International Journal of Sport Nutrition and Exercise Metabolism, 2005, 14, 75-83

Assessment of the Effects of Eleutherococcus Senticosus on Endurance Performance

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The use of nutritional ergogenic aids containing Eleutherococcus senticosus (ES), a plant which is also known as ciwujia or Siberian ginseng, is relatively common among endurance athletes. Eleutherococcus senticosus has been suggested to improve cardiorespiratory fitness (CF) and fat metabolism (FAM) and, therefore, endurance performance (EP). This article reviews the studies that evaluated the effects of ES during endurance exercise, three of which suggest that ES substantially improves CF, FAM, and EP. However, each of these reports contains severe methodological flaws, which seriously threaten their internal validity, thereby rendering hazardous the generalization of the results. On the other hand, 5 studies that used rigorous research protocols show no benefit of ES on CF, FAM, and EP. It is therefore concluded that ES supplementation (up to 1000 to 1200 mg/d for 1 to 6 wk) offers no advantage during exercise ranging in duration from 6 to 120 min.

Key Words: ginseng, ciwujia, nutritional ergogenic aid, exercise, muscle strength

It is well documented that endurance training, because of structural and metabolic adaptations, enables muscle cells to derive a greater proportion of fuel supply from fat (14). This physiological adaptation is of crucial importance for endurance athletes, because a greater fat utilization attenuates the rate of endogenous carbohydrate depletion (12, 13, 14), which could theoretically increase the time period during which prolonged exercise can be performed (13). Hence, endurance athletes who desire to perform at their best during competitions would have an advantage from maximizing fat metabolism (FAM) (16). In the hope of enhancing FAM beyond physiological limits, many endurance athletes use nutritional ergogenic aids (NEA) claiming to increase fat utilization, decrease muscle glycogen utilization, and enhance endurance performance (EP). Examples of such NEA are caffeine (13), L-carnitine (13), long- (12) and medium-chain triglycerides (12), and Eleutherococcus senticosus (ES) (2). Among the previously mentioned NEA, ES is probably the one that has received the least attention from researchers. Therefore, the goal of this article is to review the literature that verified the effects of ES during endurance exercise.

In addition to its ''lipotropic'' claims (26), ES has also been purported to improve EP (1), increase maximal oxygen consumption (VO_{2max}) (21) and anaerobic

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threshold (AT) (26), decrease heart rate (HR) (26), reduce lactate accumulation (LA) (26), and accelerate HR recovery (26). Likewise, unpublished reports (15) that examined the effects of Endurox™ (PacificHealth Laboratories, Inc., Matawan, NJ), a popular compound whose active ingredient is ciwujia suggest that it can increase FAM by 43%, oxygen consumption (VO_2) and AT by 5 to 13% and 12%, respectively, decrease HR by 7%, reduce LA by 32%, and accelerate HR recovery by 22%. These results, however, should be viewed with skepticism until the studies are published in peer-reviewed journals, and replicated by independent laboratories (3). Although some studies ascribe beneficial effects to ES during endurance exercise, there are a number of studies that demonstrate no ergogenic advantage when comparing ES with the use of a placebo (4, 8, 9, 18, 19). The likely cause for these discrepancies in results could be attributed to the type of research designs that were utilized (10). In fact, the studies reporting positive effects of ES utilized flawed research protocols, whereas those that did not report beneficial effects used robust research settings appropriate for the study of NEA. Though relatively few studies have examined the effects of ES, a brief review is justified because a) little scientific attention has been brought to the substance; b) ES is promoted to customers as an efficient NEA (15) and; c) a consensus among well-conducted studies (4, 8, 9,18, 19) suggests no effect of the compound during endurance exercise.

Information on Eleutherococcus Senticosus

Eleutherococcus senticosus is a plant that has been used by the Chinese for the last 2000 years as a medicinal remedy to treat infections, fatigue, and strengthen the immune system (15). Eleutherococcus senticosus is also known under the popular names of ciwujia, Siberian ginseng, Russian ginseng, Radix Acanthopanax senticosus, eleuthero, eleuthero ginseng, touch-me-not, and devil's bush (9, 19). The term ginseng must not be confused with that of ES. In fact, ginseng is the generic term given to all species of Panax (the plant genus), which derive from the Araliaceous plant (2), a plant that is completely different from ES. The three most popular species of Panax currently recognized are Panax quinquefolius (American ginseng), Panax ginseng (Chinese/Korean ginseng), and Panax japonicus (Japanese ginseng).

Despite the fact that ginseng and ES are two different plants, they nevertheless are derived from the same plant family (Araliaceae). Although ES extracts can contain several substances including vitamins, minerals, cellulose, and ethanol, all of which can induce various physiological responses, the substances responsible for its purported ergogenic effects are eleutherosides (root of ES) (2) and ciwujianosides (leaf of ES) (22), as opposed to ginsenosides (root of ginseng) (2) for the species of Panax. While the structure of ginsenosides is similar to that of eleutherosides and ciwujianosides, it should be noted that all three are chemically distinct (22). Therefore, the terms eleutherosides and ciwujianosides should, theoretically, not be used interchangeably and their respective effects should be evaluated separately. As eleutherosides and ciwujianosides are derived from the same plant, however, and their effects (4, 8, 9, 18, 19) during endurance exercise have been shown to be similar, in this article the term ES is used to encompass the effects of both eleutherosides and ciwujianosides. Eleutherococcus senticosus is reported to be medically safe (15). There are, however, possible side effects, because its ingestion

in some individuals can cause stomach irritation, diarrhea, and, if taken too close to bedtime, insomnia (17, 22). Pregnant or nursing women, as well as individuals with uncontrolled high blood pressure or taking hormonal drugs, should not consume ES without adequate medical supervision (22). The use of ES is not banned by the International Olympic Committee (2).

Literature Review

Positive Findings

Of the studies reviewed, three suggest that ES offers an ergogenic advantage during endurance exercise (1, 21, 26). Each of these studies, however, suffers from several methodological weaknesses, making the generalization of the results questionable. Although these studies were published in peer-reviewed journals, these journals were nonexercise/nutrition science journals. These studies, as well as those reporting negative findings, are summarized in Table 1.

Asano et al. (1) were the first to report that ES supplementation improves EP compared with a placebo. First, subjects completed three cycling tests to exhaustion (step-incremented VO_{2max} tests) over three consecutive days without any form of supplementation. Then, subjects were supplemented with the placebo for 8 d after which they underwent another cycling test. After the placebo trial, subjects were supplemented for 8 d with ES (300 mg/d) and then performed a final cycling test. The treatments were administered in a single-blind fashion and subjects served as their own control. Compared with the placebo, ES increased cycling time to exhaustion and total work capacity by 10 and 15%, respectively. Despite these improvements, there were no differences between treatments for VO_{2max} and oxygen pulse. Compared with the pre-supplementation trials, however, ES improved VO_{2max} and oxygen pulse as well as cycling time to exhaustion (16%) and total work capacity (23%). Asano et al. (1) speculated that the efficacy of ES could be caused by the fact that it increases the number of mitochondria in muscle cells. Their findings, however, should be interpreted with caution, because the experimental design contains important methodological errors, which seriously threaten the internal validity of the observed results (10). First, only a single-blind protocol was used. Second, the researchers did not employ a crossover design. Instead, they had the subjects perform three pre-supplementation trials first, then the placebo and, finally, the ES trial. Thus, an order/training effect, and not the effect of ES per se, could be responsible for the observed results.

Wu et al. (26) evaluated the effects of ES on cardiorespiratory fitness (CF) and FAM during a step-incremented submaximal cycling exercise. Eight subjects were given the placebo for 3 d, after which they underwent a first test. Following this trial, they were supplemented with 800 mg/d of ES for 14 d and then underwent a second test. The submaximal cycling test started at an initial load of 60 W for 3 min, after which it was increased every 3 min by 30 W, up to 210 W. Compared with the placebo, ES decreased HR. ES also significantly reduced LA by 33%, increased the load and VO_2 at AT (defined as 4 mmol/L) by 12 and 7%, respectively, and enhanced FAM by 43%. Fifteen minutes after the test, ES significantly decreased LA and HR by 34 and 13%, respectively. The Wu et al. study (26) possesses methodological flaws similar to those of Asano et al. (1), thereby making its results hard to interpret and difficult to generalize to the athletic population.

Table 1 Summary of Studies That Evaluated the Effects of ES During Endurance Exercise

Reference	Number of subjects, gender, and age	Duration of supplementation	Daily dose and preparation type	Study design	Results
Positive Findings					
Asano et al. (1)	6 men; 21-22 y	8 d	300 mg (Eleutheroccocus senticosus Maxim, root of ES)	PPC, SB, PC, DC	∅ on VO_{2max} and oxygen pulse; ↑ cycling time to exhaustion and total work
Wu et al. (26)	8 men; 25-35 y	14 d	800 mg (Endurox™, leaf of ES)	PPC PPC	↓ HR and LA; ↑ the load and VO_2 at AT; ↑ fat utilization; ↑↑ HR and lactate recovery
Szolomicki et al. (21)	31; gender not specified; 21-73 y	30 d	75 drops (Taigutan™, root of ES)	PPC	∅ on VCO_2, HR and RER; ↑ VO_{2max} and maximal V_E
Negative Findings					
McNaughton et al. (18)	15 women and 15 men; age not specified	42 d	1000 mg (Russian ginseng, root of ES)	R, DB, CO, PC	∅ on VO_{2max}, HR recovery and grip strength; ↑ pectoral and quadriceps strength
Dowling et al. (8)	4 women and 16 men; 37 ± 8 y	42 d	3.4 mL (Eleutherococcus senticosus Maxim L, root of ES)	M, R, DB, PC, FT	∅ on EP, VO_2, V_E, V_E/VO_2, RER, HR, LA, and PE
Plowman et al. (19)	5 women and 5 men; 23 ± 1.8 y	10 d	800 mg (Endurox™, leaf of ES)	R, DB, CO, PC, DC, WP	∅ on VO_2, RER, HR, LA, and PE
Cheuvront et al. (4)	10 men; 24 ± 4.3 y	7 d	800 mg (Endurox™, leaf of ES)	R, DB, CO, PC, DC, WP	∅ on VO_2, V_E, V_E/VO_2, RER, HR, plasma glycerol, LA, PE, energy expenditure and rate of fat oxidation
Eschbach et al. (9)	9 men; 28 ± 2 y	7 d	1200 mg (Endurox™, leaf of ES)	R, DB, CO, PC, FT, DC, WP	∅ on EP, VO_2, RER, HR, LA, PE, and plasma glucose

Note. PPC, pre–post comparison; M, ES vs. matched placebo group; R, randomized; DB, double blind; SB, single blind; CO, crossover; PC, placebo-controlled; FT, familiarization trial; DC, diet controlled; WP, washout period; ∅, no effect; ↑, increased; ↓, decreased; ↑↑, accelerated.

Researchers from Poland investigated the effects of ES on CF and FAM during a VO_{2max} test (21). A pre/post comparison design, with no placebo, was used. Thirty-one healthy subjects were tested for VO_{2max} and, upon exhaustion, measures of VO_2, VCO_2, HR, respiratory exchange ratio (RER), and minute ventilation (V_E) were taken. For a period of 30 d between trials, subjects were supplemented with 25 drops of ES three times daily. Compared with the pre-supplementation trial, ES significantly improved VO_{2max} and maximal V_E. There were, however, no differences between trials for the remaining variables. Unfortunately, because of the failure to include a placebo, the interpretation of the results is problematic.

Negative Findings

Five studies reported that ES does not improve EP nor CF and FAM during endurance exercise (4, 8, 9, 18, 19). Contrary to the studies suggesting positive benefits of ES, these reports used robust protocols, thereby allowing inferences. Each of these studies was published in peer-reviewed exercise/nutrition-oriented journals.

McNaughton et al. (18) evaluated the effects of ES, Chinese ginseng, and a placebo on VO_{2max}, HR recovery, and strength. Thirty trained runners were randomly assigned to three groups. Every 6 wk, the groups were administrated at random ES (1000 mg/d), Chinese ginseng, or the placebo. Following the first 6 wk of supplementation, and every 6 wk thereafter, subjects returned to the laboratory for testing. The results revealed that ES did not improve VO_{2max}, HR recovery, or grip strength compared with the placebo. ES did, however, significantly increase pectoral and quadriceps strength by 15 and 13%, respectively. Interestingly, Chinese ginseng significantly improved VO_{2max}, pectoral (22%), and quadriceps (18%) strength compared with the placebo. Results of this study suggest that ES improves muscular strength, but has no effect on either VO_{2max} or HR recovery in trained athletes.

The effects of ES on EP, CF, and FAM during submaximal and maximal running were evaluated by Dowling et al. (8). Following a familiarization phase, 20 trained distance runners were randomly assigned in matched pairs to either the placebo or ES group. Subjects were supplemented (3.4 mL/d) in a double-blind manner with ES or the placebo for 6 wk. Subjects maintained a similar training routine throughout the study and completed five running trials: one at baseline, one at weeks 2, 4, and 6, and a final one 2 wk after the withdrawal of ES supplementation. The test consisted of a 10-min run at the subjects' 10-km race pace followed by a 5-min recovery period and a run to exhaustion. During the running and recovery periods, VO_2, V_E, ventilatory equivalent for oxygen uptake (V_E/VO_2), RER, and HR were measured. Lactate accumulation was measured at rest before the first run and at 2 min following both running bouts. Perceived exertion (PE) was measured during both running periods. Time to achieve exhaustion was taken as the measure of EP. There were no differences between groups for any of the variables studied, suggesting that ES does not improve EP, CF, nor FAM in trained distance runners.

Plowman et al. (19) studied whether ES supplementation could improve CF and FAM during a steady-state submaximal stair-stepping exercise. Using a randomized, double-blind crossover protocol, 10 recreationally active subjects were administered either 800 mg/d of ES or a placebo for 10 d. A washout period of 5 d separated the supplementation periods. Throughout the study, subjects maintained

their training routine and diet. Subjects were requested to eat a standardized breakfast 2 to 3 h before each trial along with 800 mg of ES. During the first trial subjects exercised for 25 min on a StairMaster™ (The Nautilus Group, Vancouver, WA) at an individually selected intensity. The same workout was repeated for the second trial. Subjects were tested at the same time of day on the same day of the week for both trials. During the tests, measures of VO_2, RER, HR, LA, and PE were taken. Results were not different between treatments, thereby suggesting that recreational exercisers do not benefit from ES supplementation.

Cheuvront et al. (4) used a double-blind crossover protocol to determine the effects of ES supplementation on CF and FAM during steady-state submaximal cycling. Ten healthy males were randomly assigned to consume either 800 mg/d of ES or a placebo for 7 d. A washout period of 7 d took place before reciprocal supplementation. Subjects followed a similar diet for the last 48 h prior to the trials and, in addition, abstained from exercise for the last 24 h prior to each trial. The trials were performed at the same time and day of the week. On the seventh day of supplementation, and after a fast of 8 h, a cycling test was performed for 30 min at 25% of peak VO_2, followed by 10 additional minutes at 65% of peak VO_2. Oxygen consumption, V_E, V_E/VO_2, RER, HR, glycerol, and LA were measured before, during, and after exercise. Perceived exertion was measured during both bouts of exercise. Energy expenditure and rate of fat oxidation were measured during the bout of exercise conducted at 25% of peak VO_2. None of the results differed between treatments, indicating that during exercise conducted at low intensity, ES does not improve CF nor FAM in recreational cyclists.

Using a randomized, double-blind crossover design, Eschbach et al. (9) evaluated the effects of ES supplementation on EP, CF, and FAM during prolonged cycling. Nine trained males cycled during 120 min at ~ 60% of VO_{2max}, which was immediately followed by a simulated 10-km time trial. Before the first trial, subjects were familiarized with the exercise protocol by performing 45 min of cycling (~ 60% VO_{2max}) and the time trial. Subjects were then supplemented with either ES (1200 mg/d) or a placebo for 7 d. After the first trial, subjects underwent a washout period of 7 d before reciprocal supplementation. The trials were performed at the same time of the day, and subjects followed the same diet for the last 72 h prior to each trial. Subjects abstained from exercise for 24 h prior to each trial. During the steady-state cycling period, VO_2, RER, and HR were recorded every 30 min, whereas LA, PE, and plasma glucose were measured every 20 min. Compared with the placebo, ES did not improve any of the variables measured. These results therefore suggest that ES does not improve EP, CF, nor FAM in trained cyclists.

Conclusions

This article reviewed 8 studies that investigated the effects of ES supplementation during endurance exercise. Of the 8 studies, three (1, 21, 26) reported that ES enhances exercise capacity during such exercise. Taken together, their results suggest that ES improves EP, VO_2, VO_{2max}, maximal V_E, AT, fat utilization, and decreases HR and LA. These reports, however, suffer from serious problems of internal validity, thereby making difficult the generalization of the findings to the athletic population. As for the remaining 5 reports (4, 8, 9, 18, 19), their results indicate that ES has no effect on EP, VO_2, VO_{2max}, V_E, V_E/VO_2, LA, plasma glucose, fat

utilization, HR, and PE. Among these studies, however, one suggests that ES could potentially be beneficial for muscular strength (18). Importantly, these 5 studies used experimental protocols respecting the basic scientific principles underlying research with NEA. Therefore, it is appropriate to draw inferences from these studies. The paucity of literature, and especially of well-controlled studies, makes it difficult to draw definitive conclusions as to the effects of ES during endurance exercise. Nevertheless, based on the best scientific evidence available, ES supplementation (300 to 1200 mg/d for 7 to 42 d) appears to offer no ergogenic advantage for recreational or trained athletes during exercise less than or equal to 2 h. There is, however, some evidence suggesting that ES could increase the muscular strength of large muscles. This deserves further investigation given that increased muscle strength could directly or indirectly contribute to improve EP.

Suggestions for Further Research

Based on the results obtained from the well-conducted studies, it would seem hardly justifiable, at least with the products that were utilized, to conduct further studies verifying the effects of ES during exercises less than 2 h. Whether ES could improve exercise capacity during exercises greater than 2 h remains unknown and needs to be determined, because athletes often use ES in such circumstances in the hope of improving EP. Future studies need to observe how ES influences mitochondrial volume, muscle capillary density, storage of intracellular fat, lipoprotein lipase, and aerobic enzyme activity. Any positive change in these variables should favor fat oxidation, which is the main pathway by which ES is purported to improve EP. Moreover, the effects of ES on muscle glycogen storage capacity and utilization during prolonged exercise should be determined, because a favorable improvement could be associated with an increase in EP.

Research is needed to determine the effects and possible mechanisms of action of ES on muscular strength. It would be relevant to study the effects of ES on strength in endurance-trained/resistance-trained athletes as well as in the elderly (especially those suffering from sarcopenia), for whom only a small increase in strength can have a dramatic impact on physical capacity and quality of life (20). Ciwujianosides D_1 and C_1 have been shown to inhibit the release of histamine in rat peritoneal mast cells (24). Histamine is an important chemical mediator of the inflammatory process. Therefore, it is not impossible that ES could reduce the intensity of muscular inflammation following prolonged, strenuous exercise, which could help the recovery process of athletes. Whether this is a viable hypothesis remains to be determined in future studies.

The active constituents of ES are a series of ciwujianosides (leaf of ES) and eleutherosides (root of ES). To determine which constituents affect CF, FAM, or EP, research will need to isolate and verify the effects of each ciwujianoside and eleutheroside during endurance exercise. The dose necessary to attain and maintain eleutherosides/ciwujianosides blood saturation is presently unknown. Therefore, it would be important that future research determines the dose of ES (versus a given body weight) needed to reach eleutherosides/ciwujianosides blood saturation as well as the length of time the saturation would persist. Future studies must use robust experimental protocols and, in addition, ensure the compliance of subjects to all demands of the study, including that on the consumption of ES and the placebo.

In addition to using a questionnaire to determine the compliance of subjects to ES consumption, researchers could also verify compliance through the measurement of specific urinary biomarkers (6, 7, 23). With the exception of 1 study (8), none of the previously reviewed reports verified the content of the preparations administered. This constitutes a potential research limitation, because it has been demonstrated that the concentration of active ingredients found in ginseng and ES preparations is highly variable (5, 11). On top of this, it has been reported that certain ginseng products do not even contain the ingredients indicated on the label (25).

Accordingly, it would make sense to recommend that future studies on ES verify the content of the compounds administered. It must be known, however, that the verification of the content of a preparation is difficult. First, to the best of our knowledge, there is no commercial standardized ES extract (such as G115 for Panax ginseng) against which to compare HPLC analyses of over-the-counter ES preparations. Second, laboratory analyses to qualify and quantify ingredients from eleutherosides/ciwujianosides preparations are possible, but require specialized equipment and a high order of analytical skill (11). The assessment of the claims of NEA containing ES as it is advertised will, however, always remain an extremely important scientific piece of information for both the consumer and researcher.

Acknowledgments

Both authors are supported by the Canadian Institutes of Health Research. The authors recognize the help of Michel O. Mélaçon in the preparation of this article.

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