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**EFFECTS OF ENDUROX™ (CIWUJIA) SUPPLEMENTATION ON ENDURANCE
 PERFORMANCE AND THE METABOLIC RESPONSES TO ENDURANCE EXERCISE:
 A BRIEF REVIEW**

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ABSTRACT

EFFECTS OF ENDUROX™ (CIWUJIA) SUPPLEMENTATION ON ENDURANCE PERFORMANCE AND THE METABOLIC RESPONSES TO ENDURANCE EXERCISE: A BRIEF REVIEW. **Eric D.B. Goulet, and Isabelle J. Dionne. JEPonline.** 2004;7(1):30-36. Today's elite level athletes are bombarded with claims from sports supplement companies for how they require nutritional ergogenic aids to perform to their full genetic potential. Over the past years, ENDUROX™ (EN), whose purported benefits would be attributable to constituents (ciwujianosides) found in the leaf of the plant ciwujia, also known as *Eleutherococcus senticosus*, has been publicized as being capable to improve endurance performance by

altering the metabolic responses to endurance exercise. The goal of this brief review is to revise the available literature about the effects of EN during endurance exercise. Though the results of three unpublished studies conducted by the manufacturer of EN and those of a published study suggest that, indeed, this substance could improve fat metabolism and cardiac parameters, the fact that these studies used weak research protocols makes any inference difficult. On the other hand, the results of three published studies, which used experimental designs respecting the basic principles underlying research with putative nutritional ergogenic aids, show that EN does not improve performance, cardiorespiratory fitness, and fat metabolism during endurance exercise. Based on the best scientific data available to this day, it appears that EN supplementation (800-1200 mg/day for 7-10 days) offers no advantage beyond those potentially provided by a placebo.

Key Words: Ciwujia, Ginseng, Nutritional Ergogenic Aids, Exercise, Fat

BACKGROUND

Glycogen depletion has been identified as being a primary factor limiting the capacity of one to perform prolonged, strenuous exercise (1). Increasing the proportion of fuel derived from the oxidation of fat during exercise decreases the utilization of glycogen (2), thereby increasing the time-period during which prolonged exercise can be performed (3). Accordingly, serious, competitive endurance athletes always attempt to maximize their ability to burn fat. In order to attain such a goal, some athletes rely solely on training techniques (e.g., slow, uninterrupted long distance training, lactate threshold training, etc.). Others, in the hope of enhancing fat utilization beyond the adaptations brought by training alone, add nutritional ergogenic aids to their regimented training routine based on manufacturer claims that are often unsupported by research. One such supplement that is used by athletes is ENDUROX™ ([EN], not to be confounded with the recovery/performance drink EN R⁴™), which is available in capsules of 400 (EN) and 600 (EN EXCEL™) mg. The manufacturer of EN claims that "during a workout EN shifts the body's workout energy source from carbohydrate to fat. This carbohydrate shift increases fat metabolism and slows the lactic acid build-up that causes muscle soreness and fatigue." As a result of these attractive claims, it is thus not surprising that many amateur as well as professional athletes regularly use this substance (personal observations). The goal of this brief review is to revise the available literature about the effects of EN on performance, fat metabolism, and cardiac functions during endurance exercise. ENDUROX™ supposedly exerts its effects through compounds (ciwujianosides) found in the leaf of the plant ciwujia. Though the aim of this paper is to revise the effectiveness of EN as it is commercialized, it is important to note that, to our knowledge, there exist no studies in the literature that have examined the effects of ciwujianosides *per se* during endurance exercise.

WHAT IS ENDUROX™?

The capsules of EN and EN EXCEL are composed of many ingredients, but the principal constituent is a plant called ciwujia, which is also known as *Eleutherococcus senticosus*. More specifically, a capsule of EN is composed of ciwujia (400 mg) and calcium (65 mg). The capsule of EN EXCEL, in turn, is composed of 600 mg of ciwujia and 30 I.U. of vitamin E. In addition to the foregoing constituents, these capsules also contain stearic acid, magnesium stearate, titanium dioxide, hydroxypropyl cellulose, caramel color, and annato. As previously indicated, the active ingredients in ciwujia are chemicals called ciwujianosides, which are a series of triterpenoid saponins (A₁, A₂, A₃, A₄, B, C₁, C₂, C₃, C₄, D₁, D₂, D₃ and E) that have been isolated from the leaf of ciwujia (4,5). The manufacturer of EN does not indicate by which mechanism (s) EN (ciwujianosides) could potentially alter muscle metabolism and cardiac functions

Probably due to the lack of demonstrated effectiveness of EN in altering physiological functions, no mechanistic studies have yet attempted to delineate the potential role(s) played by ciwujianosides during exercise. However, a recent study (6) showed that ciwujianosides (D₁ and C₁) inhibit the release of histamine in rat peritoneal mast cells. This finding could potentially have implications for those athletes supplementing with EN. In fact, histamine is known to be an important chemical mediator of the inflammatory process (7).

Therefore, it is possible that EN could reduce the intensity of inflammation following a strenuous period of exercise, thereby facilitating, and diminishing the duration of, the recovery process of athletes. However, this is only pure speculation, since no studies to our knowledge has evaluated the effects of ciwujianosides on histamine synthesis and the inflammatory process *in vivo*. This could constitute an interesting track of research for futures studies.

Ciwujia is a plant that has been used by traditional Chinese medicine for almost 1700 years to treat fatigue and bolster the immune system (8). This herb is medically safe and not known to produce stimulant effects (9). As to possible side effects, its ingestion in certain individuals can trigger stomach irritation and diarrhea (9). Pregnant and nursing women are advised not to consume ciwujia (9). Finally, the use of EN is not banned by the International Olympic Committee.

LITERATURE REVIEW

Results of unpublished studies conducted by the manufacturer of ENDUROX™

The manufacturer of EN (PacificHealth Laboratories) makes available, upon request, a laboratory report that contains three studies reporting the effects of this nutritional ergogenic aid during endurance exercise (8). Collectively, results of these studies show that 10 to 14 days of supplementation with EN at a daily dose of 800-1200 mg can alter physiological functions during cycling and running exercises of a duration of 10-60 min, characterized by increased fat utilization by 43%, oxygen consumption (VO₂) by 5-13% and anaerobic threshold by 12%. In addition, claims also state accompanied decreases in exercise heart rate by 7%, reduced lactate accumulation by 32%, and an accelerated heart rate recovery by 22%.

At first glance, these results look appealing. However, they should be interpreted with great caution, as the experimental designs that were used are far from being robust. For instance, in the first and third study, subjects were tested for a first time during their first visit to the laboratory, then were supplemented for 10-14 days with EN, after which time they were tested a second time. This type of design (pre-post comparison) is weak in that it cannot adequately protect against learning, training and Hawthorne effects. Hence, it can be argued that an order effect is responsible for the observed effects. Additionally, these studies did not use placebo-controlled trials. In the second study, the description of the protocol read as follows: "sixteen subjects, eight in the control group and eight in the EN group (1200 mg/day for 14 days), underwent a 10-min exercise on the treadmill at 3.5 miles/hr." Thus, it appears that 1) no placebo was used; 2) the treatments were not administrated in a blind fashion, and 3) the subjects were not divided in a random fashion into control and EN groups. Moreover, in none of the studies was it mentioned that the effects of training-induced fatigue, diet and circadian rhythm were controlled for. Finally, for all three studies, it is not indicated whether inferential statistics were performed; only percentage changes were reported. Clearly, it would be imprudent to draw any conclusions from these studies.

RESULTS OF PUBLISHED STUDIES ON ENDUROX™

Different groups of University-based researchers have conducted studies in order to determine whether EN could potentially improve endurance performance and the metabolic responses to endurance exercise. The sum of evidence provided by these studies suggests that EN is of no value for improving either one of them. These studies, as well as those conducted by the manufacturer of EN, are briefly summarized in table 1.

Of all the reviewed studies, only one (10) shows that EN provides beneficial effects during endurance exercise. This study examined the effects of EN supplementation on aerobic power in eight male subjects. Subjects were first supplemented for three days with a placebo, after which they underwent a first aerobic power test. Following this test, they were supplemented with EN for 14 days (800 mg/day) and then performed a second aerobic power test. The aerobic power test began at an initial load of 60 Watts for 3 min after which it was increased 30 Watts every 3 min to 210 Watts. The results showed that, compared with the placebo, EN decreased heart rate at all workloads. In addition, EN enhanced fat utilization by 43%, increased the load and VO₂ at the onset of blood lactate accumulation (4 mmol/L criterion) by 12 and 7%, respectively,

and reduced lactate accumulation at the end of exercise by 33%. Fifteen min after the test, EN decreased lactate accumulation by 34% and heart rate by 13%.

Table 1. Summary of studies on the effects of ENDUROX™ during endurance exercise.

Reference	Subjects	Duration of supplementation (days)	Daily dose (mg)	Exercise	Study design	Results
<i>Kaman (8) Study 1</i>	8 males	14	800	Cycling exercise. Workload ? (from 60 to 210 Watts) by 30 Watts every 3 min.	Pre-post comparison; no placebo; not double blind.	? lactate accumulation; ? fat utilization and anaerobic threshold; ? heart rate recovery.
<i>Kaman (8) Study 2</i>	16	14	1200	10 min of running at 5.6 km/hr.	Control vs EN group; no placebo; not mentioned if subjects were randomly assigned to the groups; not double blind.	? fat utilization.
<i>Kaman (8) Study 3</i>	10 males	10	800	60 min of cycling at 100 Watts.	Pre-post comparison; no placebo; not double blind.	? heart rate; ? fat utilization; ? VO ₂ during the recovery period.
<i>Wu et al. (10)</i>	8 males	14	800	Identical to the test of the first study of Kaman (8).	Subjects were supplemented with a placebo for three days after which they underwent a first test. Then they were supplemented with EN for 14 days after which they were again tested; not double blind.	? heart rate; ? lactate accumulation; ? the load and VO ₂ at anaerobic threshold; ? fat utilization; ? heart rate and lactate recovery.
<i>Eschbach et al. (11)</i>	10 males	7	1200	2 hr of cycling at 60% VO ₂ max followed by a 10 km time trial.	Placebo controlled; double blind; crossover; balanced randomization; a washout period separated the trials.	? VO ₂ RER, heart rate, lactate accumulation, perceived exertion, plasma glucose and endurance performance.
<i>Plowman et al. (12)</i>	5 females and 5 males	10	800	25 min of stair stepping exercise at a self selected intensity.	Placebo controlled; double blind; crossover; balanced randomization; a washout period separated the trials.	? VO ₂ , RER, heart rate, lactate accumulation and perceived exertion.
<i>Chevront et al. (13)</i>	10 males	7	800	30 min of cycling at 25% VO ₂ peak followed by 10 min at 65% VO ₂ peak.	Placebo controlled; double blind; crossover; balanced randomization; a washout period separated the trials.	? VO ₂ , V _E , V _E /VO ₂ , RER, heart rate, plasma glycerol, lactate accumulation, perceived exertion, energy expenditure and rate of fat oxidation.

? = increased; ? = decreased; ? = accelerated; ? = no effect

Obviously, the aforementioned study contains multiple design errors, which make valid data interpretation difficult. First, the subjects served as their own control in a pre-post comparison protocol, which may have given rise to a training effect. Therefore, it could be argued that an order effect is responsible for the observed results. Second, the study was manifestly only single blind (the researchers knew what substance they were given), as the subjects were supplemented with the placebo for only three days, as opposed to 14

days for EN. In that kind of study, it is better to use a design that is double blind to prevent the Rosenthal effect. Of importance is the fact that nowhere in the paper the authors mentioned having controlled for the effects of training-induced fatigue, diet and circadian rhythm. Additionally, the description of the statistics used is not provided. Finally, it is of interest to note that the authors indicated that EN was "provided by PacificHealth Laboratories", therefore placing the scientists and the manufacturer of EN in a potential conflict of interest. For all these reasons, the generalization of the present findings to the athletic population is difficult.

The effects of EN supplementation on substrate utilization and performance during prolonged cycling were studied by Eschbach et al. (11). Using a randomized, double-blind crossover design, 10 trained men, with a maximal VO_2 ($\text{VO}_{2\text{max}}$) of 57 ml/kg/min, cycled during a period of 2 hr at ~ 60% $\text{VO}_{2\text{max}}$, followed by a simulated 10 km time trial. Subjects were familiarized with the exercise protocol and the time trial. Subjects maintained an identical diet for the last 72 hr before each trial. The day before both trials, subjects refrained from training. The trials were separated by at least 13 days and performed at approximately the same time of the day. Subjects were supplemented with either EN (1200 mg/day) or a placebo for seven days before trial one. After the first trial, subjects underwent a washout period of seven days before being supplemented again for another period of seven days. During the 2 hr cycling period, VO_2 , respiratory exchange ratio (RER) and heart rate were recorded every 30 min, whereas lactate, perceived exertion, and plasma glucose were recorded every 20 min. The results show that there were no significant differences between the placebo and EN group for diet composition before each trial, VO_2 , RER, heart rate, lactate, perceived exertion, plasma glucose, and for the time required to complete the 10 km time trial. These results thus suggest that EN supplementation does not improve endurance performance in trained cyclists.

Whether EN could increase fat utilization and decrease lactate production, heart rate and perceived exertion during moderate exercise was studied by Plowman et al. (12). Ten recreationally active subjects (5 females/5males) volunteered to participate in the study. A randomized, double-blind crossover protocol was used. Subjects were given either 800 mg of EN/day or a placebo for 10 consecutive days. A washout period of five days was performed before reciprocal supplementation. Subjects were tested at the same time of day and on the same day of the week for both trials. For the last 24 hr before each trial, subjects consumed an identical diet and performed the same activities. Before each trial, subjects consumed a standardized meal and ingested either two capsules of EN or a placebo. After a 5 min warm-up, subjects exercised for 25 min on a StairMaster™ (all subjects were familiarized with this equipment) at an intensity (mean of 138 W; 69 steps/min) that was individually selected. The same workout was repeated for the second trial. During the trials, VO_2 , RER, heart rate and perceived exertion were recorded each min, whereas lactate was recorded at rest and at min 10, 20 and 30. No significant differences were observed between treatments for each dependent variable studied, suggesting no effects of EN on metabolic responses during endurance exercise in recreational athletes.

Cheuvront et al. (13) studied the effects of EN on the metabolic responses to submaximal cycling exercise. Ten healthy males (VO_2 peak of 52 ml/kg/min), using a double-blind crossover protocol, were randomly assigned to consume either 800 mg of EN/day or 400 mg of placebo for seven days. The day before each trial subjects refrained from exercise and alcohol and caffeine consumption. Each trial was performed at the same time of the day and on the same day of the week. Subjects consumed an identical diet for the last 48 hr before each trial. After the first trial, subjects underwent a 7-day washout period before reciprocal supplementation and further testing. On the seventh day of supplementation, and after an 8 hr fast, a cycling test was performed for 30 min at 25%, followed by 10 additional min at 65% VO_2 peak. Oxygen consumption, minute ventilation (V_E), ventilatory equivalent for oxygen uptake (V_E/VO_2), RER, heart rate, lactate, perceived exertion and blood glycerol (an indirect marker of lipolysis) were measured before, during, and after exercise and then compared to determine any treatment effects. Results showed that there were no significant differences between the placebo and EN group for VO_2 , V_E , V_E/VO_2 , RER, heart rate, lactate, perceived exertion, and blood glycerol. Again, these results suggest that EN is unable to improve the metabolic responses to endurance exercise in moderately trained athletes.

CONCLUSIONS

The study of Wu et al. (10) showed that EN might be useful for endurance athletes: however, it is possible that factors (e.g., training, diet and learning effects) other than the effect of the treatment *per se* could account for the observed results. Hence, it is difficult to generalize their findings. Oppositely, the studies of Eschbach et al. (11), Plowman et al. (12) and Chevront et al. (13) used experimental protocols that controlled for the major factors that could have confounded their results. And the evidence provided by these studies suggest that supplementation (800-1200 mg/day for 7-10 days) with EN is an ineffective means to improve fat burning and ventilation, decrease lactate production, heart rate and perceived exertion, or enhance endurance performance. Of importance, however, is the fact that none of the four previously mentioned studies verified, through appropriate analysis, the content of the capsules of EN. However, the manufacturer of EN guarantees the assurance of quality for extraction and standardization. Nevertheless, in future studies, it would be important, before evaluating the effects of EN, that the purity and content of the capsules be verified. In fact, it has been demonstrated that certain ginseng preparations contain unacceptable levels of pesticides and lead (14) and, additionally, that the concentration of active ingredients found in ginseng and ciwujia preparations is highly variable (15). Equally troubling is the fact that it has been shown that some ginseng products available on the market do not even contain ginseng (16). Moreover, in 1993 a Swedish athlete tested positive for ephedrine. The athlete indicated that he was consuming a ginseng preparation called "Up your gas". Later analyses of this preparation revealed that it contained large amounts of ephedrine (17). It should be known that the verification of the content of the capsules of EN could be difficult. In fact, to our knowledge there is no commercial standardized extract of the leaf of ciwujia (as it is the case for Panax ginseng with G115) against which to compare HPLC analyses of EN. Laboratory analyses to quantify and qualify ingredients from EN are however possible, but require significant skills and equipment (4,5,14). Future studies must focus on the potential mechanism (s) of action of ciwujianosides during rest and exercise.

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