



Research Packet

Rev2.1

Contents:	Page/s
Corporate Philosophy	2
Mission	2
Commitment to Research	2
Commitment to Quality	2
Certificate of Analysis	2
Safe and Legal	3
Supplement Facts Panel	4
How OPTYGEN-HP Works	5-7
Optygen Study (South Dakota State U)	8-9
Optygen Study (Luther College)	10-11
Rhodiola Research	12
abstracts	13-15
references	16
Cordyceps Sinensis CS-4 Research	17
abstracts	18-19
references	20
Chromium Chelate Research	21
abstracts	22
references	23
Beta-Alanine Research	24-25
Beta-Alanine Q & A	26-27
ATPro Matrix Biochemistry	28



Corporate Philosophy:

Our Mission

Integrate our passion for racing, knowledge of sports nutrition, integrity, and values to provide endurance athletes with the ultimate, scientifically validated, high-performance racing formulations.

Research Philosophy

Research is the most important value at First Endurance. We are driven by a desire to ensure our products are proven to enhance endurance performance and have scientific validation. At First Endurance, we refuse to reduce costs by using "pixie dust" amounts of ingredients just to dress up the label. Our formulations utilize the same levels (sometimes more) of the active ingredients that were used in the actual human scientific research. We assure effective products by using the same ingredients used in the human clinical studies. We are meticulous about research and go out of our way to make sure we have addressed each of our stringent requirements. All products that First Endurance develops are based on human scientific research.

Commitment to Quality


First Endurance uses only the finest ingredients and follows stringent quality control. Supplements can be easily ruined. Even if you buy the right ingredients, they can degrade quickly and lose their efficacy if they aren't handled under the most stringent controls. We are determined to ensure nothing goes wrong with any step of the way. For example, **OPTYGEN-HP** is packaged in an blue glass bottle and utilizes colored capsules to reduce UV light, oxygen and moisture degradation, ensuring the highest quality, potency, and purity.

Certificate of Analysis:

A Certificate of Analysis (C of A) is a document which states every active and inactive substance used to manufacture a product. A C of A also shows that there are no additional ingredients added to the OPTYGEN formulation. In order to assure the safety and efficacy of OPTYGEN-HP, First Endurance provides a C of A with every bottle of OPTYGEN-HP.

CERTIFICATE OF ANALYSIS		
Product: Optygen-HP		Lot: 07255
Company: First Endurance		
Formula Ingredients	Specification	Formula Amount
Fermentation Cordyceps	NLT 7% cordycepic acid	conforms
Calcium Pyruvate	NLT 15% Ca, MT 58% PA	conforms
Rhodiola Extract	NLT 5% rosavins	conforms
Sodium Phosphate	Assay NLT 98% (dry basis)	conforms
Potassium Phosphate	Assay NLT 98% (dry basis)	conforms
d-Ribose	Conforms to patent	conforms
Chromium Chelavite	Conforms to patent	conforms
Adenosine Triphosphate	NLT 96%	conforms
Beta Alanine	NLT 98%	conforms
Capsule Type	00 Gelatin Capsule	conforms
Net Capsule Weight	Per Official Specifications	conforms
Total Plate Count	<100,000/g	conforms
Total Coliforms	<100cfu/g	Pass
Yeast & Mold	<1,000 CFU	conforms
E. Coli	<10 cfu/g	Pass
Salmonella	Negative	negative
S. aureus	<10 cfu/g	Pass

This product lot number is certified as described above to be manufactured in accordance with the official formulation specification and based on input. Said specifications include the requirements that no additional ingredients can be added beyond those described above.

Certified by: 
Jeffrey W. Bancroft
VP, Science and Technology

The raw material specifications for each ingredient are based on the certification of each supplier. Each supplier has been carefully selected and approved for the production of this product to ensure conformance with the Official Formulation and Production Specifications.

The raw material specifications for each ingredient are based on the certification of each supplier. Each supplier has been carefully selected and approved for the production of this product to assure conformance with the Official Formulation and Production Specifications.

Safe and Legal:

First Endurance is committed to developing the most advanced endurance supplements on the market. First Endurance has taken additional measures to assure that our products are safe legal and stimulant free. First Endurance supplements are legal to use in any sporting event governed by the World Anti-Doping Association (WADA), the US anti-doping association (USADA) and by the UCI (Union Cycliste International). One or more of the aforementioned governing bodies govern all US Cycling, International Cycling, US Triathlon and International Triathlon.

Some commonalties among these governing bodies include banned substances which fall into one or more of the following categories as listed in Section I A-E of the UCI Prohibited Classes of substance and Prohibited Methods document. A) Stimulants B) Narcotics C) Anabolic agents D) Diuretics and E) Peptide hormones, mimetics and analogues. This document goes on to list banned substances within each of these classes. Regulations also ban 'Compounds chemically or pharmacologically related to the products mentioned'.

OPTYGEN contains NO ingredients, which are explicitly listed under the banned substance list, nor are any of the ingredients related chemically or pharmacologically. First Endurance has also contacted the USADA and received verbal confirmation that our ingredients are not banned based on their regulations. Note: USADA, WADA and UCI do not offer any certification or written confirmation.

First Endurance manufactures its formulations to the highest GMP (Good Manufacturing Practice) standards available. In addition we use a proprietary manufacturing method for added safety and assurance. Following the Supplement Facts panel you will notice we list 'NO processing aids' under Other Ingredients. The only ingredients found in Optygen, are those listed in the Supplement Facts Panel.

Part XIV Article 7 of the Anti-doping Examination Regulations contains the following warning: *riders must refrain from using any substance, foodstuff or drink of which they do not know the composition. It must be emphasized that the composition indicated on a product is not always complete. The product may contain prohibited substances not listed in the composition.*

For a complete list of regulations and banned substances please use one of the following links:

[UCI Banned Substance List](#)

[WADA](#)

[USADA](#)

Supplement Facts Panel:

OPTIMIZE + OXYGEN = OPTYGEN™

OPTYGEN is an innovative formula designed to help elite athletes optimize performance, maximize oxygen utilization and provide the necessary adaptogens to achieve greatness.

OPTYGEN is a priority patent protected, legal and stimulant-free formulation that is designed specifically to optimize performance for endurance athletes. This revolutionary formula is based on clinical trials and the latest scientific research. OPTYGEN is designed to increase VO2Max, increase the body's ability to adapt to high levels of physical stress, increase anaerobic threshold and reduce lactic acid. It also has a 100% performance guarantee.

The adaptogens in OPTYGEN have been studied extensively for their ability to:

- Increase VO2Max
- Increase the body's ability to acclimatize to high levels of physical stress
- Increase anaerobic threshold and reduce lactic acid.

Dosage recommendations: Take 4 capsules daily with a meal.

Supplement Facts		
Serving Size: 4 Capsules		
Servings per Container: 30		
	Amount Per Serving	%DV
Chromium (as Chelavite® amino acid chelate)	200mcg	167%
Rhodiola Extract (<i>Rhodiola Rosea</i>)(root) Minimum 3% rosavins	300mg	*
Cordyceps CS-4 (<i>Cordyceps Sinensis</i>) (mycelia biomass) minimum 7% cordycepic acid	1000mg	*
Beta-Alanine	1000mg	*
ATPro™ Matrix (Calcium Pyruvate, Sodium Phosphate, Potassium Phosphate, Ribose, Adenosine)	800mg	*
*Daily Value Not Established		

Other Ingredients: Glycerine Capsule

Chelavite® is a registered trademark of Albion Laboratories, Inc.

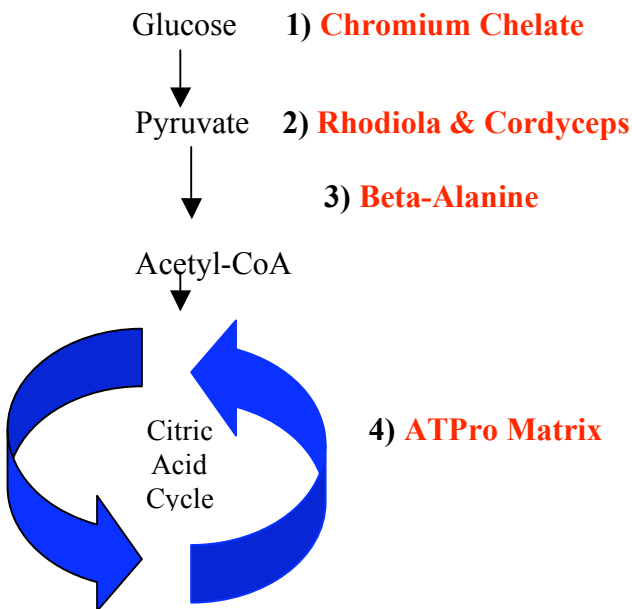
Covered by Albion International, Inc., U.S. Patent 5,614,553.

How **OPTYGEN-HP** works

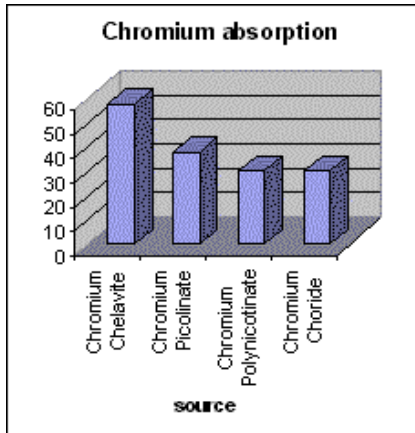
Intro: Optygen-HP™ works on four different levels all working synergistically with the goal of increasing endurance. Endurance is defined your ability to perform work over a period of time where there is sufficient oxygen delivered to the muscles. There are three critical components necessary to increase your endurance capacity.

- 1) Efficient Glucose Metabolism
- 2) Efficient Oxygen Transfer
- 3) Lactate synthesis
- 4) ATP production

Optygen targets all three of these components:



Efficient Glucose Metabolism: The first part of the Optygen-HP formula utilizes chromium for its ability to break down fuel. Chromium is an essential trace mineral that aids in glucose metabolism, regulation of insulin levels, and maintenance of healthy blood levels of cholesterol and other lipids. Chromium forms part of a compound in the body known as glucose tolerance factor (GTF), which is involved in regulating the actions of insulin in maintaining blood sugar levels and, possibly, in helping to control appetite. It is critical that any drink, bar or pre-race meal consumed prior to a race or exercise gets broken down efficiently in order to maximize your fuel delivery. Insulin spikes or lack of insulin response can cause the nutrients to either be rushed into your bloodstream too quickly or not quickly enough. Chromium regulates this nutrient breakdown so you have equal and sustained nutrient delivery to the working muscles. The most widely available sources are chromium salts such as chromium polynicotinate and chromium picolinate. Optygen-HP uses Chromium chelate, a unique form of chromium patented for its superior absorption and bioavailability properties compared to other sources.



*Chelavite, is a patented (US Patent #5,614,553) chelated form of Chromium with enhanced bioavailability and uptake.†

Efficient Oxygen Transfer: The second part of the Optygen-HP formula uses adaptogenic herbs to improve oxygen efficiency. Originally, these two adaptogenic herbs were gathered by Tibetan Sherpas for use in their tea. The Sherpas used these herbs to give them energy to climb Everest, which they did without the use of supplemental oxygen. One of the adaptogenic applications of Rhodiola that has received considerable research attention recently is for aiding in adaptation to high altitude, thus, as a preventive treatment for hypoxia or mountain sickness. In June 2002, Dr Rulin Xiu was awarded a patent for her work showing Rhodiola's ability to oxygenate blood. Clinical studies on Cordyceps have proven its ability to increase endurance through more efficient enzyme activity, mobilization of free fatty acids and beta-oxidation. In a 1998 study, Dr. Edmond Burke observed that Cordyceps has the ability to improve lactate energy metabolism within the cell. All these mechanisms clearly show how these two adaptogenic herbs improve the efficiency of oxygen transfer in the cell leading to improvements in oxygen uptake and VO₂max.

Lactate Synthesis: The third part of the Optygen-HP formula uses Beta-Alanine to efficiently synthesize lactate to be re-used as fuel. Beta-alanine is a non-essential beta-amino acid. L-Carnosine enters the digestive system and is hydrolyzed into histidine and beta-alanine, which is then synthesized back into carnosine by skeletal muscle. It is with intense training that athletes improve their muscle carnosine content by up to 87% (Harris, 2005). With intense training, you can increase your carnosine levels with a limiting factor: the body cannot produce enough Beta-Alanine to allow the body to continue to increase carnosine levels. Clinical studies show that supplementing with Beta-Alanine allows the body to produce significantly higher carnosine levels. Through its effect on carnosine levels, beta-alanine synthesizes lactic acid to be re-used as fuel. The result is a highly effective mechanism for the metabolism of lactate, which in-turn improves endurance capacity allowing you to train and race at a higher level.

ATP Production: The final step of the Optygen formulation puts all the necessary components together to assure efficient Adenosine Triphosphate (ATP) production. Clinical research has shown that endurance athletes diminish their ATP stores in exhaustive exercise, which can lead to a reduction in aerobic metabolism and endurance. Optygen's proprietary ATP^{Pro}™ matrix of five key nutrients is designed to assure ATP production. Since ATP is the final step in aerobic energy production, it is critical that the nutrients feeding the ATP cycle are readily available. Calcium pyruvate, sodium phosphate, potassium phosphate, adenosine and d-ribose all play critical roles in glycolysis and the citric acid cycle, leading to efficient ATP production. Endurance athlete's VO₂max is directly proportional to their ability to efficiently produce ATP.

A complete diagram outlining these nutrients in the citric acid cycle can be found at www.firstendurance.com/atpro.html

A synergistic formula: The combination of the four components of Optygen-HP create a synergy with the sole purpose of improving race performance through increased VO₂max, reduced lactic acid and

increased endurance. Though Cordyceps and Rhodiola taken by themselves would offer enhanced performance, the combination including Chromium Chelate, Beta-Alanine and the ATPro™ matrix complete the formulation. It is this synergistic combination of key ingredients that make Optygen-HP such a powerful and complete endurance formula.

OPTYGEN pilot study

In a pilot study conducted by Dr. Andrew Creer of South Dakota State University, highly trained collegiate runners used Optygen over an 8 week period.

It was anticipated that supplementation would reduce stress and improve performance over training without the supplement. Though changes in the performance variables (VO₂max, VT, RE16, lactate16, event time improvement) measured during the course of this study were similar between groups, Cortisol levels as well as the T/C ratio declined over the training period in S runners. Furthermore, training volume was 21% greater in S compared to P, but weekly stress scores were nearly identical. These findings suggest that although performance variables were not directly affected, use of a commercial herbal-based supplement may have helped counteract physiological stresses accompanied with high volume training.

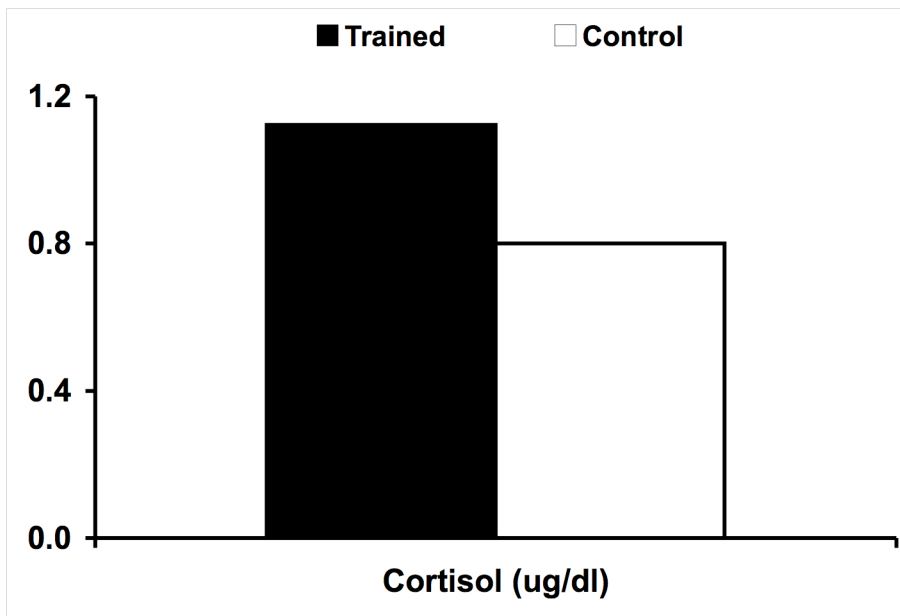
Normally trained runners (~50 miles/wk) have been reported to have low resting testosterone levels as well as cortisol levels in the high-normal range. Recent data from our laboratory show resting cortisol levels in collegiate runners to be 30% greater than age matched control data (Figure 1), and although testosterone levels were only slightly lower in runners (4%; Figure 2), the T/C ratio was 41% lower in runners coming off a ~ 60 mile week (unpublished observations). These findings are consistent with those of Houmard et al., and suggest an elevated baseline physiological stress in runners as a result of large training volumes.

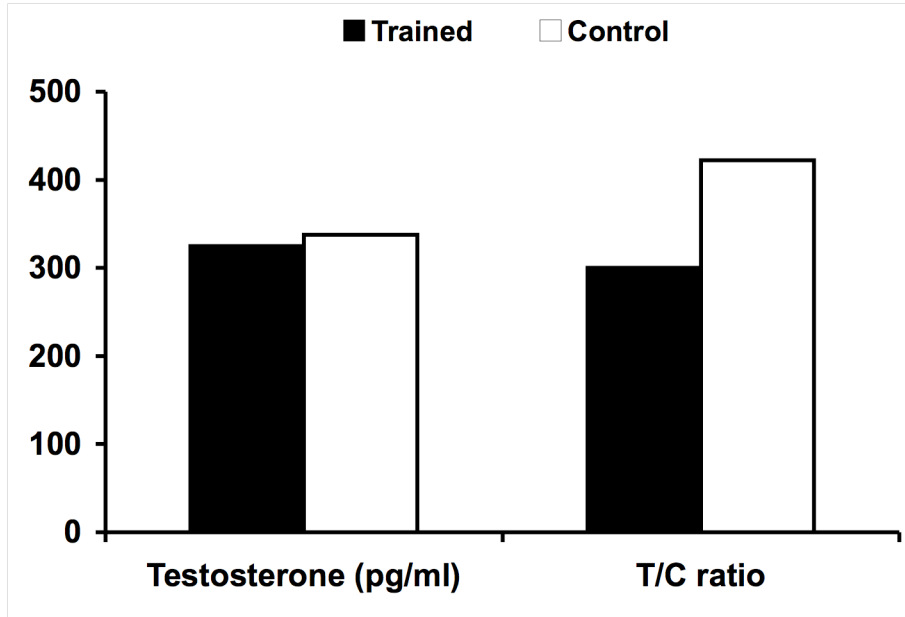
Table 1. Training volume and weekly mean stress scores from the 8-week training period. Also included are % changes in event performance from pre to post training. km•wk⁻¹ Stress Score Performance Δ

Supplement 127 ± 16* 3.7 ± 0.4 -2.3 ± 1.1 %

Placebo 100 ± 3 3.8 ± 0.2 -1.8 ± 0.2 %

* Signifies a difference between groups at p < 0.05.





Summary: Over the course of the project, runners assigned to S trained on average 27 km•wk-1 more than P; however, salivary cortisol levels seen in S decreased by 26%, contributing to a 36% increase in the T/C ratio by the end of the study. These findings would indicate that S was under less physiologic stress compared to P. If this were indeed the case, supplementation would allow an athlete to train at higher volumes without experiencing an increase in cortisol levels and a reduction in the T/C ratio, which are considered symptoms of overreaching/overtraining. Therefore, utilization of Optygen proves beneficial to trained athletes undergoing high training volumes by decreasing baseline stress and improving training sessions, leading to an overall improvement in performance.

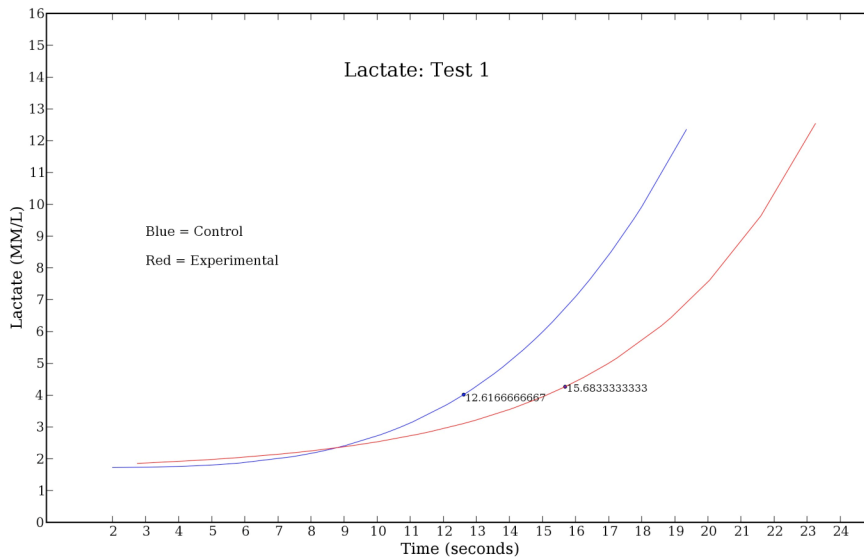
Supplementation Using A Commercial Herbal-based Product (Optygen) May Increase Running Performance in Highly Trained Collegiate Distance Runners: a pilot study. Dec 2007

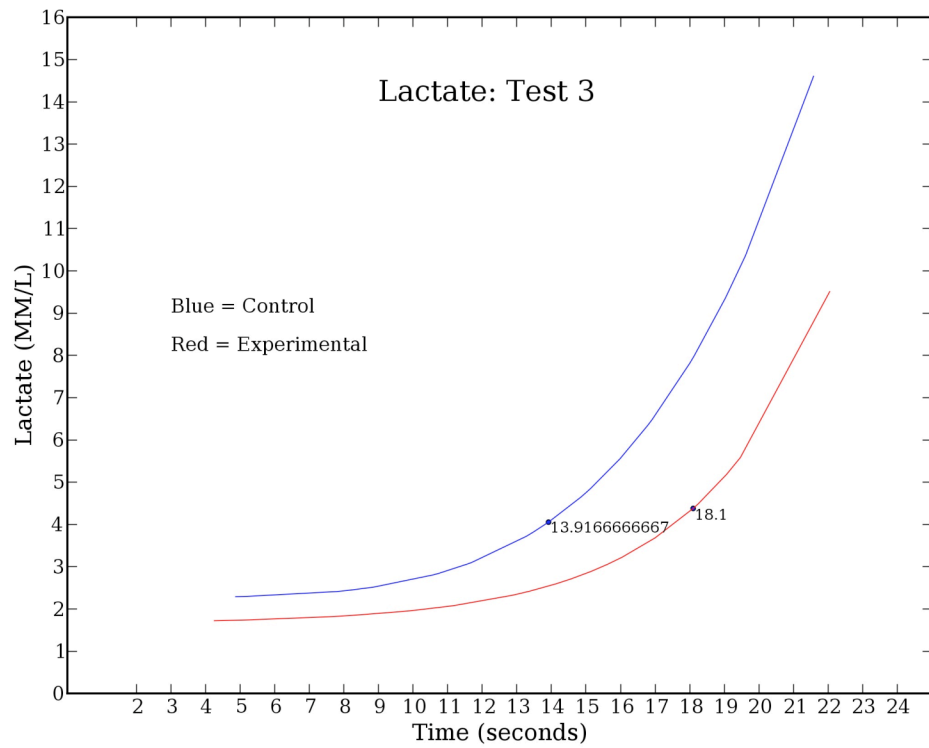
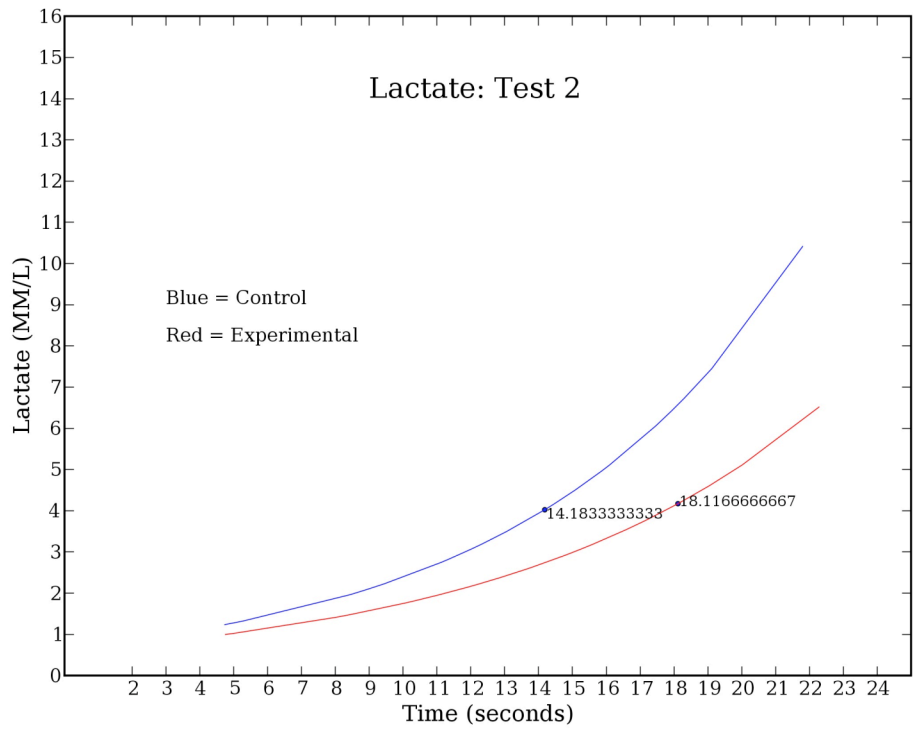
Principal Investigator:
Karlton R. Larson, PhD
H.P.E Department,
Luther College,
Decorah, IA 52101

Summary.

The purpose of this study was to determine the effects on highly trained distance runners of a commercial herbal-based supplement purported to improve endurance performance by increasing oxygen uptake, assisting recovery, and reducing lactic acid production. Though changes in performance variables (VO_2 max, hemoglobin, serum ferritin and salivary cortisol) were similar between groups, time to onset of lactate threshold was nearly 42% greater in E=experimental vs C=control group. These findings suggest that although some performance variables were not directly affected, use of a commercial-herbal based supplement may have helped improve lactate threshold levels significantly.

Importance. Over the course of the study, individuals were randomly placed into control(C, $n=4$, 20.5 ± 1.0 years, 71.1 ± 2.55 in, 157.75 ± 8.88 lb, 70.3 ± 5.92 ml/kg/min) and experimental (E, $n=5$, 21.2 ± 2.05 years, 70.7 ± 3.15 in, 148.44 ± 16 lb, 65.68 ± 3.76 ml/kg/min) groups. Supplementation occurred during a 7-week period that corresponded with an increase in training volume in preparation for competition in the fall cross country season. Results do suggest supplementation being effective in reducing lactic acid production and delaying onset of lactate threshold and therefore improving endurance in distance runners.





Rhodiola Rosea Research:

Rhodiola Background: Rhodiola is comprised of many different species and is generally found in the high mountain region of Siberia above 7,000 feet or on the Tibetan plateau above 12,000 feet. For many years, Russian athletes and scientists have touted the strong medicinal properties of this rare herb. The root of the plant, sometimes referred to as golden root, is used in current medicinal applications.

Aided Adaptation to high altitude is one of the applications of rhodiola that has received considerable research and attention recently thus, as a preventive treatment for hypoxia or mountain sickness (Zhang Weiyun, 1997; Wang Liang, 1999; Qian Yancong, et al., 1999).

There are six known polyphenol active compounds in Rhodiola. The two most active are salidroside and rosavins. Many of the clinical studies on hypoxia and oxygen transfer characteristics isolate these two active compounds.

Mechanism of Action: Recent clinical research supports the energizing and anti-hypoxic effects claimed by Traditional Chinese Medicine (TCM) and Russian researchers. In the 1986 study by Kuruov it was concluded that Rhodiola extended life significantly in states of hypoxia. Rhodiola exhibited this effect through a lowering of arterial pressure, reduced heart rate and lengthening the phases of cardiac contractions. (Kurukov 1986). Researcher Carl Germano concludes that Rhodiola has the ability to rapidly normalize lactic acid accumulation. A newly issued patent on Rhodiola proved that Rhodiola has the ability to increase blood oxygen, improve cardiac function and improve mitochondrial oxidative phosphorylation. (Xiu, 2002) Researchers believe the tissue differentiation or plasmodesmata within the compact callus aggregates (CCA) may provide capillaries for improving transport of oxygen and other nutrients. (Xu J, 1998).



Toxicity: Rhodiola was found to be safe in both acute and subacute toxicity studies. (Rege, NN, 1999)

Clinically Effective Dose: 50mg – 600mg

Rhodiola Rosea Patent and Abstracts:

United States Patent: 6,399,116
Xiu: June 4, 2002

Blood Oxygenating properties of Rhodiola:

The present invention relates to Rhodiola to treat various conditions and diseases in mammals. Rhodiola is a Tibetan herb that has been shown to **improve endurance performance**. Rhodiola is especially preferred to **enhance blood oxygen levels**, increase working capacity and endurance, heighten memory and concentration, **amplify cardiac and cardiovascular function**, provide antioxidant effects, protect against oxidation, modulate testosterone and estradiol levels, modulate sleep, and enhance sexual ability (such as improve sexual performance).

Inventors: Xiu; Rulin (2010 Kalorama Rd., NW., Suite 44, Washington, DC 20009)
Appl. No.: 559830
Filed: April 28, 2000
Current U.S. Class: 424/773; 424/725
Intern'l Class: A61K 035/78
Field of Search: 424/725,773

Rhodiola enhances blood oxygenation in humans:

A randomized placebo-controlled human clinical study was done by Xi'an Medical School in Xi'an China. The study which was published in the "Journal of China Sports Medicine" (Vol 15, No.4. 1996) clinically proved that Rhodiola can increase blood oxygenation. This study found that taking rhodiola for eight days can:

- **Enhance blood oxygenation by 11% (2% in placebo group)**
- Increasing the skeletal ATP content
- Enhancing mitochondrial oxidative phosphorylation
- **Decrease the blood lactate content**
- Reduce blood viscosity by 16% (7.8% in placebo group)
- Improve antioxidant activity
- Promote general well-being
- **Increase anaerobic threshold (AT)* by more than 14%**
- Enhance physical work capacity (PWC170)** by 13%. It positively affects the performance even 7 days after the subjects stopping taking the supplement.

*Anaerobic threshold (AT), also called known as the lactate threshold, is the point where lactate (lactic acid) begins to accumulate in the bloodstream during exercise.

** Physical work capacity at a heart rate of 170 (PWC170) is another important indicators of aerobic performance abilities.

Rhodiola has the ability to increase stamina and accelerate recovery:

In an article written for the August 1998 Issue of the Vitamin Retailer Carl Germano* RD, CNS, LDN reviewed the literature on the Tibetan herb Rhodiola and its powerful properties. Germano states "Adaptogens have been scientifically reported through clinical and laboratory studies for more than 40 years with their actions well documented and safety confirmed." Germano adds "In addition to Rhodiola's ability to increase physical endurance, Dr. Utkin, a Russian Botanist and nutritionist discovered that the plant increases sexual activity." Germano explains that the most active phytochemicals found in Rhodiola are salidroside and rosavins. **Most importantly, Germano reviewed the Russian literature and concluded "Through experiments on swimmers, skiers and other athletes, scientists around the world have reliably demonstrated the value of Rhodiola as an adaptogen, increasing stamina and accelerating recovery processes after physical exertion with no side effects."** A study confirmed that the effectiveness of Rhodiola on physical rehabilitative processes may be attributed to a rapid normalization of lactic and uric acid during recovery. Rhodiola has the ability to improve muscle-to-fat ratio, to increase hemoglobin and erythrocyte levels, to raise the total level of

protein content in the blood, and to reduce the build-up of lactic and uric acid. It is worth noting that Rhodiola is four-times less potentially toxic than Korean ginseng even in high doses.

*Carl Germano, RD, CNS, LDN is a director of product development and technical services for a leading vitamin and herb company

Rhodiola extract improves the volume of repeat work:

Chapter VIII of the book titled “Rhodiola Rosea-valuable medicinal plant”, published by Russian professor Saratkov AC, Tomsk 1987 reviews the Russian clinical research on Rhodiola Rosea. The following quotes are referenced directly from this chapter:

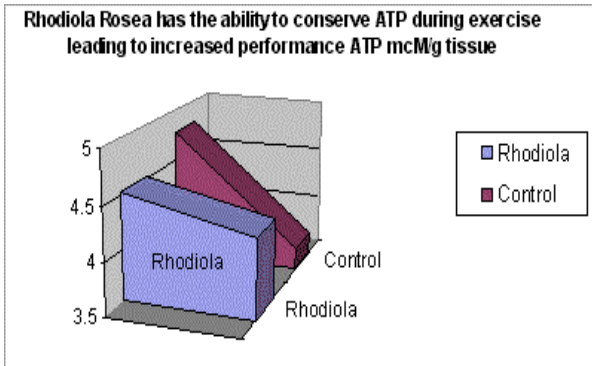
- “Under the influence of Rhodiola extract, the volume of repeat work performed after preceding proportioned work increased by 28%, whereas without baseline fatigue, the increase in the duration of work was about 12%.”
 - “What is especially important is the shortening of the recovery period, defined in terms of the time of normalization of the heart rate and the arterial pressure, where observed by the end of the study.”
 - “O. I Dalziger investigated the influence of Rhodiola extract on work capacity. Observations were carried out on groups of highly qualified skiers (42 individuals, 20-25 years of age; masters of sport and first rank Russian athletes) during training races and trial heats over a distance of 30km. Thus, 30 minutes after completing the distance the Heart Rate of the Rhodiola group was 104-106% in relation to initial baseline, while the control group was 128.7%(p<0.02).”
 - “An oxyhemographic investigation of the saturation of arterial blood with oxygen in skiers participating in a 30-km race revealed a significant increase in the duration of hypoxemic phases and a shortening of the recovery phase. These shifts attest to the greater resistance of the subjects to hypoxia, the more economical expenditure of oxygen, the better adaptation of the organism to hypoxemia and the acceleration of the restitutional processes.”
 - “In a study involving a college baseball team, it was revealed that all four parameters of work capacity (including Bo2max, O2 pulse max, total work and exhaustion time) showed significantly larger increases when Rhodiola was administered. After administering Rhodiola in an experiment on 140 athletes, 74% of the test subjects obtained their best results in a 3,000m run. The experiment group induced a 64% increase in work endurance, with reduced blood lactate levels and consistently lower blood pressures.”
 - “Through extensive experiments on swimmers, skiers and other athletes, scientists around the world have reliably demonstrated the value of adaptogens for increasing stamina and accelerating the recovery process after physical exertion.”
 - “There were no side effects noted in any of the mentioned studies.”
 - “All of these factors indicate that Rhodiola rosea extract will, by positively changing the protein balance in athletes, increase the mass of contractile muscle fibers as the result of increase work loads. This greatly helps competitive athletic performance by supporting the level of physical training even during the periods of lower activity, which precede competitions (tapering).”
-

Rhodiola administration has pronounced anti-hypoxic effects:

Russian scientist Kurmukov discovered that the administration of Rhodiola rosea polyphenols extended the life of isolated heart exposed to low oxygen conditions called hypoxia. In a second study also conducted by Kurmukov, 20mgs of polyphenolic compounds, purified from Rhodiola Rosea, extended life by 60% to experimental animals exposed to high 27,000 ft altitude (low oxygen). According to these results Rhodiola exhibits a pronounced antihypoxic effect. Rhodiola Rosea was found to exhibit a pronounced anti-hypoxic effect in different models of hypoxia (hypoxic, cytotoxic and hemic), and relieve isolated heart contracture. At these doses (of polyphenols), Rhodiola produced a transient lowering of arterial pressure, a decrease in heart rate and lengthened the phases of cardiac contractions. (Kurukov Et al, 1986).

Rhodiola extract administration reduces oxygen consumption in dogs:

A double blind placebo controlled study on dogs looked at oxygen consumption of the myocardium and coronary blood flow. Dogs were placed in one of two groups. The group which was administered Rhodiola Rosea capsules, experienced a significant reduction in oxygen consumption of the myocardium. There was also a significant decrease in coronary artery resistance with no marked effect on coronary blood flow. In addition, the Rhodiola administered group had lower heart-rate at equivalent cardiac output. Researchers concluded that Rhodiola Rosea may increase cardiac function. (Zhongguo Zhong, 1998).



Rhodiola Rosea References:

Xiu; Journal of China Sports Medicine (Vol 15, No.4. 1996)

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Saratikov AS and Krasnov EA. Rhodiola rosea-valuable medicinal plant. Chapter VIII "Clinical Study of Rhodiola Rosea" Medicinal Academy of Sciences, Tomsk 1987

Kurukov AG., Aisikov MI and Pakhimov SS (1986) Pharmacology of the plant polyphenol epigaloxin from Rhodiola. Pharmacology and Toxicology 1986; 49(2): 45-8

Cheng XJ; Di L; Wu Y; Zhao QC; Du GZ; Liu YQ (1993) Studies on the hypoglycemic effect of Rhodiola sachelinensis A. Bor. Polysaccharides Academy of Traditional Chinese Medicine and Meteria Medica of Jilin Province, Changchun. Chung Kuo Ching Yao Tsa Chih, 18(9): 557-559.

Maslova LV; Kondrateve Biu; Maslov LN; Lishamon IB (1994) The cardioprotective and antiadrenergic activity of an extract of Rhodiola rosea in stress Experimental and Clinical Pharmacology, 57(6): 61-3 Nov Dec.

Plozny AV., Revyakina NV., Kim EF., Sviridova TF. 1985 Rhodiola Rosea or Golden-root. Biology of Siberian plants requiring protection. Novosibirsk.p.85-114.

Saratikov AS., Salnik BU., Revina TA 1968. Biochemical Characteristics of the Stimulative action of Rodosine during prescribed muscular workloads. Proceedings of Siberian Department of Academy of sciences of the USSR. Biological Sciences, 5: 108-115.

Dr. Zakir Ramazanov and Dr Maria del Mar Bernal Suarez; Using Rhodiola Rosea and Rhododendron Caucasicum.(1999) ATN/Safe Goods Publishing.

Zhongguo Zhong Yao Za Zhi; The effect of Rhodiola on oxygen consumption of myocardium and coronary artery blood flow in dogs. 1998 Feb; 23(2): 104-106

Xu J; Xie J; Feng P; Su Z; Oxygen transfer characteristics in the compact callus aggregates of Rhodiola. Chinese Journal of Biotechnology; 1998; 14(2): 99-107.

Rege, NN et al; Phytotherapy Research; Ayurvedic Research Centre, Department of Pharmacology and Therapeutics, Seth GS Medical College, Parel, Mumbai, India. 1999 June; 13(4): 275-291.

Zhang Weiyun, *Recent development on application of Rhodiola spp. and its preparations*, Journal of the Gansu College of Traditional Chinese Medicine 1997; 14(4); 41-42.

Wang Liang, *Progress of research on the pharmacology of rhodiola*, Li Shizhen Medicine and Materia Medica Research 1999; 10(4): 295-296.

Qian Yancong, et al., *Survey of research on Rhodiola kirilowii*, Acta Chinese Medicine and Pharmacology 1999; (5): 34-35.

Cordyceps Sinensis CS-4 Research:

Cordyceps Sinensis CS-4 Background: Cordyceps Sinensis is a highly valued medicinal mushroom in Traditional Chinese Medicine (TCM). Cordyceps has long been used to treat lung disease and fatigue. The Cordyceps mushroom grows primarily on the plateau of China and Tibet above 12,000 feet. Some researchers believe it is the mushroom's ability to survive at high altitude, which give it its blood oxygenating properties.

The CS-4, is a fermentable strain of the mycelia (*Paecilomyces hepiali* C.) isolated from the natural Cordyceps Sinensis collected from the QuinHai. CS-4 is used to produce fermented mycelia product that contains the same pharmacologically active compounds as the natural Cordyceps Sinensis, specifically cordycepic acid. It is important to note, the clinical research on endurance, fatigue and VO₂max has only been done with the CS-4 strain.

Mechanism of action: Recent clinical research supports the anti-fatigue claims of Cordyceps Sinensis in TCM. Cordyceps CS-4 research shows that it can increase endurance and energy through more efficient enzyme activity of Red Blood Cells while improving lung and kidney function. CS-4 mobilizes free fatty acids and beta-oxidation, thereby preserving glycogen usage during prolonged exercise. (Medicine & Science in Sports & Exercise, 2001) In both animal and human studies CS-4 has proved to support the enzyme superoxide dismutase (SOD). (J. Zhu, 1999). In a human study, Cordyceps has proved to improve lactate energy metabolism within the cell. (Burke, Edmund 1998)

Toxicity: None indicated (Rege, et al, 1999)

Clinically Effective Dose: 1000mg to 3000mg

Cordyceps Sinensis Abstracts:

Effects of Cordyceps CS-4 on endurance performance in humans:

A study presented at The ACSM annual meeting, Baltimore, MD, June 2001, on elite athletes looked at the effects of Cordyceps CS-4 on endurance performance parameters. The study (which took place in Encinitas, California) concluded that supplementation with Cordyceps CS-4 extract promotes fat metabolism during prolonged exercise. Cordyceps CS-4 supplementation resulted in improved circulatory and metabolic effects during submaximal exercise in endurance-conditioned athletes. The abstract of the study which was published in the *Medicine & Science in Sports & Exercise Journal*, 2001, concluded that CS-4 supports normal fat mobilization and beta-oxidation, thereby preserving glycogen usage during prolonged exercise. (*Medicine & Science in Sports & Exercise*, 2001)

Effects of Cordyceps CS-4 on VO₂max in humans:

A study presented at The Experimental Biology 2001 (FASEB meeting) in Orlando, FL. (April 1, 2001) examined the effects of Cordyceps CS-4 on aerobic capacity of healthy humans. Christopher B. Cooper M.D. professor of medicine and physiology from the University of California, Los Angeles devised the study. The study was published in *The Chinese Journal of Gerontology*, 2001 edition. Exercise performance was tested before and after six weeks of a treatment using a symptom-limited, incremental work rate protocol on a cycle ergometer. The study, which took place in Beijing, China, concluded that after taking Cordyceps CS-4 for 6 weeks, VO₂max significantly increased while the placebo group remained unchanged. The Cordyceps administered group experienced a 6% increase in maximum oxygen uptake from 1.88 to 2.00 liters per minute. These findings support the belief that Cordyceps Sinensis CS-4 has potential for promoting aerobic capacity and resistance to fatigue. (*Medicine & Science in Sports & Exercise*, 1999)

Effects of Cordyceps CS-4 on endurance in mice:

A double blind, placebo-controlled Chinese study done on mice was conducted to determine if oral administration of Cordyceps CS-4 resulted in enhanced endurance and resistance to fatigue. After three weeks of administration, the groups given CS-4 were able to swim significantly longer than the control groups. The results of the study were dose dependent with results of one group showing a 30% increase in endurance and the second group showing a 73% increase in endurance. The study concluded that the cardiogenic action, inhibition of tracheal constrictions and relaxation of vascular contractions (which CS-4 evokes) elevates the ability and endurance of exercise. (Akinobu, et al. 1995).

Effects of Cordyceps CS-4 on ATP in mice:

A double blind, placebo controlled study looked at the effects of Cordyceps CS-4 on ATP/Pi ratio. The ATP/Pi ratio represents the high-energy state in mice. The study concluded that the CS-4 extract group showed significant increase in the ATP/Pi ratio at weeks 1-3 following Cordyceps Sinensis administration. These results suggest that the high-energy state of the liver in the CS extract-treated mice is a primary effect of repeated administration of the CS extract (Noboru, et. al, 1996).

The effects of Cordyceps extracts on the energy state of mice were examined using in vivo NMR spectroscopy. In the seven days that the CS-4 extract was administered, the ratio of Adenosine Triphosphate (ATP) to inorganic phosphate (Pi) in the liver was significantly increased by an average of 45% to 55% as compared to the placebo controlled group (Manabe, 1996).

Effects of adaptogens (Cordyceps Sinensis) on lactic acid in humans:

In a double-blind, randomized, placebo-controlled study led by S. Morrissey of Beijing Medical University Sports Research Institute, researchers evaluated the effects of an adaptogen-based formula on lactic acid clearance following maximal exercise. The formulation, which included Cordyceps Sinensis, was administered to 30 male subjects who were then assigned to one of three groups. The control group received a placebo, a second group received 500mg of the formula and a third group received 1000mg of the formula. Researchers took the subjects blood lactate measurements before exercise, at VO₂max and 15 minutes after exercise. At the end of the two weeks the group which received 1000mg/day of the formula experienced significantly improved lactate clearance ($p < .001$). This trend continued through week four. **Researchers concluded that lactate clearance improved due to improved lactate energy metabolism within the cell.** The author concluded that using this herbal formulation would enhance lactate clearance and allow athletes greater anaerobic performance. (Burke, Edmund, 1998).

Chinese fungus (Cordyceps Sinensis) lead World Record Runners:

The 1994 winter issue of American Entomologist published an article on the incredible rapid ascendancy of the Chinese women's track team. Chinese coach Ma Zunren stated that intense, high-altitude training and a stress-releiving tonic (prepared from Cordyceps Sinensis) were the factors responsible for record-breaking performance by the athletes. At the Chinese National Games in Beijing, three world records were broken in the 3,000, 5,000 and 10,000-meter events. Statements from the Chinese attribute the intense training to the athlete's success rather than dietary supplements, **yet the stress relieving properties of Cordyceps intrigued scientists** to study this further. (American Entomologist, 1994)

Effects of Cordyceps CS-4 on oxygen consumption during state of hypoxia in mice:

Researchers examined oxygen consumption in mice and their ability to survive in a hypoxic (lack of oxygen) environment following Cordyceps CS-4 administration. Under conditions of stimulation of oxygen consumption, subcutaneous injections of CS-4 extract significantly **reduced oxygen consumption by 41% to 49%** within 10 minutes and by 30% to 36% in the second 10 minutes. In a low oxygen environment, the mice lived 2 to 3 times longer after the CS-4 treatment. The CS-4 induced reduction of oxygen consumption and the prolonged survival of treated animals in a hypoxic environment **indicated a more efficient use of oxygen and a greater tolerance to hypoxia-induced acidosis than that of controls** (Lou et al., 1986)

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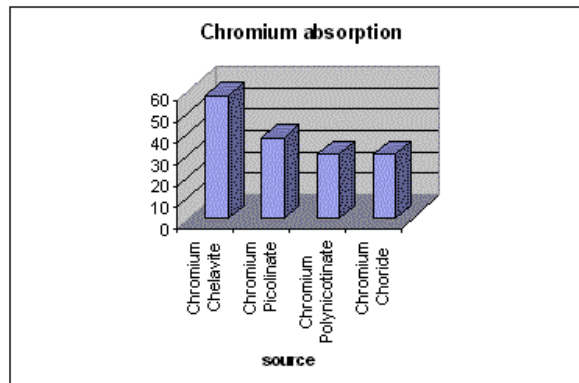
Chromium (as Chelate) research:

Chromium Chelavite®: Chromium is an essential trace mineral that aids in glucose metabolism, regulation of insulin levels, and maintenance of healthy blood levels of cholesterol and other lipids. Chromium forms part of a compound in the body known as glucose tolerance factor (GTF), which is involved in regulating the actions of insulin in maintaining blood sugar levels and, possibly, in helping to control appetite. Food sources include brewer's yeast, whole grain cereals, broccoli, prunes, mushrooms and beer. The most widely available supplements are chromium salts such as chromium polynicotinate, chromium picolinate and chromium chelated - which help increase the absorption and availability compared to isolated chromium.

Chelavite® is a patented (US Patent #5,614,553) chelated form of Chromium with enhanced bioavailability and uptake.†

†Chelavite® is a registered trademark of Albion Laboratories, Inc. Covered by Albion International, Inc., U.S. Patent 5,614,553.

Albion Research Notes, Newsletter, June 1995



Mechanism of Action: Chromium forms part of a compound in the body known as glucose tolerance factor (GTF), which is involved in regulating the actions of insulin in maintaining blood sugar levels and, possibly, in helping to control appetite. Since chromium helps regulate the actions of insulin (as a constituent of glucose tolerance factor), chromium supplements may help support the many functions of insulin in the body, such as maintaining blood sugar. (Williams, 1995)

Toxicity: Trivalent chromium may cause skin irritation at high doses given parenterally but is not toxic at the lower doses given orally. It is not recommended to exceed 400mcg of Chromium daily though toxicity will not occur until levels of 1200mcg or more per day are consumed for an extended period of time. (Cerulli, 1998)

Clinically Effective Dose: 50mcg – 200mcg: The Food and Nutrition Board of the NAS/NRC states that a safe, adequate intake of chromium for an adult is 50 to 200 mcg/day.

Chromium abstracts:

Endurance training increases chromium use:

In a series of studies done by RA Anderson, chromium secretion levels were measured in runners and cyclists. It is thought that chromium is mobilized from stores into the blood to be carried to a target organ like muscle to enhance insulin function. Once chromium is mobilized in the blood, it cannot be reabsorbed and is lost in the urine. The studies showed 24-hour chromium losses were twice as high on the day of exercise as on a rest day.

- Following a 6 mile run, serum chromium levels were increased immediately after exercise, and these levels remained elevated for 2 hours.
 - Twelve minutes of cycling at 80% of an aerobic threshold resulted in increased plasma chromium twelve minutes after the exercise. (Anderson, 1991)
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Chromium is essential for endurance athletes:

Chromium is considered to be an essential component of the glucose-tolerance factor associated with insulin in the proper metabolism of blood glucose. In essence, chromium potentiates the activity of insulin and thus may also influence lipid and protein metabolism. In addition to maintenance of blood glucose levels, chromium may be involved in the formation of glycogen in muscle tissue and may facilitate the transport of amino acids into the muscles. (Williams, 1995)

Chromium increases endurance in rats

Impairment in carbohydrate metabolism would not be conducive to optimal performance in endurance events, whereas decreased amino acid transport into the muscle could limit the benefits from training. Anderson, linked chromium to carbohydrate and protein metabolism during exercise. Anderson's research led him to believe that strenuous exercise may increase the need for chromium supplementation. Three important factors regarding endurance athletes and chromium have been observed.

- 1) Increased intensity and duration of exercise may increase chromium excretion.
- 2) Athletes who consume substantial amounts of carbohydrates may need more chromium to process glucose.
- 3) Athletes who lose weight for competition may decrease dietary intake of chromium.

Chromium supplementation benefits endurance athletes by improving insulin sensitivity and carbohydrate metabolism during exercise. (Anderson, 1998)

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Beta-Alanine Research:

Beta-Alanine: is a non-essential beta-amino acid. L-Carnosine enters the digestive system and is hydrolyzed into histidine and beta-alanine, which is then synthesized back into carnosine by skeletal muscle. It is with intense training that athletes improve their muscle carnosine content by up to 87% (Harris, 2005). With intense training, you can increase your carnosine levels with a limiting factor: the body cannot produce enough Beta-Alanine to allow the body to continue to increase carnosine levels. Clinical studies show that supplementing with Beta-Alanine allows the body to produce significantly higher carnosine levels (Dunnett, 1999). Through its effect on carnosine levels, beta-alanine synthesizes lactic acid to be re-used as fuel. The result is a highly effective mechanism for the metabolism of lactate, which in-turn improves endurance capacity allowing you to train and race at a higher level.

Influence of beta-alanine supplementation on skeletal muscle carnosine concentrations in high intensity cycling capacity:

A study conducted at the University of Chichester, U.K. examined the effects of beta-alanine supplementation on muscle carnosine content. Male subjects were supplemented with beta-alanine for 4 weeks. Subjects were tested for total work done at 110% of their maximum power. After 4 and 8 weeks, muscle carnosine content increased by 58.8% and 80.1% with beta-alanine supplementation. **Total work done increased by 13% after 4 weeks and by 16.2% after 8 weeks.** These findings support that supplementation with beta-alanine increases total work done and carnosine content in muscle during high intensity cycling. (Hill, et.al., 2007).

Effects of beta-alanine supplementation on the onset of neuromuscular fatigue and ventilatory threshold in women.

A study conducted at the University of Oklahoma examined the effects of 28 days of beta-alanine supplementation on physical work capacity at fatigue, ventilatory threshold and maximal oxygen consumption in women. Twenty two women participated and were randomly assigned to either a beta-alanine group or placebo. Before (PRE) and after (POST) subjects performed a continuous incremental cycle ergometry test to exhaustion to determine their physical work capacity. **After 4 weeks of supplementation subjects improved Ventilatory threshold by 13.9%, physical work capacity by 12.6%, and time to exhaustion by 2.5% with no significant changes in the placebo group.** Results of this study indicate that the beta-alanine supplementation delays the onset of neuromuscular fatigue and the ventilatory threshold and increases time to exhaustion. Researchers theorize that beta-alanine's ability to increase carnosine levels resulting in an **improved ability to buffer hydrogen ions led to improved performance parameters.** (Stout, et.al., 2007)

Effects of beta-alanine and creatine supplementation on aerobic power, ventilatory and lactate thresholds, and time to exhaustion.

A study conducted at Florida Atlantic University examined the effects of 28 days of beta-alanine and beta-alanine and creatine combination on aerobic exercise performance. Fifty five men participated in the double-blind placebo controlled study and were randomly assigned to one of 4 groups; placebo, creatine, beta-alanine and beta-alanine plus creatine. Subjects performed a graded cycle ergometer test pre and post supplementation to determine VO₂peak, time to exhaustion, power output and percent Vo₂peak associated with ventilatory threshold and lactate threshold. Within groups significant time to exhaustion improvements were found in the beta-alanine/creatine group.

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The study conducted at the University of Tsukuba, Japan examined the relation among the skeletal muscle carnosine concentration, fiber type and high-intensity exercise capacity. Eleven healthy men were tested using a cycle ergometer to determine high intensity exercise performance. The histidine-containing dipeptide carnosine (beta-alanyl-L-histidine) has been shown to significantly contribute to the physicochemical buffering in skeletal muscles, which maintains acid-base balance when a large quantity of H⁺ is produced in association with lactic acid accumulation during high-intensity exercise. The carnosine concentration was significantly correlated with the mean power per body mass ($r=0.785$, $p<0.01$) during the 30-s sprinting. When dividing the sprinting into 6 phases (0-5, 6-10, 11-15, 16-20, 21-25, 26-30 s), significant correlations were observed between the carnosine concentration and the mean power per body mass of the final 2 phases (21-25 s: $r=0.694$, $p<0.05$; 26-30 s: $r=0.660$, $p<0.05$). These results indicated that the carnosine concentration could be an important factor in determining the high-intensity exercise performance. (Suzuki et.al., 2002)

Beta-Alanine References:

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Q: How is OPTYGEN-HP different than the original Optygen formula?

A: Optygen-HP is the next-generation of OPTYGEN. This revolutionary formula is the result of human clinical trials and the latest scientific research on increasing endurance and performance. New features include Beta-Alanine as well as the most potent Rhodiola available.

Q: What is Beta-Alanine and how does it work?

A: Beta-Alanine is a beta-amino acid that is a precursor to L-Carnosine in muscle. L-Carnosine is synthesized in muscle when Beta-Alanine is bound to histidine, another amino acid. With intense training, you can increase your carnosine levels with a limiting factor: the body cannot produce enough Beta-Alanine to allow the body to continue to increase carnosine levels. Clinical studies show that supplementing with Beta-Alanine allows the body to produce significantly higher carnosine levels. Through its effect on carnosine levels, beta-alanine synthesizes lactic acid to be re-used as fuel. The result is a highly effective mechanism for the metabolism of lactate, which in-turn improves endurance capacity allowing you to train and race at a higher level.

Q: What are the benefits of taking Beta-Alanine?

A: Cutting edge human clinical studies show Beta-Alanine supplementation significantly improves muscular endurance, exercise capacity (so you can exercise longer) and total work done. The mechanism supporting Beta-Alanine works synergistically with the adaptogens, chelated chromium and ATPPro in OPTYGEN-HP to help endurance athletes maximize performance.

- Increases Total Work Done by 13%
- Boosts strength
- Increases endurance capacity
- Improves Ventilatory Threshold
- Delays onset of neuromuscular fatigue

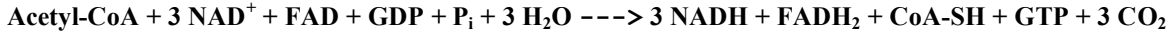
Q: What is the itching/tingling I feel after I take Optygen-HP?

A: A very small percentage of athletes will feel an itching or tingling sensation when they first start using Optygen-HP. This tingling is due to the Beta-Alanine. Researchers theorize that it is caused by the activation of dorsal root ganglion (DRG) neurons being activated by Beta-Alanine. In the presence of Beta-Alanine, DRG neurons cause multiple action potentials, whereas in the absence only a single action potentials occur. There is no cause for concern. The tingling & itching called paraesthesia should go away after a week of use. Athletes can also split up their dose to two capsules in the AM and two in the PM which should also help reduce the acute tingling/itching sensation.

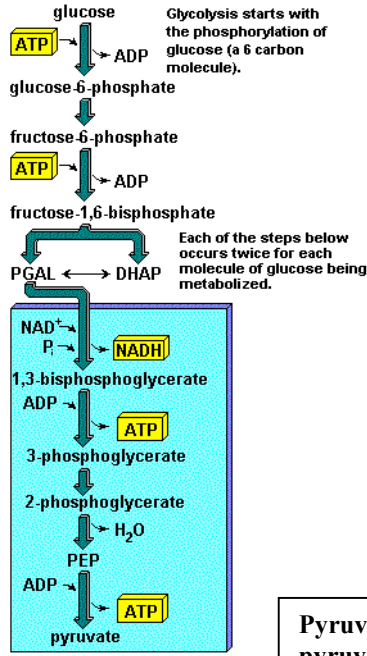
Q: Do I have to load with OPTYGEN-HP?

A: No, with the addition of Beta-Alanine and the more potent Rhodiola there is no need to load initially.

ATPro™ Matrix: Optygen's proprietary ATPro™ matrix of five key nutrients is designed to assure Adenosine Triphosphate (ATP) production. Calcium pyruvate, sodium phosphate, potassium phosphate, adenosine and d-ribose all play critical roles in glycolysis and the citric acid cycle outlined below. It is this complex set of chemical reactions which produce ATP aerobically. Clinical research has shown that endurance athletes diminish their ATP stores in exhaustive exercise which can lead to a reduction in aerobic metabolism and endurance. One's VO₂max is directly proportional to their ability to produce ATP which is also known as the body's high energy state.

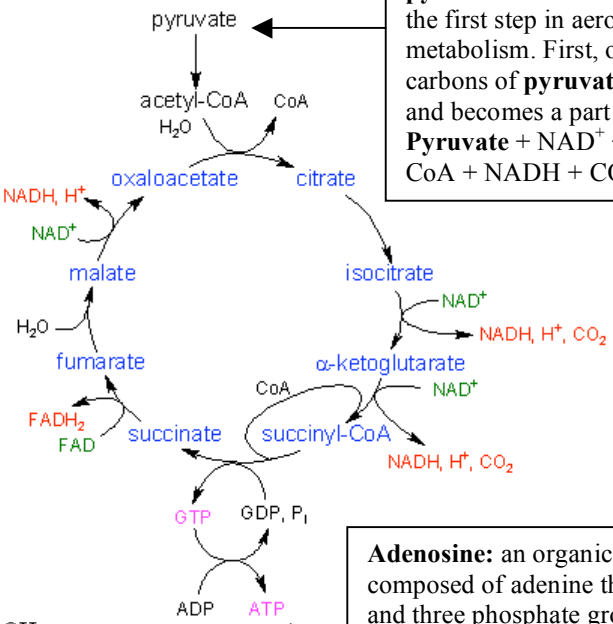


Organic Phosphates (**Sodium phosphate & Potassium phosphate**) play an important role in metabolism. For example, in the metabolism of sugars (which have hydroxyl groups, -OH, in their molecules), **phosphate** esters are often formed as an intermediate compound. Formation of these esters is called phosphorylation. Nucleotides are phosphate esters that play an important role in the conservation and use of the energy released in the metabolism of foods in the body.



Pyruvate: The oxidation of pyruvate to form Acetyl CoA is the first step in aerobic metabolism. First, one of the three carbons of pyruvate splits apart and becomes a part of CO₂.
Pyruvate + NAD⁺ + CoA Acetyl-CoA + NADH + CO₂

D-Ribose: serves as a precursor to the adenine nucleotides found in deoxyribonucleic acid (DNA), ribonucleic acid (RNA), ATP (adenosine triphosphate), and several other molecules essential to life.



Adenosine: an organic compound composed of adenine the sugar **d-ribose** and three phosphate groups. ATP serves as the major energy source within the cell to drive a number of biological processes such as muscle contraction, and the synthesis of proteins.

