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The Effect of Eight Weeks of Supplementation with *Eleutherococcus senticosus* on Endurance Capacity and Metabolism in Human

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Abstract

The aim of this study was to examine the effects of *Eleutherococcus senticosus* (ES) supplementation on endurance capacity, cardiovascular functions and metabolism of recreationally trained males for 8 weeks. Nine recreationally trained males in college consumed 800 mg/d of ES or starch placebo (P) for 8 weeks according to a double-blind, randomized, placebo controlled and crossover design with a washout period of 4 weeks between the cycling trials. Subjects cycled at 75% $\dot{V}O_2$ peak until exhaustion. The examined physiological variables included endurance time, maximal heart rate during exhaustion exercise, $\dot{V}O_2$, rating of perceived exertion and respiratory exchange ratio. The biochemical variables including the plasma free fatty acid (FFA) and glucose were measured at rest, 15 min, 30 min and exhaustion. The major finding of this study was the $\dot{V}O_2$ peak of the subjects elevated 12% ($P < 0.05$), endurance time improved 23% ($P < 0.05$) and the highest heart rate increased 4% ($P < 0.05$) significantly. The second finding was at 30 min of 75% $\dot{V}O_2$ peak cycling, the production of plasma FFA was increased and the glucose level was decreased both significantly ($P < 0.05$) over 8-week ES supplementation. This is the first well-conducted study that shows that 8-week ES supplementation enhances endurance capacity, elevates cardiovascular functions and alters the metabolism for sparing glycogen in recreationally trained males.

Key Words: ciwujia, ergogenic aid, aerobic exercise

Introduction

Athletes use a variety of nutritional ergogenic aids to enhance performance. Most nutritional aids can be categorized as a potential energy source, an anabolic enhancer, a cellular component, or a recovery aids (1). *Eleutherococcus senticosus* (ES) is also known as Siberian ginseng, ciwujia or eleuthero. It is a thin, thorny shrub native to forests in southeastern Russia, northern China, Japan and Korea (5). Active ingredients of ES are a complex group of chemicals called eleutherosides (13) derived from the root and rhizome of ES. Also, ciwujianosides come from the leaf of ES. ES is reported to be medically safe but

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some of the subjects may have possible side effects such as diarrhea and insomnia (17). It is very important that ES is not banned by the International Olympic Committee and the World Anti-Doping Agency (3).

ES has been documented in three studies to improve endurance exercise, oxygen uptake and overall performance in athletes (2, 20, 22). The studies of Asano *et al*. (2) and Wu *et al*. (22) both suffered from important methodological flaws. Although Asano *et al*. (2) have shown that ES improved the use of oxygen by the exercising muscle, they only used a single-blind protocol and did not employ a crossover design. Wu *et al*. (22) also did not employ a crossover design and the observed results might be due to order and training effects. Szolomicki *et al*. (20) did not have a placebo control group. In contrast, in the review studies of Goulet and Dionne (9), five well-conducted studies which used rigorous research protocols had shown no effect of ES supplementation on cardiorespiratory fitness, fat metabolism and endurance performance. It seems, therefore, that up to 800 to 1200 mg/d for 1 to 6 weeks ES supplementation offers no advantage during exercise ranging in duration from 6 to 120 min. In this study, we supplemented subjects for 8 weeks whereas the past studies supplemented subjects for no more than six weeks.

This is the first published, double-blind, placebo-controlled and cross-over design study to examine the effects of ES supplementation for more than 8 weeks in a population of recreationally trained college students. The purpose of the present study was to test the hypothesis that 800 mg/d of ES supplementation for 8 weeks would be associated with improvements in endurance time, highest heart rate (HHR) attained and $\dot{V}O_2$ peak. We would also like to know if ES supplement could alter the metabolism of fat oxidation on sparing glucose during aerobically intense cycling at 75% $\dot{V}O_2$ peak in recreationally trained males.

Materials and Methods

Subjects

Nine recreationally trained college male students (Table 1) volunteered to participate in the study. Subjects were engaged in a tennis school team and training for 15-16 h per week prior to and during the testing period; none were using any conflicting medications. All subjects were informed orally and in writing of the experimental protocol and associated risks of the study before written informed consents were obtained. These subjects were screened to ensure they were not consuming ES or any other nutritional supplement prior to enrollment into this study. Prior to participation, each subject completed a health history questionnaire. All subjects were free of any cardiovascular or orthopedic condition that would influence exercise testing or training. The experimental protocol was approved by the Human Subjects Committee of Fu Jen Catholic University.

Table 1. Characteristics of the subjects (n = 9)

Characteristics	Mean	SD
Age (y)	19.0	2.1
Weight (kg)	66.4	7.2
Height (cm)	172.5	6.6
Body fat (%)	16.1	3.5
$\dot{V}O_2$ peak (ml/min/kg)	45.3	5.2

Table 2. Dietary intake of macronutrients of the subjects' diets for 1 day before the experimental trial

	After education ES group		After education P group	
	Mean	SD	Mean	SD
Energy (kJ)	11715	320	11632	606
Carbohydrate (g)	409.68	45.90	415.83	35.26
Carbohydrate (%)	58.5		59.8	
Protein (g)	115.55	14.28	114.12	14.89
Protein (%)	16.5		16.4	
Fat (g)	77.78	11.42	71.6	13.96
Fat (%)	25		23.8	

All results are expressed as mean values and standard deviation (n = 9). ES, *Eleutherococcus Senticosus*; P, placebo. No significant differences were observed between ES and P group after they educated by registered dietitian.

Eleutherococcus senticosus (ES) Supplementation and Starch Placebo (P)

ES and P were both manufactured by a cGMP-quality pharmaceutical plant (Chung Mei Pharmaceutical Co., Ltd. Changhua, 35342, Taiwan) in the same capsule form. The contents of the ES capsules were from the root and rhizome of the plant of ES, or starch in placebo (P). In this study, we carefully analyzed and verified the content of the capsules with 2 institutes: 1) Pharmaceutical Industry Technology and Development Center in Wugu Shiang, Taipei County, Taiwan, and 2) Super Laboratory in Wugu Shiang, Taipei County, Taiwan. The results indicated that both capsules did not contained caffeine, ephedrine and no harmful heavy metals as determined by TLC method. Two primary eleutherosides have been identified and it was shown that the ES capsules contained

0.11% of eleutheroside B (Syringin) and 0.12% of eleutheroside E as determined by HPLC. Subjects ingested 4 capsules of either ES (100 mg per capsule) or P twice a day before breakfast and before dinner for 8 weeks.

Pre-Experimental Protocol

The peak oxygen uptake ($\dot{V}O_2$ peak) was tested in the pre-experimental protocol performed 4 days before the start of the actual study. $\dot{V}O_2$ peak was determined by a portable cardiopulmonary indirect breath-by-breath calorimetry system (MetaMax 3B, Cortex Biophysik, Leipzig, Germany). The MetaMax was fixed onto a chest harness worn by the subjects while havinh an incremental exercise test on a cycle ergometer (Monark 834E, Ergoline, Bitz, Germany) until exhaustion. The protocol was started at 60 W for 3 min, with resistance raised by 25 W each additional minute until $\dot{V}O_2$ peak was achieved. The following criteria were used to determine the attainment of $\dot{V}O_2$ peak: 1) Subjects reported the rating of perceived exertion (RPE) using Borg's 20-grade rating scale when greater than 19; 2) Respiratory exchange ratio (RER) in excess of 1.1, and 3) Reaching age-predicted maximum heart rate (220-age) ±10% tested by a heart rate monitor (Polar S625X, Polar Electro, Kempele, Finland).

Study Design

This study was a randomized, double-blind, placebo-controlled and crossover design. Supplementation of either ES or P at 800 mg/day was initiated after first a familiarization trial (4 days after the pre-experimental protocol) and was continued for 8 weeks. There was a 4-week washout period between the experimental trials. Then the capsules were switched and supplementation was continued for another 8 weeks. This study used a conventional crossover protocol. Each subject completed four experimental trials: The two pre-supplementation periods served to familiarize the subjects with the tests. They then reported the placebo and ES results after 8 weeks of supplementation. Subjects were asked to maintain their normal training patterns and diet habits during the 20-week period of this experiment. They were asked specially to refrain from exercise, caffeine and alcohol consumption 24 h before each trial and to consume their typical pretest meal (1632 kJ) 1 h prior to each trial. The subjects were tested at the same time of the day for each exhaustion ride.

Nutritional Education

To ensure healthy and balanced food intake for the subjects during the experimental period, subjects were educated by a registered dietitian at the beginning of this study. Take-home instructions were given to assure intake compliance. Education included dietary reference intakes (DRIs), balanced dietary intake patterns and showed food models to subjects for understanding the concept of portion. Subjects interviewed by the registered dietitian were asked to keep a detailed 24-hour dietary record prior to each experimental trial for compliance and were asked to maintain a consistent diet 1 day before and to keep a balanced diet during the experimental period. Dietitian used the nutrition analysis software (e-kitchen, version 2003, Taichung, Taiwan) to analyze the diets of the subjects.

Endurance Time Trial Testing Protocol (Experimental Trials)

On the day of the experiment, subjects attended the laboratory at 06.00-08.00 h following a 9-10 h of overnight fast and were tested at the same time of the day for each exhaustion ride. A standardized breakfast consisting of 60 g carbohydrates, 16 g protein and 9.5 g fat was ingested (1632 kJ). Baseline physiological data were collected while the subjects were sitting quietly on the cycle ergometer (model 834E, Monark, Varberg, Sweden) for 10 min prior to commencing the cycling test. Heart rate (HR) was monitored by a Polar heart rate monitor (Polar S625X, Polar Electro, Kempele, Finland) and RPE was evaluated using the Borg's 20-grade rating scale. Subjects then commenced a 5-min warm-up at a cycling speed equivalent to 55% $\dot{V}O_2$ peak. The cycling speed was then increased to a pace equivalent to 75% $\dot{V}O_2$ peak of the subjects. Subjects were blinded to the endurance time (ET) and HR. The ET trial was equivalent to a cumulative time of work of the subject cycled at 75% $\dot{V}O_2$ peak until exhaustion. Exhaustion was defined as the point at which subjects could no longer maintain the required cycling speed (rpm > 60). RPE, RER, HR and $\dot{V}O_2$ peak were collected at rest, 15, 30 min and exhaustion.

Blood Analysis

An indwelling catheter was inserted into the antecubital vein for blood sampling. Venous blood samples (~20 ml) were drawn when 1) prior to the exercise (at rest), 2) at 15 min during exercise, 3) at 30 min during exercise, and 4) at exhaustion. At each sampling time, 5 ml blood was taken. Whole blood glucose concentration was measured by a glucometer (Roche Diagnostics Accu-Chek EASY, Roche Diagnostics, New Zealand). Then blood sample was drawn into a heparinized tube. After centrifugation, samples (plasma) were stored at -80°C and later analyzed for plasma free fatty acid (FFA) measured by an en-

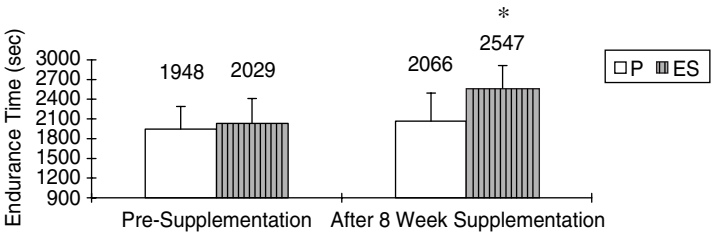

Fig. 1. Endurance time before and after 8 weeks of supplementation of *Eleutherococcus senticosus* (ES) and Placebo (P). All results are expressed as mean values and standard deviation (n = 9). Statistical differences between each group were determined by paired *t* test, group with * indicate significant difference between groups ($P < 0.05$).

Table 3. Effects of *Eleutherococcus senticosus* (ES) and Placebo (P) supplementation after 8 weeks of supplementation on mean physiological and biochemical data during cycling exercise

Parameter	Trial	Rest	15 min	30 min	At the end of the endurance exercise
Rating of perceived exertion (RPE)	ES	2 ± 0	13 ± 1	15 ± 1*	19 ± 1
	P	2 ± 0	14 ± 1	18 ± 2	19 ± 1
Heart rate (HR) (beats/min)	ES	68 ± 4	150 ± 2	171 ± 6	190 ± 4*
	P	72 ± 6	152 ± 3	76 ± 5	182 ± 7
$\dot{V}O_2$ (oxygen uptake) (l/min)	ES	0.36 ± 0.01	2.34 ± 0.05	2.55 ± 0.09	3.02 ± 0.14*
	P	0.36 ± 0.02	2.32 ± 0.06	2.78 ± 0.10	2.92 ± 0.17
Respiratory exchange ratio (RER)	ES	0.83 ± 0.01	0.91 ± 0.01	0.90 ± 0.02*	1.13 ± 0.02*
	P	0.84 ± 0.02	0.93 ± 0.02	0.96 ± 0.03	1.10 ± 0.05
Plasma free fatty acid (FFA) (μM)	ES	122 ± 78	214 ± 66	298 ± 79*	343 ± 86*
	P	169 ± 101	246 ± 90	265 ± 110	287 ± 72
Blood glucose (mg/dl)	ES	99.4 ± 20.8	89.2 ± 15.1	82.4 ± 20.1*	86.6 ± 12.3*
	P	97.2 ± 18.3	90.6 ± 17.4	88.6 ± 17.4	92.8 ± 20.1

All results are expressed as mean values and standard deviation (n = 9). Group with * indicated significant differences between ES and P groups ($P < 0.05$) determined by paired *t* test.

zymatic colorimetric method using a commercially available kit (WAKO NEFA C, Wako Chemicals, Richmond, VA, USA). Glutamate oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), blood urea nitrogen (BUN) and creatinine were determined by a spectrophotometric technique (Johnson & Johnson Vitros Ektachem DT-60 analyzer, Orthoclinical Diagnostics, Rochester, NY, USA) using a kit (Ektachem slide, Kodak Co. Roehester, NY, USA) for examining liver and kidney functions.

Statistical Analyses

All values are presented as means ± standard deviation (SD). Statistical analyses were carried out using SPSS 11.0 for Windows (Chicago, IL, USA). Paired *t* test was used to evaluate significant differences between ES and P groups after 8 weeks of supplementation. Statistical significance was accepted at $P < 0.05$.

Results

Effect of ES on Endurance Capacity and Cardiovascular Functions

Prior to supplementation, $\dot{V}O_2$ peak of subjects were 45.3 ± 5.2 ml/kg/min. After the 8-week supplementation, $\dot{V}O_2$ peak of the *P* group was 46.7 ± 5.3 ml/kg/min, compared to 50.9 ± 5.1 ml/kg/min in the ES group ($P < 0.05$), showing a significant difference in response to the ES supplementation. The two pre-supplementation periods served to familiarize the subjects with the tests and showed no significant differences between the groups. After the 8-week supplementation, endurance time was significantly increased with ES (ES = 2547 ± 367 s, P = 2066 ± 429 s) ($P < 0.05$) (Fig. 1). Measurements of RPE, HR, $\dot{V}O_2$, RER, blood glucose and plasma FFA are shown in Table 3. Data were analyzed in the time period at

the beginning of exercise (rest), 15 min, 30 min and at exhaustion during the 75% $\dot{V}O_2$ peak exercise. RPE increased slightly over time in the P and ES groups and there was a significant difference between the groups (ES = 15 ± 1, P = 18 ± 2) at 30 min during 75% $\dot{V}O_2$ peak exercise ($P < 0.05$). Resting heart rate showed no significant difference between the groups. Maximal heart rate (MHR) showed a significant difference with the ES group (ES = 190 ± 4 beats/min, P = 182 ± 7 beats/min ($P < 0.05$). $\dot{V}O_2$ increased significantly with the ES group at exhaustion (ES = 3.02 ± 0.14 l/min, P = 2.92 ± 0.17 l/min) ($P < 0.05$). As shown in Table 3, the *t* tests revealed significant differences between the groups of RER at 30 min (ES = 0.90 ± 0.02, P = 0.96 ± 0.03) and at exhaustion (ES = 1.13 ± 0.02, P = 1.10 ± 0.05) ($P < 0.05$).

Blood Parameters

As shown in Table 3, FFA levels were affected by ES supplementation which was increased at 30 min (ES = 298 ± 79 μM, P = 265 ± 110 μM) and at exhaustion (ES= 343 ± 86 μM, P = 287 ± 72 μM) with significance ($P < 0.05$) between the groups. Also, glucose levels were affected by ES supplementation and decreased at 30 min (ES = 82.4 ± 20.1 mg/dl, P = 88.6 ± 17.4 mg/dl) and at exhaustion (ES = 86.6 ± 12.3 mg/dl, P = 92.8 ± 20.1 mg/dl) with significance ($P < 0.05$) between the groups.

Subjects were asked whether they noticed any side effects that may be related to the intake of supplementation every 4 weeks. Within the 20-week experimental period, only one subject suffered from minor insomnia on the first day during ES supplementation. No other side effects were reported for both groups. Three subjects felt more powerful and comfortable during the practice sessions of tennis. The blood parameters GOT, GPT, BUN and creatinine were all in the normal range in both groups and showed no significant differences after the 8-week supplementation (Table 4).

Table 4. Comparison of liver and kidney parameters after 8 weeks of *Eleutherococcus senticosus* (ES) and Placebo (P) supplementation

	ES group		P group	
	mean	SD	mean	SD
GOT (U/l)	28.75	4.57	28.88	4.45
GPT (U/l)	21.36	8.53	20.94	7.97
BUN (mg/dl)	13.81	3.38	13.96	3.45
Creatinine (mg/dl)	1.1	0.69	1.2	0.71

All results are expressed as mean values and standard deviation (n = 9). GOT, Glutamate oxaloacetate transaminase; GPT, Glutamate pyruvate transaminase; BUN, Blood urea nitrogen. No significant differences were observed between ES and P group determined by paired *t* test.

Discussion

The data presented in this study indicated that in recreationally trained males, eight weeks of *Eleutherococcus senticosus* supplementation markedly enhances endurance time, elevates cardiovascular functions and alters the metabolism of plasma free fatty acid and glucose during the 75% $\dot{V}O_2$ peak exercise to exhaustion on a bicycle ergometer. These findings are based on one placebo result and one ES result after a 8-week supplementation. To our knowledge, this is the first well-controlled study that showed positive effects of ES on endurance exercise capacity in human clinical studies.

In contrast to previous works, several well-conducted studies (4, 6, 7, 16, 19) reported no effect of 800 to 1200 mg per day for 1 to 6 weeks of ES supplementation on endurance performance such as heart rate, lactate level at relative workloads, steady state oxygen consumption ($\dot{V}O_2$), maximal oxygen consumption ($\dot{V}O_2$ max), ratings of perceived exertion (RPE) or respiratory exchange ratio (RER) during treadmill or cycling duration of up to approximately 50-min. While all the well-conducted studies found in the literature showed no effect of ES on endurance performance, we obtained positive results in our hypothesis. It seems likely that this ergogenic effects are dependent on the length of duration of ES supplementation: 8 weeks and 800 mg dosage had been shown to be safe to human body.

In this study, there is no diet variation and training effect between the test groups. The nutrients content of the diets of the subjects was one of the major determinants of effectiveness in their response to exercise. It has been well established that variations or modifications of food intake in the days and hours prior to exercise can have a significant impact on substrate utilization (10). Therefore, the pre-exercise dietary control must be considered. In this study, we controlled the diets of all the subjects' to consume their typical pretest meal (1632 kJ) 1 h prior to each trial to demonstrate no diet variation with the pre-exercise diet between the ES and P groups after education from a dietitian. These emphasized that the beneficial effect of ES on endurance exercise documented in this study was not accompanied by any significant alteration in diet.

Peak oxygen intake ($\dot{V}O_2$ peak) represents the sum of effective oxygen supply and oxygen consumption in tissues and defines physical fitness sufficiently well. In this study, we have shown that ES

did affect $\dot{V}O_2$ peak significantly between the test and control groups ($P < 0.05$), and increased oxygen uptake as well. Endurance time was also increased significantly ($P < 0.05$) accompanied by an increase of oxygen uptake. Compared to the study of Eschbach *et al*. (7), we noted that the effects of ES may be more pronounced in persons with lesser aerobic capacity (< 50 ml/kg/min) than in those with higher $\dot{V}O_2$ max levels (> 55 ml/kg/min). And in the study of Szolomicki *et al.* (20), thirty-one healthy subjects were tested for $\dot{V}O_2$ max and, upon exhaustion, measures of $\dot{V}O_2$, VCO_2, HR, 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 $\dot{V}O_2$ max 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.

High-intensity endurance exercise is often associated with discomfort. Heart rate is a more precise method to measure the intensity involved in a workout. Compared with the P group, the ES group increased HR 4.0% during the endurance exercise after the 8-week supplementation. This result demonstrated that the subjects in the ES group were able to tolerate greater heart work load that could be benefits to endurance exercise. This index indicated that ES might positively affect oxygen consumption during metabolic processes in tissues. Because both the HRmax and metabolism index increased significantly, it suggests that the increased $\dot{V}O_2$ peak in the ES group was contributed by aerobic metabolism of tissues and the stronger cardiovascular functions. These changes were not resulting from physical training because the subjects were in a maintenance phase of their training which would help to control for any training effect between the experimental periods in these 8 weeks. This study utilized a randomized, double-blind, placebo-controlled and crossover design as well as a familization trial to control for potential learning effects and to minimize the between-test variance. As expected, with these metabolic effects, the endurance time and oxygen uptake with ES improved after 8 weeks of ES supplementation.

Ergogenic aids are believed to increase performance by some of the following mechanisms: renewing or increasing energy storages in the body facilitating biochemical reactions that yield energy (12, 16). The beneficial effect of ES was also accompanied by significant alterations in metabolism expressed as plasma free fatty acid (FFA) and blood glucose in a shift towards aerobic source of energy. Compared to previous studies as we have mentioned before, in this study ES produced a significant decrease in RER (from 0.96 decreased to 0.90 ($P < 0.05$) at 30 min of 75% $\dot{V}O_2$ peak exercise. That suggests a 20% shift in the metabolism from carbohydrate to fat indicating that the reason for lower RER is the response of glucose and lipid metabolism with ES supplementation, which appears to increase FFA and lower glucose level during 30 min and exhaustion with significance ($P < 0.05$). Plasma FFA are the main substrates used during exercises performed at half or less aerobic capacity. Moderate exercise induces endocrine and metabolic changes that seem to be associated with the improvement of FFA oxidation. A classical concept has been FFA/TAG (triacylglycerol) recycling (21) which might play a role in the regulation of lipid metabolism during and after exercises. FFA is released by the action of hormone-sensitive lipase and fatty acids are the preferred fuel of muscle during endurance exercise. Fatty acids utilization changes during the recovery through changes of the levels of insulin and glucose in the plasma (15). Endurance exercise causes pronounced increases in the lipolysis rate in the adipose tissue (11). At the 30 min and exhaustion of 75% $\dot{V}O_2$ peak exercise, the FFA concentration of the ES group was significantly higher by 12% and 19%, respectively, than the P group ($P < 0.05$). The higher FFA at exhaustion in the ES trial was not only related to the longer exercise duration, but also because ES elevated lipid utilization and decreased glucose oxidation simultaneously. The elevated insulin concentration might suppress fat metabolism, and increase muscle glucose uptake as well as carbohydrate oxidation during subsequent exercises (8). The data indicate that ES may activate the adrenal system, elevate the c-AMP in blood and liver, and activate the lipase to increase lipolysis (8). Therefore, the present study indicated that ES supplementation did appear to enhance endurance time during intense submaximal exercises with concomitant increases in free fatty acid availability and utilization in preference over glucose for cellular energy demands. Liu *et al*. (14) recently suggested that Syringin has an ability to augment insulin release resulting in a plasma glucose lowering action. In this study, the ES capsules contained 0.11% of eleutheroside B (Syringin). These biochemical results indicate that ES has an effect on the elevation of fat oxidation sparing muscle glycogen.

The limitation of this study was that the content of the ES capsules could not be completely analyzed because there it was difficult to get all the standards for the eleutherosides (eleutheroside A, B, C, D, E, F, G) against which to compare the HPLC analysis data. Results showed that the ES used in this study contained the active compounds of the plant extract: eleutheroside B and eleutherside E. These compounds may activate the adenylate cyclase system for lowering

glucose (18). The effects on blood glucose could be considered ergolytic for endurance exercise performance. In future studies, we would like to examine the possible mechanism underlying the beneficial effect of ES supplementation on endurance exercise. Future studies should be investigated in the volume, number of mitochondria and the activity of muscle mitochondrial enzymes: citrate synthase and cytochrome *c* oxidase.

In conclusion, this study indicates that the 8-week ES supplementation has ergogenic benefit for recreationally trained males. These data are novel as this was the first well-controlled study of ES supplementation and had ergogenic effects in which ES may enhance the endurance capacity, improve the cardiovascular function and alter metabolic functions. It is concluded that *Eleutherococcus senticosus* is an effective nutritional ergogenic aids for people who perform endurance exercises, but the exact mechanisms involved need further investigation.

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