



## **OptygenHP Research Packet**

Rev4.0

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## **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.

### ***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-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*.

CERTIFICATE OF ANALYSIS		
Product: Optygen-HP		Lot: 07255
Company: First Endurance		
<u>Formula Ingredients</u>	<u>Specification</u>	<u>Formula Amount</u>
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 confidence 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.

## 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>		
<b>Serving Size: 4 Capsules</b>		
	Amount Per Serving	%DV
Chromium (from Chelavite® amino acid chelate)	200mcg	167%
Ashwagandha Extract ( <i>Withania Somnifera</i> )(root)	150mg	*
Rhodiola Extract ( <i>Rhodiola Rosea</i> )(root)	150mg	*
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

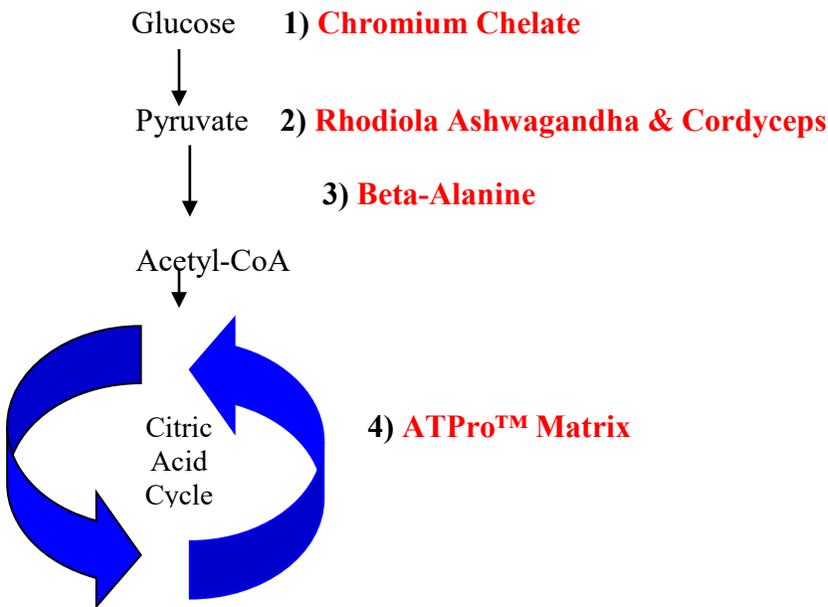
Chelavite® is a registered trademark of Albion Laboratories, Inc.  
Covered by Albion International, Inc., U.S. Patent 5,614,553.

# How **OPTYGEN-HP** works

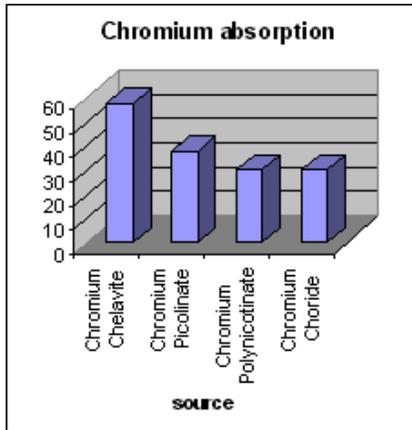
**Intro:** *OPTYGEN-HP*<sup>TM</sup> works on four different levels – synergistically – with the goal of increasing endurance. Endurance is defined as the ability to perform work over a period of time during which there is sufficient oxygen delivered to the muscles. There are four critical components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

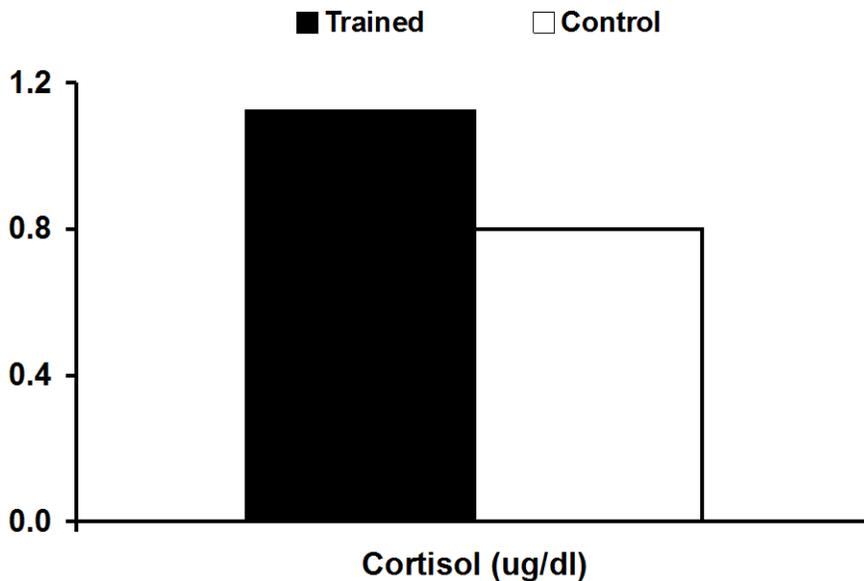
Normally trained runners (~50 miles/wk) have been reported to have low resting testosterone levels as well as cortisol levels in the high-normal range. Recent data from our laboratory show resting cortisol levels in collegiate runners to be 30% greater than age matched control data (Figure 1), and although 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.

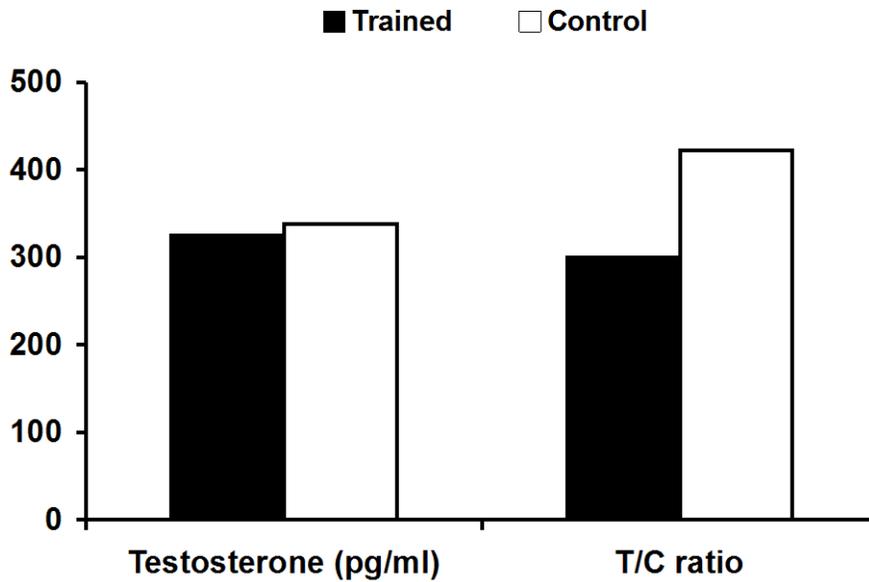
*Table 1.* Training volume and weekly mean stress scores from the 8-week training period. Also included are % changes in event performance from pre to post training. km•wk<sup>-1</sup> Stress Score Performance Δ

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 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

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## **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

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### **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.

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### **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.

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## **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

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## **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 restitutive 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).”
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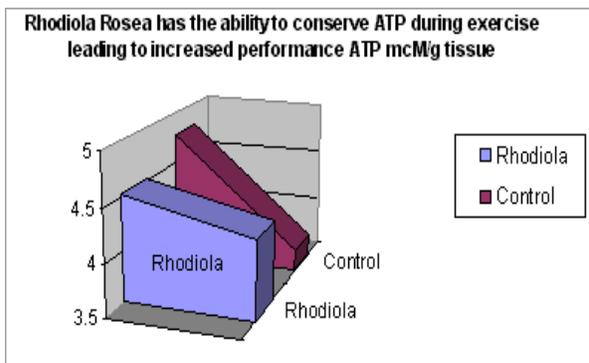
### **Rhodiola administration has pronounced anti-hypoxic effects:**

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).

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### **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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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.

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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 VO<sub>2</sub>max 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 VO2 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 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 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 VO<sub>2</sub> 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.

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## **Ashwagandha Research:**

Ashwagandha root extract is a perennial shrub cultivated in India and China. It's a medicinal ayurvedic herb used for thousands of years for its ability to release tension, improve breathing, reduce stress and aid in fertility. Its name comes from the Sanskrit language and means ashva- 'horse' and gandha- 'smell'. The root has a strong smell that is described as horse-like. Its botanical name is *Withania somnifera*, however it's also known as winter cherry or gooseberry. Its primary activity comes from the standardization of withanolides which are triterpene lactones.

In preclinical studies, *Withania Somnifera* has shown anti-microbial, anti-inflammatory, anti-tumor, anti-stress, neuroprotective, cardioprotective, and anti-diabetic properties. (8). Additionally, it has demonstrated the ability to reduce reactive oxygen species, modulate mitochondrial function, regulate apoptosis, reduce inflammation and enhance endothelial function.(8) Several studies have also looked at the efficacy of this herb for infertile men (5, 6, 7). These studies reviewed *Withania somnifera* which showed significant improvement on serum hormonal profile, semen volume and sperm concentration. This evidence suggests that the mechanism of action of *Withania somnifera* may improve recovery from overtraining since overtraining results in low testosterone and low semen motility.

Though there are dozens of studies dating back 50 years, over the last 10 years eight separate clinical studies have shown the efficacy of this herb as it pertains to endurance athletes. Much like other adaptogenic herbs like *Rhodiola Rosea*, its primary benefit comes from its ability to modulate cortisol (stress). Ashwagandha has been shown to improve resistance to stress including a reduction in cortisol by 30%. (9) Secondary benefits include improvement in VO<sub>2</sub>max, improvement in substrate utilization (fat burning) and performance. (1,2,3,4) Studies indicate this is a systemic dose dependent ingredient that should be consumed daily for 8 weeks or longer.

40 elite male cyclists participated in the experimental study. Half the cyclist were randomly placed in a placebo group versus a treatment group where they consumed ashwagandha for 8 weeks. VO<sub>2</sub>max, respiratory exchange ratio (RER), and total time to exhaustion was measured on day 1 and at 8 weeks. The treatment group showed significant improvement in VO<sub>2</sub>max (p<.001), METS (P<.001) and time to exhaustion (P<.001). (3)

50 healthy male and female athletic adults participated in this double-blind, randomized, placebo controlled study. VO<sub>2</sub> was measured during a 20m shuttle run test. Results showed a greater increase (p<0.0001) in mean VO<sub>2</sub>max with ashwagandha versus placebo at 8 weeks and 12 weeks. Study shows ashwagandha enhances cardiorespiratory endurance in healthy athletic adults. (1)

57 young male subjects participated in an 8-week randomized double-blind placebo controlled study. Subjects in the treatment group consumed ashwagandha for 8 weeks while the control group consumed a placebo. Compared to placebo, the treatment group had significant increases in muscle strength on bench-press, leg-extension, and muscle size. The ashwagandha group also had significant reduction in muscle damage as indicated by the stabilization of creatine kinase and improvement in testosterone levels. (2)

A 2010 study using 40 normal healthy subjects, looked independently at the efficacy of both *Withania somnifera* and *Terminalia Arjuna*. This double blind study separated the subjects into four groups. One group consumed *Withania somnifera*, a second group consumed Terminalia Arjuna, a third group consumed both herbs and a fourth group consumed a placebo. After 8 weeks of supplementation significant improvements were seen with all three test groups. The group using *Withania somnifera* increased maximum velocity, power and VO<sub>2</sub>max. (4).

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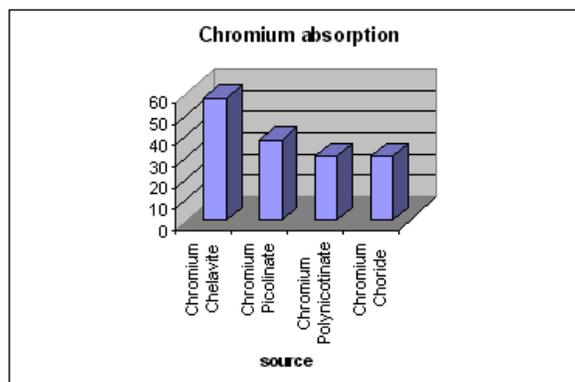
## **Chromium (as Chelate) research:**

**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 chelate - 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.

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## **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).
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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)

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### **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).

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## **Beta-Alanine Research:**

**Beta-alanine:** 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 increase, 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 (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 training and racing at a higher level.

## **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).

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### **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)

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### **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.

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### **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)

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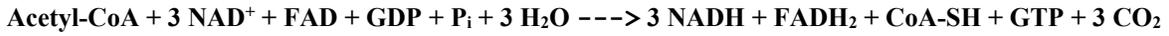
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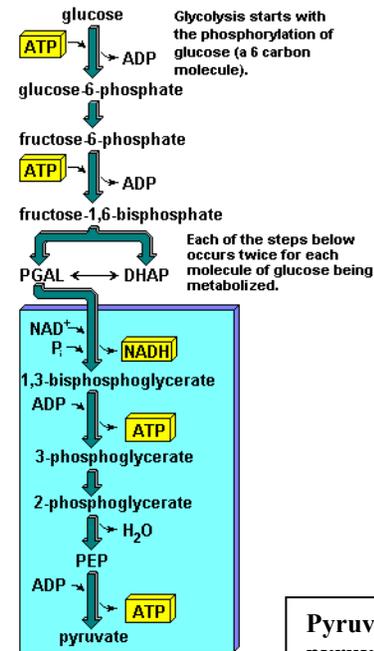
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Suzuki Y, Ito O, Mukai N, Takahashi H.; High levels of skeletal muscle carnosine contributes to the latter half of exercise performance during 30s maximal cycle ergometer sprinting. *Jap Journal of Physiology* 52 199-205, 2002.

**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.

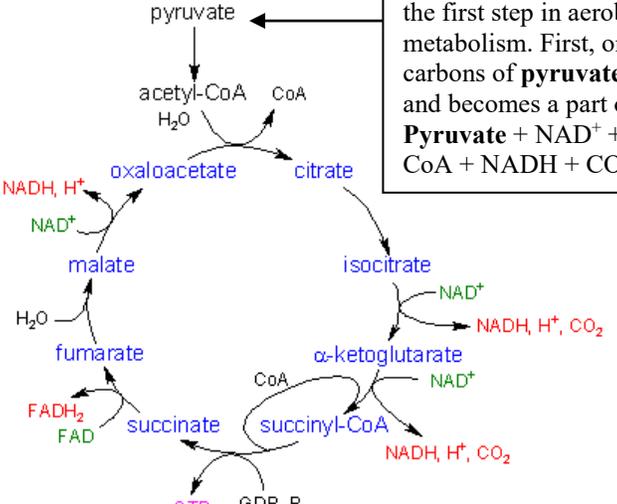


Organic Phosphates (**Sodium phosphate & Potassium phosphate**) play an important role in metabolism. For example, in the metabolism of sugars (which have hydroxyl groups, -OH, in their molecules), **phosphate** esters are often formed as an intermediate compound. Formation of these esters is called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

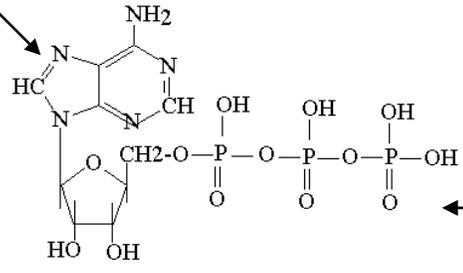


**Pyruvate:** The oxidation of **pyruvate** to form Acetyl CoA is the first step in aerobic metabolism. First, one of the three carbons of **pyruvate** splits apart and becomes a part of CO<sub>2</sub>.  
**Pyruvate + NAD<sup>+</sup> + CoA** Acetyl-CoA + NADH + CO<sub>2</sub>

**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.



adenosine triphosphate (ATP)