



## Research Packet

Rev3.0

<b>Contents:</b>	<b>Page/s</b>
Corporate Philosophy	2
Mission	2
Commitment to Research	2
Commitment to Clean Products	2
Certificate of Analysis	3
Supplement Facts Panel	4
How <i>OPTYGEN-HP</i> Works	5-7
<i>OPTYGEN-HP</i> Pilot Study	8-9
Rhodiola Research	10
Abstracts	11-13
References	14
Cordyceps Sinensis CS-4 Research	15
Abstracts	17-19
References	20
Chromium Chelate Research	21
Abstracts	22
References	23
Beta-Alanine Research	24-26
Abstracts	27-30
References	30
Q & A	31
ATPro Matrix Biochemistry	32



## **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 include at least the same levels of the active ingredients that were used in the actual human scientific research, if not more. We ensure effective products by using the same formulation of 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 Clean Products***

First Endurance was built on the premise of offering a high end product line to professional athletes and endurance athletes training at a high level. We have worked with the world's best endurance athletes since 2002. During that time there has been over 1,000 doping tests performed on our athletes with no adverse findings. This is not a coincidence. Since inception, we have had a process-based approach that was developed to ensure no cross contamination. Third party testing does NOT guarantee products are 100% free of banned substances. It only guarantees a product is free of doping substances which they have tests for. Derivatives or analogs of banned substances that do not have a testing protocol can still show up in products. Following a process-based approach allows First Endurance to retain complete control. With our process methodology we remove the risk of cross contamination.

The Process Based Approach:

- 1) First Endurance owns all of its intellectual property. This means we develop our formulas in-house, so we have complete control over sourcing our ingredients. This allows us to choose our manufacturing facilities to ensure they meet our standards and gives us the control to change ingredient suppliers at any point.
- 2) First Endurance quality standards require manufacturing facilities that are regulated by the FDA to be GMP (Good Manufacturing Practice) certified. In addition, we only use manufacturers that do not manufacture any products containing banned substances.
- 3) Our ingredients are sourced only from reputable companies that do not broker or source ANY banned substances or nutrients that have not undergone strict safety measures. Our suppliers only offer ingredients that are GRAS (Generally Recognized as Safe), have a CAS registry and offer an MSDS (Material Safety Data Sheet). In other words, we would never source an ingredient from an international distributor unless all of these processes were in place.
- 4) When ingredients are received they are tested for purity and potency before they can be released into our manufacturing facility. This two-pronged test ensures the ingredient is exactly as it states.
- 5) Every LOT of finished product produced has a corresponding Certificate of Analysis from a third party lab. This analysis assures the ingredients listed on the label are the only ingredients in the product.

Our strict standards completely eliminate the risk of inadvertent cross contamination, ensuring that our entire manufacturing process and product line remains clean and free of all banned substances.

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-HP* 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*.

The raw material specifications for each ingredient are based on the contribution 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.

## **Supplement Facts Panel:**

**OPTIMIZE + OXYGEN = *OPTYGEN-HP*™**

*OPTYGEN-HP* 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-HP* 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.

<b>Supplement Facts</b>		
Serving Size: 4 Capsules		
	Amount Per Serving	%DV
Chromium (from Chelavite® amino acid chelate)	200mcg	167%
Rhodiola Extract ( <i>Rhodiola Rosea</i> )(root) minimum 10.0% rosavins	300mg	*
Cordyceps ( <i>Sinensis</i> )(mycelia biomass) minimum 7% cordycepic acid ( <i>Militaris</i> ) (sporocarp) minimum 10% Polysaccharides	800mg	*
Beta-Alanine	1500mg	*
ActiGin Proprietary matrix (Panax notoginseng extract, Rosa Roxburghii fruit extract)	50mg	*
ATPro Matrix (Calcium Pyruvate, Sodium Phosphate, Potassium Phosphate, Ribose)	500mg	*
*Daily Value Not Established		

Other Ingredients: Vegan capsule

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

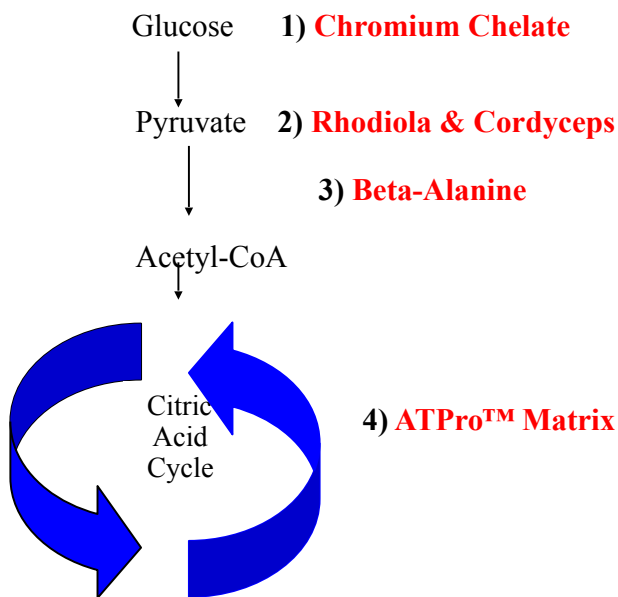
Covered by Albion International, Inc., U.S. Patent 5,614,553.

## How **OPTYGEN-HP** works

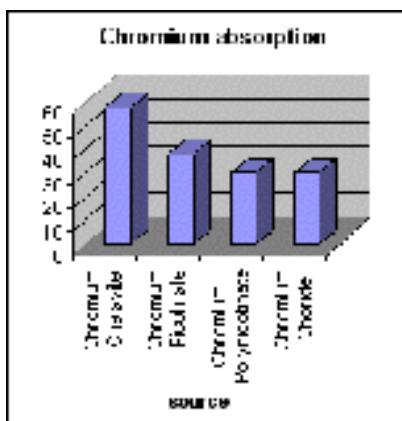
**Intro:** *OPTYGEN-HP*<sup>TM</sup> works on four different levels – synergistically – with the goal of increasing endurance. Endurance is defined as the ability to perform work over a period of time during which there is sufficient oxygen delivered to the muscles. There are four critical components necessary to increase endurance capacity:

- 1) Efficient glucose metabolism
- 2) Efficient oxygen transfer
- 3) Lactate synthesis
- 4) ATP production

*OPTYGEN-HP* targets all four 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 fuel delivery. Insulin spikes or lack of insulin response can cause the nutrients to either be rushed into the bloodstream too quickly or not quickly enough. Chromium regulates this nutrient breakdown so equal and sustained nutrients are delivered 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 in adaptation to high altitude – 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 VO<sub>2</sub>max.

**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, carnosine levels can be increased, but 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 training and racing at a higher level.

**ATP Production:** The final step of the *OPTYGEN-HP* formulation puts all the necessary components together to ensure 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-HP*'s proprietary ATPPro™ matrix of five key nutrients is designed to ensure 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. An endurance athlete's VO<sub>2</sub>max is directly proportional to the body's 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](http://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 VO<sub>2</sub>max, reduced lactic acid and increased endurance. Though Cordyceps and Rhodiola taken individually would offer enhanced performance, the combination including chromium chelate, beta-alanine and the ATPPro™ matrix complete the formulation. It is this synergistic combination of key ingredients that make *OPTYGEN-HP* such a powerful and complete endurance formula.

## ***OPTYGEN-HP* Pilot Study**

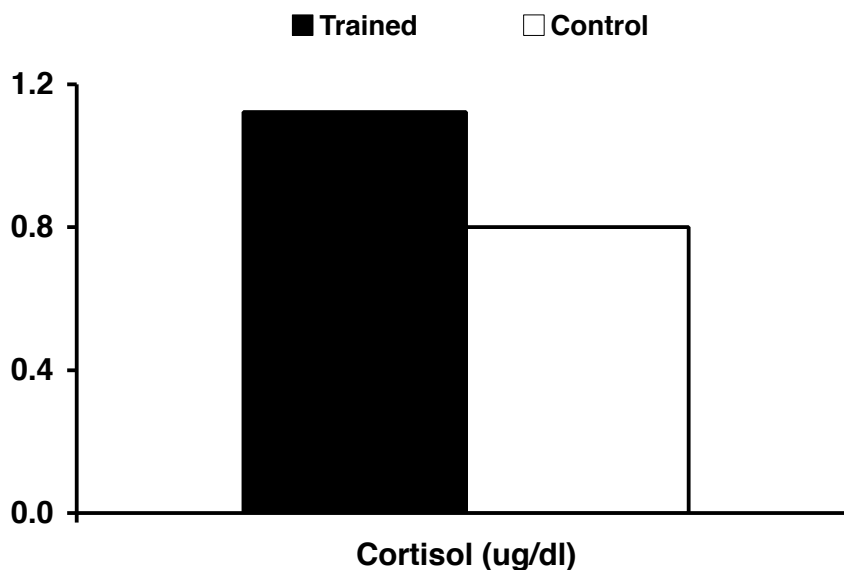
In a pilot study conducted by Dr. Andrew Creer of South Dakota State University, highly trained collegiate runners used *OPTYGEN-HP* over an 8 week period.

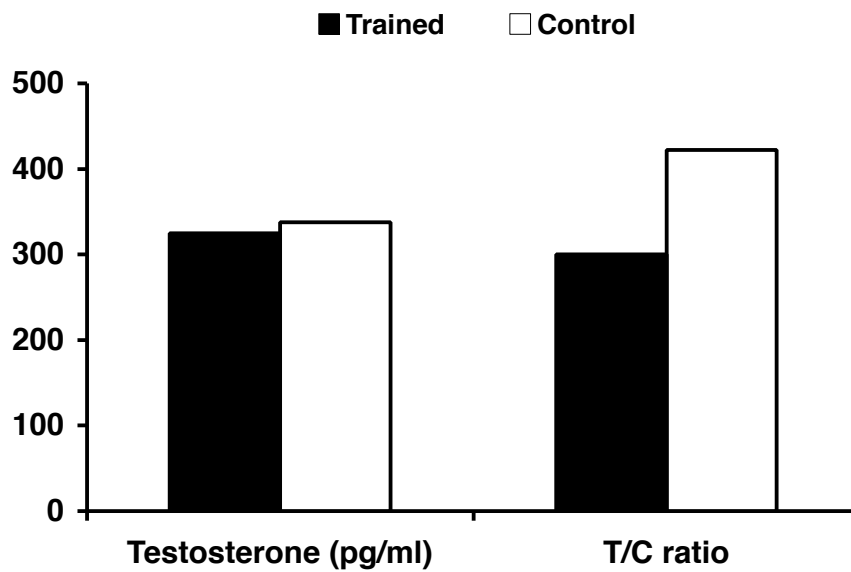
It was anticipated that supplementation would reduce stress and improve performance over training without the supplement. Though changes in the performance variables (VO<sub>2</sub>max, VT, RE16, lactate16, event time improvement) measured during the course of this study were similar between groups, 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<sup>-1</sup> 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 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-HP* proves beneficial to trained athletes undergoing high training volumes by decreasing baseline stress and improving training sessions, leading to an overall improvement in performance.



## **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 Kurukov 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

---

### **Acute dose of Rhodiola on Endurance Exercise Performance:**

A 2013 study published in the Journal of Strength and Conditioning used a randomized placebo-controlled human clinical study on athletes. Testing consisted of a 10 minute warm up followed by a 6 mile time trial on a bicycle ergometer. Rating of perceived exertion (RPE) was measured every 5 minutes during the TT. Blood lactate concentration, salivary cortisol and salivary alpha amylase were measured before warm-up, 2 minutes after warm up, and 2 minutes after TT. Testing was repeated 2-7 days later with the other conditions. Rhodiola rosea ingestion significantly decreased heart rate during the warm up. Subjects completed the TT significantly faster after Rhodiola rosea ingestion. The difference was even more pronounced when a ratio of the RPE relative to the workload was calculated.

---

### **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:**

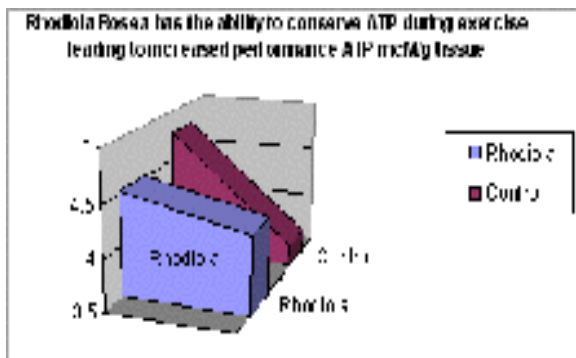
Russian scientist Kurmukov discovered that the administration of Rhodiola rosea polyphenols extended the life of isolated heart exposed to low oxygen conditions called hypoxia. In a second study also conducted by Kurmukov, 20mg of polyphenolic compounds, purified from Rhodiola Rosea, extended life by 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)

Germano, Carl RD, CNS, LDN; Vitamin Retailer (August, 1998 pp54-56) "Rhodiola: Not just another adaptogen"

Germano C, Ramazanov Z. Arctic Root-Rhodiola Rosea. 1999, Kensington Books.

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 Research:**

**Cordyceps 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 gives blood its 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 that 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 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, respiratory illness and fatigue. The Cordyceps mushroom grows primarily as a parasitic fungus on caterpillars on the plateau of China and Tibet above 12,000 feet. Tibetan sherpas would make tea from the fungus and claimed that it allowed them to climb high up Mount Everest without supplemental oxygen. Some researchers believe it is the mushroom's ability to survive at high altitude, which gives 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 VO<sub>2</sub> max has only been performed with the CS-4 strain.

The importance of Cordyceps materialized during the Chinese National Games in Beijing where athletes broke three world records in the 3,000, 5,000 and 10,000-meter events. 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-relieving tonic (prepared from Cordyceps Sinensis) were the factors responsible for record-breaking performance by the athletes. 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)

Despite these potential benefits, several studies have found no benefit to supplementation, however it seems these studies were too short in duration and/or performed using a smaller dose. In addition, recent analysis has questioned the validity of certain marketed CS-4 strains claiming they are not Cordyceps at all. This has potentially led to the questioning of the effectiveness of this adaptogen and led scientist to look for a more easily identifiable and reproducible strain like Cordyceps Militaris.

### **Cordyceps Militaris; A new strain**

Cordyceps Militaris is a mycelial biomass cultured from oats. This strain is similar to *Sinensis* yet has larger quantities of the active constituents making it an effective substitute. A 2016 study using this new strain showed significant improvements in time to exhaustion, peak power output and ventilator threshold in cyclists.

Twenty-eight healthy and trained college students underwent this double blind, placebo controlled study at the University of North Carolina using an acute and prolonged supplementation period. The average age was 22 years old with an average weight of 155lbs. Athletes were randomly placed in a placebo group or a supplementation group. The supplementation group consumed Cordyceps Militaris for three weeks and were

measured for VO<sub>2</sub>, time to exhaustion, ventilatory threshold at baseline, week 1 and week 3.

Following one week of supplementation only time to exhaustion improved in the supplementation group. After three weeks the supplementation group increased peak power by 17% whereas the placebo group decreased by 11%. The supplementation group improved time to exhaustion by 70 seconds compared to a 5 second reduction in placebo. In addition, ventilatory threshold was further improved in week three. (Katie R. Hirsch, et. al. 2016)

**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), proving its effectiveness as an antioxidant. (J. Zhu, 1999). In a human study, Cordyceps has proved to improve lactate energy metabolism within the cell. (Burke, Edmund 1998) Its also been shown to improve oxygen utilization, blood flow and therefore help clear lactate. (Ko et. al, 2007, Zhu et. al, 1998) Supplementation has been shown to improve aerobic performance, showing improvements in maximal oxygen consumption and ventilatory threshold. (Chen et al., 2010)

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

### **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 VO<sub>2</sub> max 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, VO<sub>2</sub> max 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 cardiotonic 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 supplementation. 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 VO2 max 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)

### **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.(Lou et al., 1986)

**Conclusion:** Cordyceps has a long history of use with both endurance and power athletes with strong anecdotal evidence supporting its benefits. For over 30 years researcher have gone back and forth publishing studies supporting positive activity and studies showing no activity. Two likely culprits to these non-activity study results are the recent findings that show strains that are not truly cordyceps and study designs that lacked enough supplementation time or effective dose.

Using these new findings, the 2016 Cordyceps Militaris study was able to prove positive performance enhancements with healthy human athletes using a prolonged supplementation period. There is still considerable evidence in support of Cordyceps CS-4 and with proper analytical identification of a true cordyceps sinensis , proper dose and duration, athletes can expect physiological benefit.

Cordyceps has a multitude of mechanisms that allow it to improve bodily functions. We still believe however, that its primary mechanism is to aid in the modulation of stress. It is stress that both benefits athletes greatly and also derails all training and athletic gains. When stress goes unabated it quickly manifests into suppressed VO<sub>2</sub>, suppressed oxygen utilization, inflammation and poor lactate clearance. Cordyceps is an effective natural fungus that can help athletes during heavy, stressful training. The management of stress allows athletes to remain healthy and to sustain a high level of training.

### **Cordyceps Study references:**

Chinese fungus and World Record Runners: American Entomologist pp. 235-236 (winter, 1994) Georges M. Halpern: Cordyceps, Chinese Healing Mushroom, Avery Publishing, 1999.

J.Zhu, G.M. Halpern and K.Jones: The Scientific Rediscovery of and Ancient Chinese Herbal Medicine:

Cordyceps sinensis, *Alternative & Complementary Therapies*, 4(3-4),289-303,429-457.

Zhu, X. 1990. Immunosuppressive effect of cultured Cordyceps sinensis on cellular immune response. *Chinese Journal of Modern Developments in Traditional Medicine* 10:485-487,4540

Medicine & Science in Sports & Exercise abstract published in 2001;33:S164. Cordyceps CS-4: Poster presented at The ACSM annual meeting, Baltimore, MD, June 2001. Poster presented at The Experimental Biology 2001 (FASEB meeting), Orlando, FL, April 3, 2001.

Medicine & Science in Sports & Exercise abstract published in 1999;31(5):S174. Cordyceps CS-4 Poster presented at The Experimental Biology 2001 (FASEB meeting), Orlando, FL, April 1, 2001. Paper published in *Chinese J Gerontology* 2001;20(4):297-298.

Kim H, Yun J. A comparative study on the production of exopolysaccharides between two entomopathogenic fungi *Coryceps militaris* and *Cordyceps sinensis* in submerged mycelial cultures. *J Appl Microbiol*. 2005.

Chen et al., Effect of CS-4 Cordyceps Sinensis on exercise performance in healthy older subjects. *Journal of Alternative Complementary Medicine*. 2010.

Akinobu Tsunoo, Naoki Taketomo, Hiroshi Tsuboi, Masayuki Kamijo, Atsushi Nemoto, Hajime Sasaki, Masayuki Uchida; Meiji institute of Health Science. Cordyceps Sinensis: Its diverse effects on mammals *in vitro* and *in vivo*. Third International Symposium of the Mycological Society of Japan, 1995.

Noboru Manabe et. Al.; Effects of the Mycelial Extract of Cultured *Cordyceps Sinensis* on *In Vivo* Hepatic Energy Metabolism in the Mouse. *Japanese Journal of Pharmacology* 70, 85-88 (1996).

Burke, Edmund R. Herbs Enhance Lactate Metabolism. *Nutrition Science News*, V.3; N.9 P. 458 (1998)

Lou Y, Liao X, Lu Y. Cardiovascular pharmacological studies of ethanol extracts of Cordyceps mycelia and Cordyceps fermentation solution. *Chinese Traditional and Herbal Drugs* 1986; 17(5): 17-21, 209-213.

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.

Katie R. Hirsch, et. al. Cordyceps militaris Improves Tolerance to High-Intensity Exercise After Acute and Chronic Supplementation. University of North Carolina. *Journal of Dietary Supplements*. ( 2016)

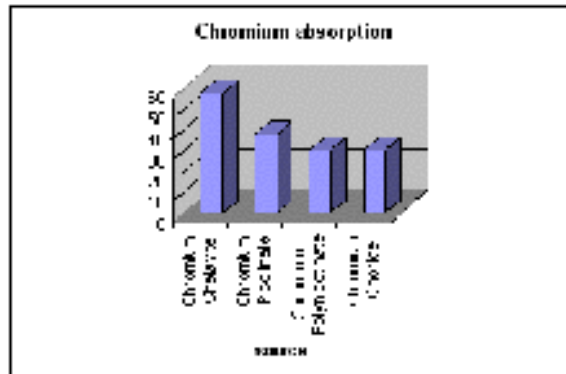
### **Chromium (as Chelate) research:**

**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 chelate - which help increase the absorption and availability compared to isolated chromium.

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

Albion Research Notes, Newsletter, June 1995



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

forms part of a compound in the body known as involved in regulating the actions of insulin in poly, in helping to control appetite. Since 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 anaerobic threshold resulted in increased plasma chromium twelve minutes after the exercise. (Anderson, 1991).
- 

### **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; and
- 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).

### **Chromium references:**

Anderson RA. Effects of chromium on body composition and weight loss. *Nutr Rev.* 1998 Sep;56(9):266-70.

Anderson, RA. 1988. Selenium, chromium, and manganese. Chromium in *Modern Nutrition in Health and Disease*, eds. M. Shils and V. Young. Philadelphia: Lea and Febiger.

Anderson, RA, Polansky MM, Bryden NA. Strenuous running: acute effects on chromium, copper, zinc, and selected clinical variables in urine and serum of male runners. *Biology Trace elements res.* 1984; 6: 327-336

Anderson, RA, Polansky MM, Bryden NA. Effects of carbohydrate loading and underwater exercise on circulating cortisol, insulin and urinary losses of chromium and zinc. *Eur Journal of Applied Physiology*, 1991;3:289-293.

Williams, M, 1995, Chromium, *Nutrition for Fitness and Sport*, Brown and Benchmark publications.

Cerulli J, Grabe DW, Gauthier I, Malone M, McGoldrick MD. Chromium picolinate toxicity. *Ann Pharmacother.* 1998 Apr;32(4):428-31.

McCarty MF. Chromium and other insulin sensitizers may enhance glucagon secretion: implications for hypoglycemia and weight control. *Med Hypotheses.* 1996 Feb;46(2):77-80.

Reading SA. Chromium picolinate. *J Fla Med Assoc.* 1996 Jan;83(1):29-31.

Trent LK, Thieding-Cancel D. Effects of chromium picolinate on body composition. *J Sports Med Phys Fitness.* 1995 Dec;35(4):273-80.

Walker LS, Bemben MG, Bemben DA, Knehans AW. Chromium picolinate effects on body composition and muscular performance in wrestlers. *Med Sci Sports Exerc.* 1998 Dec;30(12):1730-7.

## Intro

Beta-Alanine has been a staple of endurance and strength athletes for over a decade. We first introduced this naturally occurring amino acid in 2007 with the introduction of OptygenHP. Since that time, study after study has proved this nutrient to be highly beneficial for endurance and power sports. A newly published 2017 meta-analysis reviewed 40 individual studies employing 65 different exercise protocols and totaling 70 exercise measures in 1461 participants. This meta-analysis published in the British Journal of Sports Medicine concluded that "Beta-Alanine had a significant overall effect. With the greatest benefit being total exercise capacity."

**What is Beta-Alanine?** Beta-Alanine is an amino acid combining carnosine and vitamin B5, known as pantothenic acid. Though it is the carnosine in the body that allows for the enhancement of improved lactate synthesis, it is Beta-Alanine that is the rate limiting nutrient in this process. In other words, to increase carnosine content one must supplement with Beta-Alanine. When ingested, carnosine breaks down into Beta-Alanine and histidine. The more effective method to improve carnosine is therefore by ingesting Beta-Alanine instead of carnosine. Beta-alanine has become widely accepted as a highly effective nutrient for endurance training and racing. Studies have clearly shown it to be an effective tool to boost endurance training and racing through its improvement on working capacity, VO<sub>2</sub> and lactate threshold. (Pottier 2007, Stout 2007, Suzuki 2002, Van Thienen 2009, Zoeller 2006, and Smith 2009, Saunders 2017, Bellinger 2016).

## Lactate Threshold

Based on current research, Beta-Alanine's primary role appears to be its effect on lactate threshold, which in endurance training is defined as the rate at which there is equilibrium in lactic acid production and lactic acid elimination. During exercise, hydrogen ions (H<sup>+</sup>) are produced in the body and cause the pH levels in the muscles to drop. When pH levels in the muscles are low, it means muscle tissue is acidic or producing lactic acid. At this lower pH, muscles cannot balance lactic acid production with lactic acid elimination, resulting in an overall slowing of movement, decreased physical strength, and intensity. When pH levels are balanced, training can continue for longer periods at increased intensity.

Exerting effort above lactate threshold prevents endurance athletes from sustaining that effort for more than a few minutes. It's long been understood that the amino acid carnosine plays a key role in the homeostasis of pH and lactate threshold and that carnosine levels are regulated by Beta-Alanine.

### **To understand how Beta-Alanine works, you must first understand how carnosine works.**

Carnosine enters the digestive system and is hydrolyzed into histidine and Beta-Alanine, which is then synthesized back into carnosine by skeletal muscle. Intra-muscular carnosine buffers hydrogen ions, this in turn leads to an increase in pH which is necessary for the balance between production and elimination of lactic acid.

Carnosine works by soaking up hydrogen ions (H<sup>+</sup>) to prevent low pH levels, as confirmed in recent studies. Increased carnosine concentration in muscles leads to increased buffering capacity of intra-muscular hydrogen ion (H<sup>+</sup>) (Dunnet 1999 & 2002, Hill 2007), as well as regulation of intra-cellular pH of both oxidative and glycolytic muscle fibers (Damon 2003). Increased carnosine accounts for up to 30% of the pH buffering capacity of the body.

With intense training, athletes have an opportunity to improve their intra-muscular carnosine content by up to 87% (Harris, 2005), which in turn provides an increase in lactate threshold. However, though endurance training increases intra-muscular carnosine levels, oral supplementation of carnosine does not have the same result. So, even though carnosine is widely available as a supplement, it is only through the availability of beta-alanine that intra-muscular carnosine can increase.

A related study shows carnosine levels significantly drop with age, which may be a key reason older athletes tend to have a lesser ability to eliminate lactate. (Dunnett, 2002)

### **So where does Beta-Alanine come in?**

Since Beta-Alanine is the precursor to the production of intra-muscular carnosine, it must be present in order for intra-muscular carnosine levels to increase when intense training takes place. Ingestion of Beta-Alanine for 4 to 8 weeks has been shown to elevate muscle carnosine content by 42%, 47%, 64% and 65% respectively (Pottier 2007, Harris 2006, Hill 2007). Increasing intra-muscular carnosine means the body is capable of buffering more hydrogen and eliminating more lactic acid. The end result for an athlete is an improved lactate threshold. A slew of research studies on the mechanism of improved lactate threshold through the supplementation of beta-alanine have shown significant improvements in power, strength, endurance performance, and aerobic metabolism (Smith 2009, Van Thienen 2009, Stout 2007, Suzuki 2002, Pottier et al 2007). These double-blind, placebo-controlled studies were conducted in 4 and 8 week periods.

### **What does this all mean to your performance?**

The ability to sustain efforts above lactate threshold is the primary benefit associated with Beta-Alanine supplementation. Beta-Alanine supplements should be consumed daily during heavy training blocks and based on today's research, a minimum of 4 weeks is required before experiencing any significant increases in intra-muscular carnosine levels. Studies have proven the effect to be dose dependent, with an increased dosage pattern throughout the supplementation period. The buffering effects can be expected to slowly increase from the beginning of training and sustained throughout the entire training block. Using this supplementation strategy to improve interval workouts or threshold training workouts is the best method to achieve a lasting physiological change that can be carried over into races.

### **New Studies**

A 2016 study on trained cyclists in a 4000m TT showed significant improvement in performance.

Supplementation increased time to exhaustion concomitant with improved anaerobic capacity during supramaximal intensity cycling and an increase in power output during a 4000m cycling TT, resulting in an enhanced overall performance.

A 2017 study by Saunders et. al, performed on active cyclists showed that supplementation for 24 weeks improved carnosine content and exercise capacity each week. The study concluded that the maximal carnosine content achievable is therefore not known.

The third significant study proved that total Beta-Alanine consumption, not a specific dose was the primary determinant of carnosine content. Athletes consuming 1.6g Beta-Alanine per day over a long period improved carnosine content to a similar degree as those consuming an equivalent amount in a shorter time period. This study along with the 2017 Saunders study prove that consuming Beta-Alanine long term in maintenance dose can be beneficial to endurance trained athletes.

### **Studies**

- 1) Van Thienen's 2009 study done on trained cyclists showed beta-alanine can improve sprint performance at the end of an exhaustive endurance exercise by 11.4%.
- 2) The Smith 2009 double-blind study done on recreationally active college men supplementing with beta-alanine for six weeks while undergoing high-intensity interval training (HIIT) showed significant improvements in VO<sub>2</sub>peak, VO<sub>2</sub> time to fatigue versus a group using a placebo.
- 3) The Stout 2007 double-blind study done on 22 trained women supplementing with beta-alanine for 28 days performing on cycle ergometers showed a significant improvement in ventilatory threshold, physical working capacity at fatigue threshold and time to exhaustion.
- 4) The Suzuki 2002 study looked at untrained men and trained them two days per week on cycle ergometers for 8 weeks. This double-blind study showed significant increase in sustainability of high power during 30-second maximal cycle ergometer sprinting.



5) Pottier et al. 2007 investigated supplementation of beta-alanine on fifteen trained men in a 400m sprint and knee extension to exhaustion. Beta-alanine supplementation increased carnosine levels by 47% and attenuated fatigue in repeated bouts of exhaustive exercise.

#### Beta-Alanine References:

- 1) Dunnett M., R.C. Harris. Influence of oral beta-alanine and L-histidine supplementation on the carnosine content of the gluteus medius. *Equine Vet J.* 30 (suppl): 499-504, 1999.
- 2) Dunnett M., Harris RC, Dunnett CE, Harris PA. Plasma carnosine concentration: Diurnal variation and effects of age, exercise and muscle damage. *Equine Vet J Suppl*; Sept 2002. (34): 283-7
- 3) Harris R. C. Muscle Carnosine elevation with supplementation and training, and the effects of elevation on exercise performance. (ISSN conference, 2005).
- 4) Harris RC, et al; The absorption of orally supplied beta-alanine and its effect on muscle carnosine synthesis in human vastus lateralis. *Amino Acids*; 2006 May; 30 (3): 279-289.
- 5) Hill CA, Harris RC, Kim HJ, Harris BD, Sale C, Boobis LH, Kim CK, Wise JA; Influence of beta-alanine supplementation on skeletal muscle carnosine concentrations and high intensity cycling capacity. *Amino Acids*. 2007 Feb; 32(2) 225-33
- 6) Pottier, A, Ozdemir M, Reyngoudt H, Koppo K, Harris R, Wise J, Achten E, Derave W. Beta-Alanine supplementation augments muscle carnosine content and attenuates fatigue in trained sprinters. *Medicine and Health Sciences, Belgium; ECSS July 2007.*
- 7) Smith AE, Walter AA, Graef JL, Kendall KL, Moon JR, Lockwood CM, Fukuda DH, Beck TW, Cramer JT, Stout JR; Effects of Beta-Alanine supplementation and high-intensity interval training on endurance performance and body composition in men; a double-blind trial. *JISSN* 6:5 2009.
- 8) Stout JR, Cramer JT, Soeller RF, Torok D, Costa P, Hoffman JR, Harris RC, O'Koy J.; Effects of beta-alanine supplementation on the onset of neuromuscular fatigue and ventilatory threshold in women. *Amino Acids* 2007 April; 32 93): 381-6
- 9) Suzuki Y, Ito O, Mukai N, Takahashi H.; High levels of skeletal muscle carnosine contributes to the latter half of exercise performance during 30s maximal cycle ergometer sprinting. *Jap Journal of Physiology* 52 199-205, 2002.
- 10) Van Thienen R, Van Proeyen K, Vanden EB, Puype J, Lefere T, Hespel P. Beta-Alanine improves sprint performance in endurance cycling. *Med Science Sports and Exercise*; April 2009; 41(4): 898-903
- 11) Zoeller RF, Stout JR, O'Kroy JA, Torok DJ, Mielke M.; Effects of 28 days of beta-alanine and creatine monohydrate supplementation on aerobic power, ventilatory and lactate thresholds, and time to exhaustion. *Amino Acids*. 2006 Sept 5.
- 12) Bellinger et. al., Metabolic consequences of Beta-Alanine supplementation during exhaustive supramaximal cycling and 4000m TT performance. *Applied Physiology Nutrition Metabolism*: Aug 2016; 41(8):864-71. doi: 10.1139/apnm-2016-0095. Epub 2016 Apr 6.
- 13) Saunders B. et. al., Beta-Alanine supplementation to improve exercise capacity and performance: A systematic review and meta-analysis. *British Journal of Sports Med.* 2017 Apr; 51(8):658-669. doi: 10.1136/bjsports-2016-096396. Epub 2016 Oct 18.
- 14) Saunders B. et. al., Twenty-four Weeks of -Alanine Supplementation on Carnosine Content, Related Genes, and Exercise. *Medicine & Science in Sports & Exercise*: May 2017 Volume 49 p 896-906

## **Beta-Alanine Abstracts:**

### **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 VO<sub>2</sub>peak, time to exhaustion, power output and percent Vo<sub>2</sub>peak associated with ventilatory threshold and lactate threshold. Within groups significant time to exhaustion improvements were found in the beta-alanine/creatine group.

---

### **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 VO<sub>2</sub>peak, time to exhaustion, power output and percent Vo<sub>2</sub>peak associated with ventilatory threshold and lactate threshold. Within groups significant time to exhaustion improvements were found in the beta-alanine/creatine group. (Zoeller RF, et.al.,2006)

---

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

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:**

Dunnett M., R.C. Harris. Influence of oral beta-alanine and L-histidine supplementation on the carnosine content of the gluteus medius. *Equine Vet J.* 30 (suppl): 499-504, 1999.

Harris R. C. Muscle Carnosine elevation with supplementation and training, and the effects of elevation on exercise performance. (ISSN conference, 2005).

Hill CA, Harris RC, Kim HJ, Harris BD, Sale C, Boobis LH, Kim CK, Wise JA; Influence of beta-alanine supplementation on skeletal muscle carnosine concentrations and high intensity cycling capacity. *Amino Acids.* 2007 Feb; 32(2) 225-33

Stout JR, Cramer JT, Soeller RF, Torok D, Costa P, Hoffman JR, Harris RC, O'Koy J.; Effects of beta-alanine supplementation on the onset of neuromuscular fatigue and ventilatory threshold in women. *Amino Acids* 2007 April; 32 93): 381-6

Zoeller RF, Stout JR, O'Kroy JA, Torok DJ, Mielke M.; Effects of 28 days of beta-alanine and creatine monohydrate supplementation on aerobic power, ventilatory and lactate thresholds, and time to exhaustion. *Amino Acids.* 2006 Sept 5.

Suzuki Y, Ito O, Mukai N, Takahashi H.; High levels of skeletal muscle carnosine contributes to the latter half of exercise performance during 30s maximal cycle ergometer sprinting. *Jap Journal of Physiology* 52 199-205, 2002.

**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, but 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?**

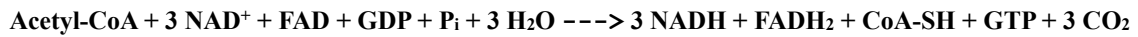
**A:** Cutting edge human clinical studies show beta-alanine supplementation significantly improves muscular endurance, exercise capacity (so you can exercise longer) and total work done. The mechanism supporting beta-alanine works synergistically with the adaptogens, chelated chromium and ATP<sup>Pro</sup><sup>TM</sup> 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

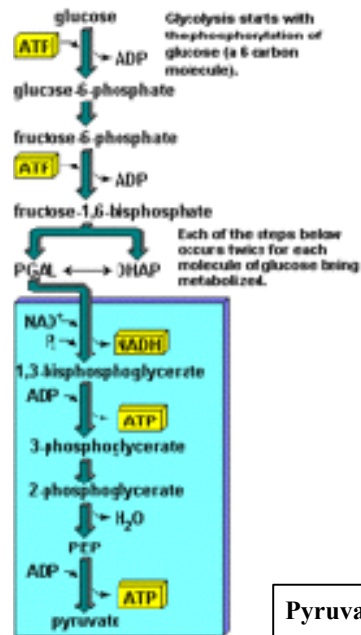
**Q: Do I have to load with *OPTYGEN-HP*?**

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

**ATPro™ Matrix:** *OPTYGEN-HP*'s proprietary ATPro™ matrix of five key nutrients is designed to ensure 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. VO<sub>2</sub>max is directly proportional to the ability to produce ATP, which is also known as the body's high energy state.

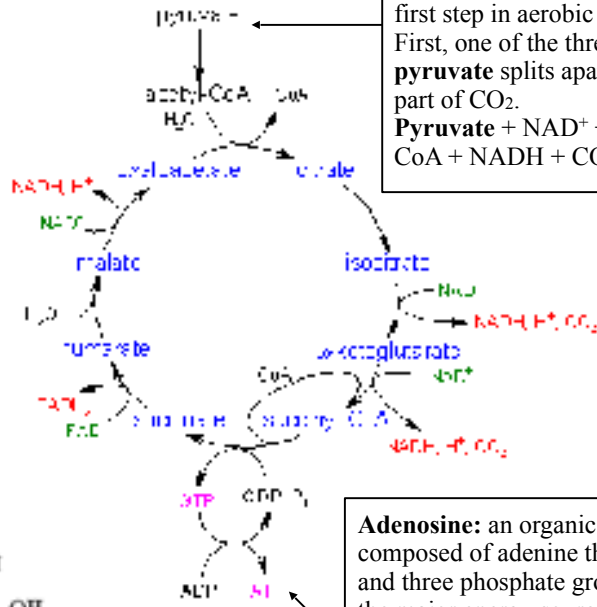


Organic Phosphates (**Sodium phosphate & Potassium phosphate**) play an important role in metabolism. For example, in the metabolism of sugars (which have hydroxyl groups, -OH, in their molecules), **phosphate** esters are often formed as an intermediate compound. Formation of these esters is called 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 CO<sub>2</sub>.  
**Pyruvate** + NAD<sup>+</sup> + CoA Acetyl-CoA + NADH + CO<sub>2</sub>

**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.

