power (Watt)      | PLA   | 27     | 1,472 ± 485      | 1,630 ± 475 | 1,507 ± 385 | Group 0.91 |
|                        | PWS   | 27     | 1,502 ± 384      | 1,602 ± 354 | 1,603 ± 466 | Time 0.01 |
|                        | PWS + S | 26    | 1,445 ± 324    | 1,605 ± 444 | 1,544 ± 403 | G x T 0.83 |
| Mean Power (Watt)      | PLA   | 27     | 647 ± 146        | 640 ± 133  | 636 ± 127  | Group 0.95 |
|                        | PWS   | 27     | 630 ± 72         | 643 ± 66  | 638 ± 69  | Time 0.23 |
|                        | PWS + S | 26    | 630 ± 114     | 656 ± 134 | 612 ± 145 | G x T 0.40 |
| Peak Power (Watt/kg)   | PLA   | 27     | 18.3 ± 5.6       | 20.2 ± 5.4 | 18.4 ± 4.0 | Group 0.90 |
|                        | PWS   | 27     | 18.6 ± 4.7       | 19.8 ± 4.6 | 19.8 ± 5.8 | Time 0.02 |
|                        | PWS + S | 26    | 18.3 ± 3.6     | 20.2 ± 5.3 | 19.4 ± 4.8 | G x T 0.80 |
| Mean Power (Watt/kg)   | PLA   | 27     | 8.0 ± 1.1        | 7.9 ± 1.0  | 7.7 ± 0.9  | Group 0.73 |
|                        | PWS   | 27     | 7.8 ± 1.2        | 8.0 ± 1.1  | 7.9 ± 1.0  | Time 0.18 |
|                        | PWS + S | 26    | 8.0 ± 1.1      | 8.2 ± 1.4 | 8.0 ± 1.2 | G x T 0.33 |
| Total Work (Joules)    | PLA   | 27     | 16,003 ± 4774    | 16,017 ± 4019 | 15,196 ± 3826 | Group 0.98 |
|                        | PWS   | 27     | 16,821 ± 2,166  | 16,319 ± 2,003 | 15,165 ± 2,095 | Time 0.17 |
|                        | PWS + S | 26    | 18,023 ± 3,431  | 16,680 ± 4,025 | 19,213 ± 3,110 | G x T 0.29 |

Values are means ± standard deviations. Strength (Bench and Leg Press) were analyzed by MANOVA. MANOVA analysis revealed overall Wilks’ Lambda group (p = 0.038), time (p < 0.001), and group x time (p = 0.29). Greenhouse-Geisser time and group x time interaction p-values are reported with univariate group p-values.
* represents p < 0.05 difference from baseline. ^ represents p < 0.05 difference from wk 4.
improvement was observed within the PWS (61.84 kg, 95% CI 24.96, 98.725) and PWS + S 44.89 kg, 95% CI 8.31, 81.47) groups, but not for PLA (36.50, 95% CI, −0-21, 73.2). Similarly, by week 8, all groups increased their LP 1RM as follows: PLA (43.28 kg, 95% CI 4.16, 82.41), PWS (79.23 kg, 95% CI 39.12, 118.54), and PWS + S (89.54 kg, 95% CI 50.55, 128.53). No between groups differences were noted at week 4 or week 8.

Similar results were observed in Wingate anaerobic capacity assessment. MANOVA analysis using baseline values and ages as covariates revealed that a significant increase in Wingate peak power for PWS + S and PLA at week 4; yet no significant differences were otherwise noted at week 8 or among other Wingate parameters examined.

Blood chemistry assessment
Tables 8, 9 and 10 show blood chemistry data analyzed during the study. MANOVA revealed some time effects in several variables indicative of individuals engaged in heavy resistance exercise training with no significant group x time interactions in muscle and liver enzymes, markers of catabolism, or blood lipids. Univariate ANOVA analysis revealed a significant quadratic effect in blood glucose values. Post-hoc analysis revealed the PLA group had a small but significant increase in blood glucose after 4-weeks of training while all groups were higher after 8-weeks of training. However, no significant differences were seen among groups and values remained within normal ranges. Table 11 shows Chi squared categorical analysis. No significant differences were observed among groups in the number of participants who observed changes in blood chemistry markers above normal baseline values.

Discussion
Numerous PWS's are sold to athletes purporting to improve acute exercise performance and/or promote greater training adaptations [1]. Preliminary assessment of the acute effects of ingesting the PWS used in this study provided some evidence that this formulation enhanced resting energy expenditure and cognitive function and that adding 20 mg of synephrine to the formulation increased resting energy expenditure to a greater degree [42, 43]. Theoretically, use of these PWS's during training would promote greater fat loss and/or training adaptations over time. Therefore, this study examined the safety and efficacy of daily ingestion of a commercially available PWS with and without synephrine for 8-weeks during training on body composition and training adaptations in resistance-trained athletes. Results indicated that while there was some evidence that PWS ingestion enhanced some measures of cognitive function and 1RM strength gains primarily after 4-weeks of training, no significant differences were seen among groups in improvement in body composition and/or cognitive and exercise performance after 8-weeks of training. Additionally, there was little evidence indicating that adding synephrine to the PWS promoted additive benefits. Results also indicated that ingesting these PWS's had no significant effects on resting heart rate or blood pressure, standard clinical chemistry panels, and/or the incidence of reported side effects. Consequently, within the confines of this study, use of these PWS's appeared to be well-tolerated.

Cognitive function
The PWS's investigated in this study contained 284 mg of caffeine, 300 mg of N-Acetyl-L-Tyrosine, and 15 mg of L-Dopa extracted from Mucuna pruriens. Numerous studies have shown that ingesting caffeine (e.g., 3-6 mg/kg) can improve exercise performance, cognitive function, and/or vigilance [5]. In the present study, participants ingested an average of 3.5 mg/kg of caffeine prior to training sessions. There is also some evidence that tyrosine supplementation can improve cognitive function.
function and/or memory [13, 14] although dosages typically studied (i.e., 50–150 mg/kg or 1.6–12 g) were much higher than the amount investigated in this study (i.e., 300 mg). Additionally, there is some evidence that L-Dopa supplementation (e.g., 150 mg) can affect cognitive function and/or reduce perceptions of fear or anxiety [15, 16] although the dosages studied in the present investigation are much lower. Thus, it is conceivable that ingesting a PWS with ergogenic levels of caffeine (and possibly tyrosine and/or L-Dopa) prior to exercise may provide some improvement in cognitive function and/or training adaptations due to a greater ability to focus on exercise training.

In the present study, analysis of mean changes from baseline with 95% CIs (Fig. 2) indicated that change in Stroop Color and Word-Color counts were significantly above baseline in the PWS group and changes in Word count, Color count, and Word-Color counts were greater in the PWS+S group after 4-weeks of training and these changes were generally greater than the placebo group. These findings are consistent with several studies that reported that acute or chronic ingestion of PWS formulations containing caffeine positively affected cognitive function, concentration, and/or perceptions of energy [5, 56, 57]. The Stroop Color-Word test assesses attention, processing speed, and executive function which have been shown to decline as one fatigues. Theoretically, maintaining cognitive function during the latter stages of competition can improve performance particularly in events that require quick decision making. However, after 8-weeks of training and supplementation in the present study, all groups observed similar improvements in Stroop Word, Color, and Word-Color counts and no differences were observed in questions related to readiness to perform. These findings are consistent with other studies reporting no overall benefit of PWS supplementation on cognitive function, concentration, and/or perceptions of energy [58, 59] and suggest that the ergogenic value observed may lessen over time. However, it is also possible that since performing the 1 RM and anaerobic sprint capacity tests

### Table 8 Muscle and Liver enzymes and Markers of Catabolism

| Variable       | Group | Number | Time (wk) | p-value | p-value |
|----------------|-------|--------|-----------|---------|---------|
|                |       |        | 0         | 4       | 8       | p-value |
| ALP (U/L)      | PLA   | 27     | 76.8 ± 15.1 | 66.4 ± 12.9 | 71.2 ± 13.4 | Group 0.24 |
|                | PWS   | 27     | 87.2 ± 24.7 | 72.3 ± 19.0 | 78.4 ± 24.9 | Time <0.001 |
|                | PWS+S | 26     | 76.4 ± 22.8 | 68.1 ± 17.3 | 74.4 ± 19.6 | G x T 0.25 |
| ALT (U/L)      | PLA   | 27     | 25.3 ± 10.0 | 25.0 ± 22.4 | 24.6 ± 13.0 | Group 0.74 |
|                | PWS   | 27     | 25.1 ± 10.1 | 26.9 ± 16.0 | 30.9 ± 17.9 | Time 0.73 |
|                | PWS+S | 26     | 26.6 ± 23.0 | 28.6 ± 20.8 | 26.0 ± 12.2 | G x T 0.55 |
| AST (U/L)      | PLA   | 27     | 29.1 ± 11.0 | 27.6 ± 17.7 | 27.1 ± 9.8  | Group 0.47 |
|                | PWS   | 27     | 28.8 ± 9.7  | 31.6 ± 26.1 | 33.1 ± 19.7 | Time 0.96 |
|                | PWS+S | 26     | 28.4 ± 15.1 | 28.4 ± 10.3 | 27.3 ± 8.5  | G x T 0.76 |
| CK (U/L)       | PLA   | 27     | 310.0 ± 217.2 | 263.1 ± 214.4 | 215.5 ± 115.1 | Group 0.34 |
|                | PWS   | 27     | 297.5 ± 160.4 | 256.9 ± 203.7 | 336.1 ± 242.0 | Time 0.79 |
|                | PWS+S | 26     | 261.2 ± 130.0 | 324.1 ± 232.2 | 274.8 ± 172.3 | G x T 0.86 |
| LDH (U/L)      | PLA   | 27     | 164.2 ± 36.2 | 153.5 ± 33.9 | 159.4 ± 29.5 | Group 0.90 |
|                | PWS   | 27     | 157.7 ± 24.2 | 160.7 ± 37.6 | 162.8 ± 24.3 | Time 0.19 |
|                | PWS+S | 26     | 158.8 ± 32.1 | 152.5 ± 24.3 | 160.4 ± 23.6 | G x T 0.44 |
| BUN (mg/dl)    | PLA   | 27     | 14.9 ± 4.9 a | 12.3 ± 6.7  | 16.2 ± 6.8  | Group 0.62 |
|                | PWS   | 27     | 12.0 ± 4.0 c | 12.3 ± 5.8  | 16.1 ± 5.3  | Time <0.001 |
|                | PWS+S | 26     | 13.6 ± 4.9  | 12.6 ± 6.6  | 16.5 ± 5.0  | G x T 0.55 |
| Creatinine (mg/dl) | PLA   | 27     | 1.15 ± 0.44 a | 0.72 ± 0.47 | 0.85 ± 0.36a | Group 0.27 |
|                | PWS   | 27     | 1.08 ± 0.41 a | 0.75 ± 0.38 | 0.95 ± 0.31 | Time <0.001 |
|                | PWS+S | 26     | 1.13 ± 0.51 a | 0.82 ± 0.43 | 1.05 ± 0.28a| G x T 0.78 |
| BUN:Creatinine | PLA   | 27     | 15.7 ± 9.6  | 24.7 ± 19.1 | 26.5 ± 23.4 | Group 0.20 |
|                | PWS   | 27     | 12.7 ± 6.8  | 22.7 ± 17.3 | 20.4 ± 15.0 | Time 0.002 |
|                | PWS+S | 26     | 15.3 ± 10.9 | 20.9 ± 15.1 | 17.9 ± 12.6 | G x T 0.63 |

Values are means ± standard deviations. All variables were analyzed by MANOVA. MANOVA analysis revealed overall Wilks’ Lambda group (p = 0.43), time (p < 0.001), and group x time (p = 0.66). Greenhouse-Geisser time and group x time (G x T) interaction p-values are reported with univariate group p-values.

* represents p < 0.05 difference from baseline. ^ represents p < 0.05 difference from wk 4.
did not require significant executive or cognitive functioning to perform, there may be benefits on other performance tasks that require more decision making and attention.

Training adaptations
The PWS’s examined in the present study contained a number of nutrients that have been purported to influence training adaptations. For example, the PWS’s contained 3 g/day of beta-alanine. Beta-alanine supplementation (e.g., 3–6 g/day for 2–4 weeks) has been reported to increase muscle carnosine levels, buffer acidity, and enhance exercise performance [6, 21–24]. Research has indicated that length of time of supplementation affects the impact that beta-alanine supplementation has on muscle carnosine levels and potential ergogenic benefit [27, 60–62]. Thus, it is possible that consuming 3 g/day of beta-alanine for 8-weeks could have provided ergogenic benefit during resistance-training. The PWS supplements also contained 2 g/day of creatine nitrate at approximately a 2:1 ratio of creatine to nitrate. While there is little evidence that ingesting 2 g/day of creatine for 8-weeks can markedly increase muscle creatine stores and/or affect exercise capacity, it is enough creatine to maintain creatine stores during training [7, 28]. The greater potential of ergogenic value from ingesting 2 g/day of creatine nitrate would theoretically be due to the nitrate content [46, 63]. There are a number of studies that indicate that nitrate supplementation prior to exercise (e.g., 300 mg) can improve exercise capacity [9, 11, 17–20]. The amount of nitrate contained in the creatine nitrate supplement used (i.e., ~1 g/day) is more consistent with dietary recommendations to help control blood pressure [64, 65]. Nevertheless, there was sufficient amount of nitrates in the PWS to provide some ergogenic benefit particularly to endurance exercise performance. The PWS’s also contained 2 g/day of arginine alpha-ketoglutarate. Prior research has reported that dietary supplementation of higher doses of arginine alpha-ketoglutarate (e.g., 12 g/day) can affect exercise capacity [12] although other studies with lower amounts have shown no benefit [66, 67]. Given that the PWS’s only contained 2 g/day of arginine alpha-ketoglutarate, it is likely that this nutrient provided minimal effects. Finally, one of the PWS’s contained 20 mg of synephrine (as *Citrus Aurantium*). Synephrine has been purported to suppress appetite [29] and promote weight loss through an enhanced thermogenesis [34–36] with no negative effects on the cardiovascular system [37, 38, 68]. Theoretically, adding synephrine to the PWS would promote greater fat loss during training and a more optimal body composition.

### Table 9: Blood Glucose and Lipid Data

| Variable     | Group | Number | 0       | 4       | 8       | p-value |
|--------------|-------|--------|---------|---------|---------|---------|
| **Glucose (mg/dl)** | PLA   | 27     | 86.6 ± 7.0 | 93.7 ± 12.8* | 93.8 ± 13.0* | Group 0.90 |
|               | PWS   | 27     | 89.4 ± 7.1 | 89.7 ± 8.9  | 95.1 ± 9.2*  | Time <0.001 |
|               | PWS + S | 26    | 90.7 ± 8.2 | 90.1 ± 5.0  | 95.4 ± 7.9*  | G x T 0.017q |
| **Cholesterol (mg/dl)** | PLA   | 27     | 159.5 ± 31.6 | 156.9 ± 34.3 | 156.1 ± 41.7 | Group 0.34 |
|               | PWS   | 27     | 164.1 ± 31.3 | 158.1 ± 26.0 | 163.3 ± 32.8 | Time 0.16 |
|               | PWS + S | 26    | 174.5 ± 42.8 | 171.9 ± 40.9 | 165.9 ± 36.1 | G x T 0.44 |
| **HDL-C (mg/dl)** | PLA   | 27     | 53.4 ± 12.6 | 51.8 ± 13.1 | 51.3 ± 15.0 | Group 0.99 |
|               | PWS   | 27     | 52.7 ± 14.7 | 50.0 ± 13.9 | 52.6 ± 14.7 | Time 0.10 |
|               | PWS + S | 26    | 53.5 ± 16.2 | 52.7 ± 12.7 | 49.6 ± 15.0 | G x T 0.24 |
| **CHL:HDL** | PLA   | 27     | 3.1 ± 0.7  | 3.1 ± 0.8  | 3.1 ± 0.7  | Group 0.38 |
|               | PWS   | 27     | 3.2 ± 0.9  | 3.3 ± 0.8  | 3.2 ± 0.7  | Time 0.35 |
|               | PWS + S | 26    | 3.9 ± 3.7  | 3.5 ± 1.8  | 4.1 ± 4.4  | G x T 0.22 |
| **LDL-C (mg/dl)** | PLA   | 27     | 106.0 ± 29.6 | 105.0 ± 31.4 | 104.7 ± 35.1 | Group 0.32 |
|               | PWS   | 27     | 111.4 ± 29.8 | 108.0 ± 23.4 | 110.6 ± 27.9 | Time 0.43 |
|               | PWS + S | 26    | 121.0 ± 35.2 | 119.2 ± 42.3 | 116.2 ± 42.2 | G x T 0.56 |
| **Triglyceride (mg/dl)** | PLA   | 27     | 74.2 ± 33.8 | 81.9 ± 31.5 | 83.6 ± 30.7 | Group 0.11 |
|               | PWS   | 27     | 92.8 ± 43.3 | 98.5 ± 37.8a | 86.5 ± 37.6 | Time 0.89 |
|               | PWS + S | 26    | 81.6 ± 36.6 | 73.9 ± 22.9b | 80.4 ± 41.9 | G x T 0.31 |

Values are means ± standard deviations. All variables were analyzed by MANOVA. MANOVA analysis revealed overall Wilks’ Lambda group (p = 0.44), time (p < 0.001), and group x time (p = 0.58). Greenhouse-Geisser time and group x time (G x T) interaction p-values are reported with univariate group p-values. q represents quadratic effect and l represents linear p-value from univariate ANOVA. * represents p < 0.05 difference from baseline. ^ represents p < 0.05 difference from wk 4.
Results of the present study provide some support that ingesting a PWS containing these nutrients enhanced training adaptations. Analysis of mean changes from baseline and 95% CI data (see Fig. 4) indicated that there was some evidence that 1RM strength gains were greater with PWS supplementation compared to placebo at both 4 and 8-weeks of training. There was also evidence that peak power, mean power, and total work during the anaerobic capacity sprint test was increased to a greater degree after 4-weeks of PWS + S supplementation (see Fig. 4). However, consistent with findings from Outlaw and colleagues [58], we did not observe a significant improvement in body composition changes in response to training as has previously been reported [56, 69]. This includes when adding 20 mg of synephrine (as Citrus Aurantium) to the formulation. These latter findings contrast reports suggesting that that Citrus Aurantium supplementation can promote weight and/or fat loss [36, 70] although it should be noted that the amount of synephrine provided (i.e., 20 mg/day) was less than that used in Kaats et al. study (i.e., 49 or 98 mg/day). Greenway and coworkers [71] reported that ingesting an herbal supplement containing 200 mg of green tea, 198 mg of caffeine (derived from guarana extract), and 9 mg of synephrine (derived from Citrus Aurantium) did not promote weight loss. Thus, it is possible that a higher dose of synephrine is needed to promote weight loss in individuals involved in intense training and/or addition of synephrine to a PWS has less effect in resistance-trained individuals.

### Table 10: Complete Blood Count Data

| Variable            | Group | Number | Time (wk)  | p-value  |
|---------------------|-------|--------|------------|----------|
|                     |       |        | 0  | 4  | 8   |                  |
| WBC Count (x10^3/μl) | PLA   | 27     | 6.09 ± 2.09 | 5.84 ± 1.17 | 6.04 ± 1.52 | Group 0.36 |
|                     | PWS   | 27     | 6.64 ± 1.54 | 6.21 ± 1.66 | 5.92 ± 1.17 | Time 0.09  |
|                     | PWS + S | 26   | 5.98 ± 1.25 | 5.66 ± 1.40 | 5.68 ± 1.74 | G x T 0.64 |
| RBC Count (x10^6/μl) | PLA   | 27     | 5.09 ± 0.72 | 4.82 ± 0.47 | 4.87 ± 0.54 | Group 0.72 |
|                     | PWS   | 27     | 4.92 ± 0.51 | 4.92 ± 0.51 | 4.88 ± 0.34 | Time 0.88  |
|                     | PWS + S | 26   | 4.87 ± 0.60 | 5.04 ± 0.56 | 5.05 ± 0.64 | G x T 0.16 |
| Hemoglobin (g/dl)   | PLA   | 27     | 15.55 ± 2.49 | 14.90 ± 1.35 | 15.12 ± 1.46 | Group 0.84 |
|                     | PWS   | 27     | 15.24 ± 1.33 | 15.26 ± 1.76 | 15.03 ± 0.95 | Time 0.97  |
|                     | PWS + S | 26   | 14.84 ± 2.13 | 15.60 ± 1.78 | 15.61 ± 1.98 | G x T 0.13 |
| Hematocrit (%)      | PLA   | 27     | 47.28 ± 6.86 | 44.66 ± 4.31 | 45.04 ± 5.08 | Group 0.76 |
|                     | PWS   | 27     | 45.84 ± 4.71 | 45.74 ± 5.60 | 45.45 ± 3.07 | Time 0.85  |
|                     | PWS + S | 26   | 45.24 ± 5.77 | 46.87 ± 5.22 | 46.77 ± 5.77 | G x T 0.16 |
| MCV (fl)            | PLA   | 27     | 92.87 ± 3.89 | 92.72 ± 3.51 | 92.48 ± 3.61 | Group 0.34 |
|                     | PWS   | 27     | 93.22 ± 3.37 | 92.98 ± 3.28 | 93.18 ± 2.86 | Time 0.32  |
|                     | PWS + S | 26   | 92.74 ± 3.03 | 92.98 ± 3.32 | 92.60 ± 3.27 | G x T 0.37 |
| MCH (pg/cell)       | PLA   | 27     | 30.53 ± 1.76 | 30.98 ± 2.09 | 31.12 ± 1.81 | Group 0.80 |
|                     | PWS   | 27     | 31.06 ± 1.44 | 31.07 ± 1.53 | 30.83 ± 1.48 | Time 0.13  |
|                     | PWS + S | 26   | 30.37 ± 1.33 | 30.96 ± 1.24 | 30.93 ± 1.60 | G x T 0.36 |
| MCHC (g/dl)         | PLA   | 27     | 32.87 ± 1.39 | 33.40 ± 1.46 | 33.69 ± 1.90 | Group 0.73 |
|                     | PWS   | 27     | 33.34 ± 1.35 | 33.41 ± 1.42 | 33.09 ± 1.22 | Time 0.11  |
|                     | PWS + S | 26   | 32.75 ± 0.91 | 33.31 ± 1.37 | 33.39 ± 1.10 | G x T 0.30 |
| RDW (%)             | PLA   | 27     | 13.38 ± 0.62 | 13.28 ± 0.51 | 12.98 ± 0.59 | Group 0.43 |
|                     | PWS   | 27     | 13.09 ± 0.58 | 13.11 ± 0.88 | 13.18 ± 0.73 | Time 0.65  |
|                     | PWS + S | 26   | 12.97 ± 0.58 | 12.99 ± 0.77 | 13.08 ± 0.72 | G x T 0.02 |
| Platelet Count (x10^3/μl) | PLA   | 27     | 220.66 ± 75.84 | 233.14 ± 53.34 | 228.96 ± 55.60 | Group 0.46 |
|                     | PWS   | 27     | 230.77 ± 45.80 | 234.11 ± 38.24 | 242.92 ± 41.94 | Time 0.58 |
|                     | PWS + S | 26   | 222.53 ± 67.23 | 222.26 ± 48.51 | 217.38 ± 51.95 | G x T 0.65 |

Values are means ± standard deviations. All variables were analyzed by MANOVA. MANOVA analysis revealed overall Wilks’ Lambda group (p = 0.78), time (p = 0.06), and group x time (p = 0.013). Greenhouse-Geisser time and group x time (G x T) interaction p-values are reported with univariate group p-values. *represents p < 0.05 from PLA. †represents p < 0.05 from PWS. ‡represents p < 0.05 from PWS + S.
Table 11: Prevalence of Blood Chemistry Changes Exceeding Normal Clinical Bounds

| Marker Category | PLA | PWS | PWS + S | p-value |
|-----------------|-----|-----|---------|---------|
| Lipids & Glucose |     |     |         |         |
| Cholesterol     | No Change | 23  | 24  | 25  | 0.42 |
|                 | Normal Baseline, Exceed at 4-weeks | 2  | 0  | 1  |     |
|                 | Normal Baseline, Exceed at 8-weeks | 0  | 1  | 0  |     |
|                 | Normal 4-weeks, Exceed 8-weeks | 2  | 2  | 0  |     |
| HDL-C           | No Change | 25  | 21  | 26  | 0.10 |
|                 | Normal Baseline, Exceed at 4-weeks | 1  | 1  | 0  |     |
|                 | Normal Baseline, Exceed at 8-weeks | 1  | 1  | 0  |     |
|                 | Normal 4-weeks, Exceed 8-weeks | 0  | 4  | 0  |     |
| LDL-C           | No Change | 15  | 15  | 17  | 0.49 |
|                 | Normal Baseline, Exceed at 4-weeks | 11 | 9  | 9  |     |
|                 | Normal Baseline, Exceed at 8-weeks | 1  | 1  | 0  |     |
|                 | Normal 4-weeks, Exceed 8-weeks | 0  | 2  | 0  |     |
| Triglycerides   | No Change | 27  | 27  | 25  | 0.35 |
|                 | Normal Baseline, Exceed at 4-weeks | 0  | 0  | 1  |     |
|                 | Normal Baseline, Exceed at 8-weeks | 0  | 0  | 0  |     |
|                 | Normal 4-weeks, Exceed 8-weeks | 0  | 0  | 1  |     |
| Glucose         | No Change | 21  | 23  | 24  | 0.49 |
|                 | Normal Baseline, Exceed at 4-weeks | 2  | 0  | 0  |     |
|                 | Normal Baseline, Exceed at 8-weeks | 1  | 1  | 0  |     |
|                 | Normal 4-weeks, Exceed 8-weeks | 3  | 3  | 2  |     |
| Muscle          | LDH  | No Change | 20  | 18  | 18  | 0.74 |
|                 | Normal Baseline, Exceed at 4-weeks | 1  | 2  | 0  |     |
|                 | Normal Baseline, Exceed at 8-weeks | 2  | 1  | 3  |     |
|                 | Normal 4-weeks, Exceed 8-weeks | 4  | 6  | 5  |     |
| Creatine Kinase | No Change | 19  | 22  | 21  | 0.42 |
|                 | Normal Baseline, Exceed at 4-weeks | 1  | 0  | 0  |     |
|                 | Normal Baseline, Exceed at 8-weeks | 0  | 1  | 2  |     |
|                 | Normal 4-weeks, Exceed 8-weeks | 7  | 4  | 3  |     |
| Kidney          | Creatinine | No Change | 23  | 25  | 23  | 0.72 |
|                 | Normal Baseline, Exceed at 4-weeks | 2  | 0  | 1  |     |
|                 | Normal Baseline, Exceed at 8-weeks | 0  | 0  | 0  |     |
|                 | Normal 4-weeks, Exceed 8-weeks | 2  | 2  | 2  |     |
| BUN             | No Change | 17  | 18  | 19  | 0.41 |
|                 | Normal Baseline, Exceed at 4-weeks | 3  | 2  | 1  |     |
|                 | Normal Baseline, Exceed at 8-weeks | 0  | 0  | 2  |     |
|                 | Normal 4-weeks, Exceed 8-weeks | 7  | 7  | 4  |     |
| Liver           | ALP  | No Change | 25  | 23  | 25  | 0.28 |
|                 | Normal Baseline, Exceed at 4-weeks | 1  | 0  | 0  |     |
|                 | Normal Baseline, Exceed at 8-weeks | 0  | 0  | 0  |     |
|                 | Normal 4-weeks, Exceed 8-weeks | 1  | 4  | 1  |     |
| ALT             | No Change | 24  | 22  | 22  | 0.72 |
|                 | Normal Baseline, Exceed at 4-weeks | 1  | 0  | 0  |     |
|                 | Normal Baseline, Exceed at 8-weeks | 1  | 2  | 1  |     |
|                 | Normal 4-weeks, Exceed 8-weeks | 1  | 3  | 3  |     |
| AST             | No Change | 23  | 21  | 21  | 0.84 |
|                 | Normal Baseline, Exceed at 4-weeks | 1  | 1  | 1  |     |
|                 | Normal Baseline, Exceed at 8-weeks | 0  | 1  | 2  |     |
|                 | Normal 4-weeks, Exceed 8-weeks | 3  | 4  | 2  |     |

Data are frequency of occurrence. Significance is by chi-square analysis.
Safety analysis

One of the criticisms regarding PWS’s is that while there may be some ergogenic benefit, the short and/or long-term safety of taking these supplements is unknown [1]. Results of the present investigation indicate that the PWS’s studied were well-tolerated and did not adversely affect markers of health. In this regard, we observed no significant changes in resting hemodynamics, clinical blood markers, or a disproportional number of reported side effects in the PWS groups. These findings are consistent with a growing body of evidence that PWS supplementation appears to be safe and well-tolerated in apparently healthy individuals [56–59, 69, 70, 72–78] and that combination of these types of nutrients in PWS does not pose undue risk.

Conclusions

Results suggest that 8-weeks of PWS and PWS + S supplementation can improve some indices of cognitive function and exercise performance during resistance training without significant side effects in apparently healthy males. However, the inclusion of synephrine did not promote additive benefits. Additional research should investigate the effects of ingesting PWS’s on cognitive and exercise performance, training adaptations, and safety of long-term use in athletes.

Acknowledgements

We would like to thank the subjects that participated in this study as well as Abigail O’Connor, Chelsea Goodenough, Felix Ayadi, Chun-Hao Chang, Jeremy Carter, and Sunday Simbo at the Exercise & Sport Nutrition Laboratory at Texas A&M University who assisted with data collection. We would also like to thank Steve Riechman, Chris Woodman, and Steve Smith for their insights on data interpretation; Katherine Kelly and Cynthia Meininger for their valuable assistance in sample analysis; the Center for Translational Research in Aging and Longevity for providing nursing support; and, Dr. JP Bramhall for providing medical oversight.

Funding

This study was supported by Nutrabolt (Bryan, TX) through an unrestricted research grant provided to Texas A&M University. The Director of Clinical Science at Nutrabolt assisted in study design, data analysis and interpretation, and provided comments on the manuscript. However, the sponsor was not involved in data collection or data entry and there were no restrictions on publication of the data or preparation of this paper. As stated below, competing interests were supervised and managed by a university approved management plan to insure that data were accurately reported.

Availability of data and materials

Data and/or statistical analyses are available upon request on a case by case basis for non-commercial scientific inquiry and/or educational use as long as IRB restrictions and research agreement terms are not violated.

Authors’ contributions

YPJ served as study coordinator and assisted with data collection, data analysis, and manuscript preparation. MK, NB and DW assisted in data collection and sample analysis. CR serves as coordinator of the Exercise and Sport Nutrition Lab and project manager. MG assisted in research design and consultation. PSM served as study quality assurance manager. CPE served as a scientific liaison to the sponsor, assisted in study design, data analysis and interpretation, and provided comments on the manuscript. However, CPE was not involved in data collection or data entry and there were no restrictions on publication of the data or preparation of this paper. RBK (corresponding author) obtained the grant, served as study PI and assisted in the design of the study, data analysis, and manuscript preparation. All authors read and approved the final manuscript.

Competing interests

CP Earnest serves as a Director of Clinical Sciences for Nutrabolt and is a Research Associate in the ESNL. RB Kreider serves as a university approved scientific advisor for Nutrabolt. PS Murano serves as quality assurance supervisor in accordance to a conflict of interest management plan that was
approved by the university’s research and compliance office, the internal review board, and office of grants and contracts and monitored by research compliance. Remaining investigators have no competing interests to declare. The results from this study do not constitute endorsement by the authors and/or the institution concerning the nutrients investigated.

Consent for publication
Not applicable.

Ethics approval and consent to participate
This study was reviewed and approved by Texas A&M University’s Institutional Review Board (IRB2014-0079FX) in compliance in accordance with the Declaration of Helsinki.

References
1. Campbell B, Wilborn C, La Bounty P, Taylor L, Nelson MT, Greenwood M, et al. International Society of Sports Nutrition position stand: energy drinks. J Int Soc Sports Nutr. 2013;10(1):1. doi:10.1186/1550-2783-10-1.

2. Kreider RB, Wilborn CD, Taylor L, Campbell B, Almada AL, Collins R, et al. International Society of Health & Kinesiology, Center for Translational Research in Aging and Longevity, Texas A&M University, College Station, TX 77843-4243, USA. 2Nutrabolt, Bryan, TX 77807, USA. 3Department of Health & Kinesiology, College Station, TX 77843-4243, USA. 4Department of Nutrition and Food Sciences, Institute for Obesity Research & Program Evaluation, Texas A&M University, College Station, TX 77843, USA.

Received: 23 January 2016 Accepted: 12 December 2016

Published online: 03 January 2017

Jung et al. Journal of the International Society of Sports Nutrition (2017) 14:1
35. Haas S, Fontaine KR, Cutter G, Limdi N, Perumean-Chaney S, Allison DB. Citrus aurantium and synephrine alkaloids in the treatment of overweight and obesity: an update. Obes Res. 2006;14(1):79–88. doi:10.1038/sj.or.6700732
36. Preuss HG, DeFerrandino D, Bagchi M, Bagchi D. Citrus aurantium as a thermogenic, weight-reduction replacement for ephedra: an overview. J Med. 2002;55(3):428–47.
37. Hansen DK, George NJ, White GE, Pellicore LS, Abdel-Rahman A, Fabricant D, et al. Physiological effects following administration of Citrus aurantium for 28 days in rats. Toxicol Appl Pharmacol. 2012;261(3):236–47. doi:10.1016/j.taap.2012.04.006.
38. Penzak SR, Jann MW, Cold JA, Hon YY, Desai HD, Gurely BJ. Seville (sour) orange juice: synephrine content and cardiovascular effects in normotensive adults. J Clin Pharmacol. 2001;41(10):1059–63.
39. Stohs SJ, Badmaev V. A Review of Natural Stimulant and Non-stimulant Thermogenic Agents. Phytother Res. 2016;30(5):732–40. doi:10.1002/ptr.5583.
40. Rahama S, Rabiei Z, Alibabaei Z, Mohktari S, Rafieian-Kopaei M, Deris F. Anti-aimensive activity of Citrus aurantium flowers extract against scopalamine-induced memory impairments in rats. Neurol Sci. 2015;36(4):553–60. doi:10.1007/s10072-014-1991-2.
41. Yang W, Ma J, Liu Z, Lu Y, Hu B, Yu H. Effect of naringin on brain insulin signalling and cognitive functions in ICR-STZ induced dementia model of rats. Neurol Sci. 2014;35:571–5. doi:10.1007/s10072-013-1594-3.
42. Cho M, Jung Y, Goodenough C, O'Connor A, Dalton R, Levers K, et al. Effects of ingesting a pre-workout supplement with and without synephrine on cognitive function, perceptions of readiness to perform, and exercise performance. J Int Soc Sports Nutr. 2014;11(1):2. doi:10.1186/1550-2783-11-s1-p36.
43. Jung Y, Goodenough C, Cho M, O'Connor A, Dalton R, Levers K, et al. Thermogenic and hemodynamic effects of ingesting a pre-workout supplement with and without synephrine. J Int Soc Sports Nutr. 2014;11(1):1–2. doi:10.1186/1550-2783-11-s1-p35.
44. Jung YP, Koozachian A, Shin S, Collins PB, Dalton R, et al. Effects Of Short-term Pre-Workout Supplement Ingestion At Different Dosages On Exercise Performance: 901 Board #217 June 1, 3: 30 PM - 5:00 PM. Med Sci Sports Exerc. 2016;48(Suppl 4):12254. doi:10.1249/01.ms.0000485764.31303.3e.
45. Kerksick CM, Wilborn CD, Campbell BJ, Roberts MD, Rasmussen CJ, Greenwood M, et al. Early-phase adaptations to a spilt-body, linear periodization resistance training program in college-aged and middle-aged men. J Strength Cond Res. 2009;23(3):962–71. doi:10.1519/JSC.0b013e3181a0baef.
46. Galvan E, Walker DK, Simbo SY, Dalton R, Levers K, O'Connor A, et al. Acute and chronic safety and efficacy of dose dependent creatine nitrate supplementation and exercise performance. J Int Soc Sports Nutr. 2016;13:1. doi:10.1186/s12970-016-0124-0.
47. Jagim AR, Oliver JM, Sanchez A, Galvan E, Fluckey J, Rechman S, et al. A buffered form of creatine does not promote greater changes in muscle creatine content, body composition, or training adaptations than creatine. J Int Soc Sports Nutr. 2012;9(1):43. doi:10.1186/1550-2783-9-43.
48. Kreider RB, Melton C, Rasmussen CJ, Greenwood M, Lantaster S, Cantler EC, et al. Long-term creatine supplementation does not significantly affect clinical markers of health in athletes. Med Cell Biochem. 2003;244(1–2):295–104.
49. Levers K, Dalton R, Galvan E, O'Connor A, Goodenough C, Simbo S, et al. Effects of powdered Monomemory tart cherry supplementation on acute endurance exercise performance in aerobically trained individuals. J Int Soc Sports Nutr. 2016;13:22. doi:10.1186/s12970-016-0133-z.
50. Kegoes RC, Ward KD, Shelton ML, Applegate WB, Cantler ED, Palmeri GM, et al. Changes in bone mineral content in male athletes. Mechanisms of action and intervention effects. JAMA. 1996;276(3):226–30.
51. Almada AL, Kreider RB, Rasmussen J, Rasmussen C, Tutko R, Milnor P, Almada AL, Kreider RB, Rasmussen J, Rasmussen C, Tutko R, Milnor P. Comparison of the reliability of repeated whole body DEXA scans to repeated spine and hip scans. J Bone Miner Res. 1999;14:243.
52. Kaminsky LA, Bryant CX, Mahler DA, Durstine JL, Humphrey RH. ACSM’s Guidelines for Exercise Testing and Prescription. 8th ed. Baltimore: Lippincott; Williams & Wilkins; 2009.
53. Golden CJ. Group version of the Stroop color and word test. J Pers Assess. 1975;39(4):386–90. doi:10.1207/s15327752ja903_104.
54. Bowling JL, Katayev A. An evaluation of the Roche Cobas c 111. Lab Med. 2010;41(7):398–402.
55. Page P. Beyond statistical significance: clinical interpretation of rehabilitation research literature. Int J Sports Phys Ther. 2014;9(5):726–36.
76. Wells AJ, Hoffman JR, Gonzalez AM, Stout JR, Fragala MS, Mangine GT, et al. Phosphatidylserine and caffeine attenuate postexercise mood disturbance and perception of fatigue in humans. Nutr Res. 2013;33(6):464–72. doi:10.1016/j.nutres.2013.03.009.

77. Seifert JG, Nelson A, Devonish J, Burke ER, Stohs SJ. Effect of acute administration of an herbal preparation on blood pressure and heart rate in humans. Int J Med Sci. 2011;8(3):192–7.

78. Stohs SJ, Preuss HG, Shara M. The safety of Citrus aurantium (bitter orange) and its primary protoalkaloid p-synephrine. Phytother Res. 2011;25(10):1421–8. doi:10.1002/ptr.3490.