

NEW RESEARCH

Following exhaustive exercise, athletes fight inflammation, battle oxidative stress, need to repair torn muscle tissue, and have depleted essential glycogen stores. Glycogen is the primary storage carbohydrate in muscles and liver totaling approximately 2,000Kcal in a trained athlete. Muscle glycogen is generally known as the main fuel for strenuous sports activity. Unlike fat, this fuel can be mobilized rapidly under anaerobic condition, which typically occurs under various acute/exhaustive physical exercises.

Glycogen re-synthesis is the process of converting consumed food into stored glycogen. Even with optimal recovery after a hard workout, full glycogen re-synthesis is difficult to attain within 24 hours and subsequent workouts can begin to suffer. This is especially true when working out or racing for multiple days back to back. Having the ability to replenish glycogen to a greater degree allows athletes to bounce back from exhaustive exercise faster and be better prepared for the next day of training or racing.

GLYCOGEN RE-SYNTHESIS

The OptyMax (PN, RR) combination extract was studied for its ability to significantly improve glycogen re-synthesis in two key studies.

A. STUDY #1 In-vitro Glycogen:

The purpose of this study was to investigate the mechanism in which OptyMax (PN, RR) fruit extracts work. An in-vitro study of this highly fractionated combination of extracts show it affects associated gene expression and proteins that would increase the glycogen synthesis in muscles. This OptyMax (PN, RR) combination extract directly up-regulates GLUT-4 allowing for a greater re-synthesis of glycogen.

Results:

This in-vitro study suggests that OptyMax (PN, RR) may up-regulate the adiponectin secretion to affect AMPK-HIG-1-GLUT4 mediated glucose absorption in muscle cells. GLUT4 transporter is specific to muscle and is responsible for glucose absorption in muscle cells. When GLUT4 is up-regulated glycogen can be restored faster and to a greater degree. Faster glycogen replenishment directly correlates to faster and more complete recovery from exhaustive exercise.

B. STUDY #2 In-vivo (Human) Glycogen:

The in-vitro study was later supported with an in-vivo human study done on trained subjects. Glycogen re-synthesis was tested using the same OptyMax

(PN, RR) combination extract. The double-blind crossover study was conducted on 14 male college students. Pre-exercise measurements of glycogen concentration levels in the quadriceps were taken along with maximum oxygen uptake and maximum heart rate. Subjects were then randomly placed into a control group and experimental group. Everyone in the study was given a high-glycemic carbohydrate meal consisting of 80% carbohydrate, 8% fat and 12% protein the night before and then again immediately after a sixty minute cycling effort at 75% of VO₂Max.

After twelve hours of fasting, subjects performed a cycling exercise at 75% VO₂max for sixty minutes. Glycogen was again measured at 0, 3h, and 24 h after exercise. The OptyMax (PN, RR) combination extract was given to the experimental group daily along with a high-glycemic meal twelve hours prior to exercise and immediately following exercise. Regular meals were administered at three hours and 24 hours post exercise.

Results:

The pre-exercise baseline glycogen showed no significant differences between groups. Post exercise, the experimental group showed a glycogen synthesis rate increase of 370% in exercised skeletal muscle in the recovery phase (0-3h) and 60% in late recovery phase (4h – 24h) after high intensity exercise.

Glycogen Synthesis Rate Study

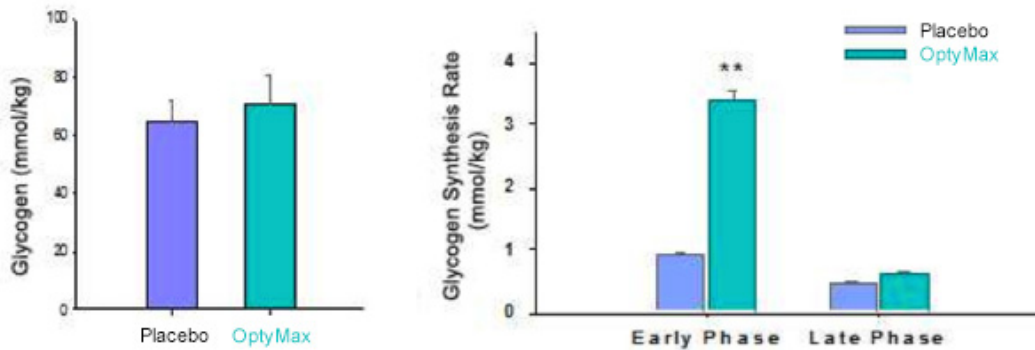


Fig. 2A. Baseline glycogen synthesis rate

Fig. 2B. Glycogen synthesis rate in early (3h) and late (24h) phase recovery

Table 2. Glycogen synthesis rate in Early Phase and Late Phase Recovery.

	Glycogen synthesis rate (mmol/kg/h)	
	Placebo	OptyMax
Early Phase Recovery	0.912 ± 0.005	3.400 ± 0.017**
Late Phase Recovery	0.459 ± 0.002	0.627 ± 0.003

** p<0.001

Discussion:

In the “glycogen study”, direct human evidence revealed that this OptyMax (PN, RR) can significantly enhance the rate of glycogen re-synthesis after one hour of exercise at a high-intensity. This suggests this ingredient matrix can be used to speed up and improve recovery from acute strenuous physical exercise, prolonged aerobic and anaerobic activities. The previous in-vitro study suggests the mechanism may up-regulate GLUT4. When GLUT4 is up-regulated glycogen can be restored faster and to a greater degree. Faster glycogen replenishment directly correlates to faster and more complete recovery from exhaustive exercise.

INSULIN SENSITIVITY

Insulin is a storage hormone that is released when carbohydrates are consumed. High-glycemic foods create a sugar rush and a subsequent insulin spike that helps regulate/lower the blood sugar. Too much insulin and one starts to get severe sugar swings. Insulin sensitivity is an individual's response to the carbohydrate meal, where some athletes are very sensitive and others are more resistant. With significantly higher glycogen re-synthesis rates, one would generally expect higher insulin sensitivity.

Note: insulin sensitivity is usually a bad thing.

C. STUDY Insulin resistance:

Insulin sensitivity was measured as a separate arm in the Glycogen study. After exercise a catheter was placed in the antecubital vein for blood sampling. Blood samples were taken before and during the 3 hour post-exercise recovery period following the high glycemic meal. During the post-exercise recovery period blood samples were collected every 30 minutes.

Results:

The experimental group who received the OptyMax (PN, RR) blend significantly improved whole-body insulin sensitivity, evidenced by better glucose tolerance with lower insulin response curve following the high-glycemic carbohydrate meal. ***This is especially impressive considering that this same group significantly improved glycogen re-synthesis.***

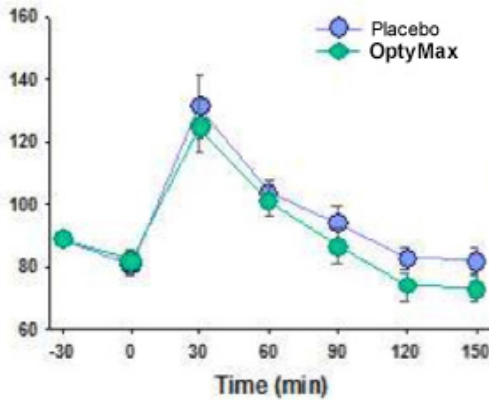


Fig. 1A. Meal Glucose Tolerance Test (MTT) after exercise

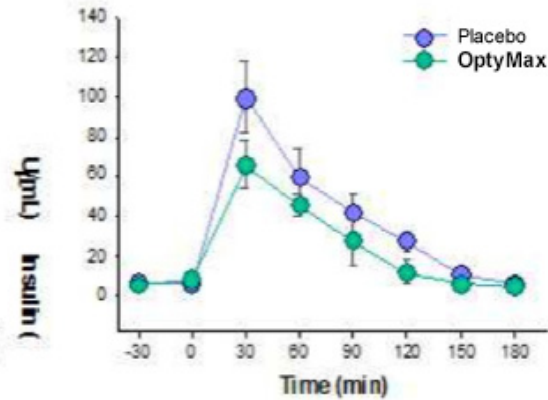


Fig. 1B. After exercise, serum insulin levels at indicated time after meal supplement.

Table1. Average decrease in blood glucose (mg/dL/min) and serum insulin (µU/mL/min) in human subjects between 30-180min.

RECOVERY MARKERS

MDA (malondialdehyde), IL-6 (cytokine interleukin-6) and CK (creatine kinase) are three well-studied and well-recognized markers of overtraining, overreaching and catabolic muscle activity. These are also known as key recovery/inflammatory

markers. Most studies have used MDA as a measurement of oxidative stress imposed by exercise. IL-6 is mainly produced, as an inflammatory response, in the muscle cells during strenuous exercise. Following exercise, lack of muscle glycogen causes muscles to secrete more IL-6. Exhaustive or very intense exercise also causes muscles to tear. When muscle fibers are damaged Creatine Kinase(CK) will appear in the blood. This is key indicator of muscle catabolism following exhaustive or intense exercise. The greater the muscle damage the greater these three key markers will show and the longer the recovery process takes. Lower values for these three markers immediately following exercise are an indication of less muscle damage, whereas lower values 24 hours post exercise are an indication of faster recovery. Athletes who train on back to back days require better recovery in order to influence their ability to train better.

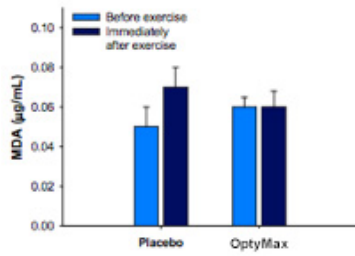
Because of the intensity required to do a one repetition (1-RM) maximum in the weight room, considerable amount of muscle fiber tears can be expected. 1-RM is a common method used to test inflammatory markers.

Study: Inflammation and Recovery Markers

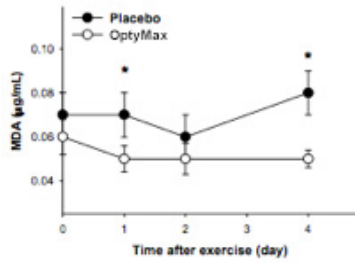
In addition to the significant results of the glycogen re-synthesis study, the OptyMax (PN, RR) combination extracts were also studied for their effects on inflammation. Sixteen highly-trained competitive swimmers voluntarily completed a double-blind crossover study after a weight-lifting exercise separated by 30 days. Competitive swimmers typically train two to 4 hours per day during the competitive swimming season. Subjects were divided into 2 groups: The experimental group received OptyMax (PN, RR) combination extracts while the control group received a placebo. Subjects were tested for their 1-RM max and then retested two weeks before the study, followed by a 30 day wash out period before the test was re-taken. Subjects were analyzed for MDA, IL-6 and CK, three key recovery/inflammatory markers associated with high intensity or exhaustive exercise. These measures were taken 1 day and 4 days post exercise.

Results:

Subjects in the experimental group significantly improved MDA levels immediately following exercise and 4 days post exercise (figure 1). IL-6 and CK levels were significantly improved at 4 days post exercise (figure 2 & 3).



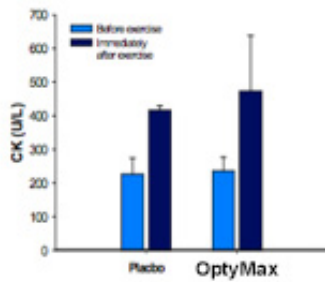
	MDA synthesis (µg/mL)	
	Placebo group	OptyMax group
Before exercise	0.05 ± 0.01	0.06 ± 0.005
Immediately after exercise	0.07 ± 0.01	0.06 ± 0.008



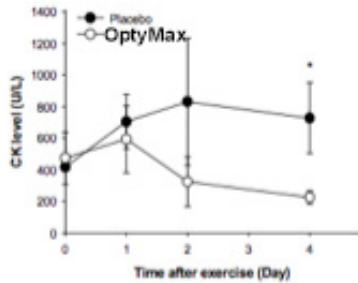
Group	MDA synthesis (µg/mL) on Day 4 after exercise	Percentage (%)
Placebo	0.080 ± 0.010	100.0
OptyMax	0.045 ± 0.004*	56.25

*p<0.05

MDA levels on Day 1 and Day 4 were significantly lower in OptyMax group (*P<0.05).



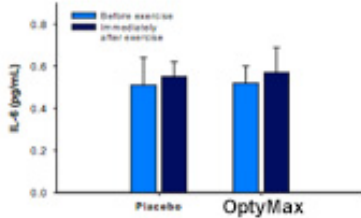
	Creatine kinase synthesis (U/L)	
	Placebo group	OptyMax group
Before exercise	226.47 ± 41.30	235.50 ± 40.72
Immediately after exercise	415.66 ± 14.03	472.83 ± 166.31



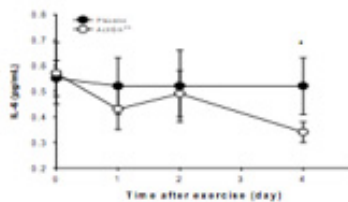
Group	CK synthesis (U/L) on Day 4 after exercise	Percentage (%)
Placebo	727.08 ± 224.53	100.0
OptyMax	224.53 ± 41.91*	30.88

*p<0.05

The study result showed that subjects in the OptyMax supplemented group had significantly lower CK levels than the subjects in the control group (*P<0.05) on the 4th days after a single resistance exercise.



	IL-6 synthesis (pg/mL)	
	Placebo group	OptyMax group
Before exercise	0.51 ± 0.13	0.52 ± 0.08
Immediately after exercise	0.55 ± 0.07	0.57 ± 0.12



Group	IL-6 synthesis (pg/mL) on Day 4 after exercise	Percentage (%)
Placebo	0.52 ± 0.11	100.0
OptyMax	0.34 ± 0.04*	65.38

* p<0.05

Discussion:

In the “anti-inflammation study” human evidence on highly trained athletes proved that the OptyMax (PN, RR) combination extracts reduces inflammation in muscles after considerable muscle damage from a 1-RM.

There is no way to eliminate all muscle damage from high intensity exercise.

In fact, to do so would not be desirable since muscle damage serves as a stimulus for muscle growth and as an internal warning/healing mechanism. However, excessive muscle damage will restrict glycogen recovery. Excessive damage on back-to-back workouts can thwart performance gains due to its catabolic nature. Limiting muscle damage through increased glycogen re-synthesis rate and by reducing inflammation in fatigued muscles to an appropriate degree would help improve recovery and aerobic and anaerobic performance training.

ENDURANCE CAPACITY:

Endurance capacity is a measure of the amount of work an athlete can accomplish over a given period of time. To improve endurance capacity you must either increase the amount of work over a given time or reduce the amount of time needed to accomplish a given amount of work. Typically endurance capacity is reserved for aerobic, or long-distance activities.

Study: Endurance Capacity Study-College Males:

A recent 2010 study published in the Chinese Journal of Physiology examined the effects of supplementing with OptyMax (ES) for 8 weeks. The aim of this study was to examine endurance capacity, cardiovascular function and metabolism of recreationally trained males. Nine college males consumed 800mg/day OptyMax (ES) or a placebo for 8 weeks in a double-blind, randomized placebo controlled crossover design with a 4 week washout period. Subjects received a placebo then cycled at 75% VO₂Peak until exhaustion. After a wash-out period the subjects received supplementation of OptyMax (ES) for four weeks. They again cycled at 75% VO₂Peak until exhaustion.

Results:

The study showed OptyMax (ES) significantly ($P > 0.05$) enhances endurance capacity by 23%, HR by 4%, VO₂Peak by 12%, and helped spare glycogen. The study also showed that free fatty acids were increased and glucose level decreased both significantly ($p < 0.05$) showing a sparing of muscle glycogen.

Study #2 Endurance Capacity Study - Endurance Runners #2:

In 2006, a study was conducted with ten endurance runners in order to evaluate the effects of OptyMax (ES) supplementation on fat utilization and performance in endurance runners. Ten endurance runners (age 19.8 ± 2.1 years, Maximal O₂ 65.3 ± 5.2 ml/min/kg) were tested before and after daily consumption of OptyMax (ES) or a placebo. Runners were randomly placed into a control group and placebo group. The energy and nutrient intake did

not differ between groups. All subjects were then tested for running time to exhaustion and max heart rate (maxHR).

Results:

After 28 days of supplementation there were statistically significant increases in running time to exhaustion ($P<0.05$) of 4%. MaxHR also increased significantly ($P<0.05$) by 13 beats/min as did the use of fatty acids as fuel ($P<0.05$).

Discussion:

OptyMax (ES-*Eleutherooccus Senticosus*) has been around for thousands of years. There are many studies supporting its effectiveness as a modulator of stress and consequent improvement in related physiological endurance parameters. The two studies outlined are simply recent further evidence of the effectiveness of this adaptogenic herb.

Volume of oxygen (V_{O2}), endurance capacity and max heart rate are all endurance performance parameters used to measure athletes progress. Human physiology is very complex and all mechanisms affect one another. Sparing of glycogen through more efficient use of lactate and fat mobilization in itself can improve endurance performance. OptyMax (ES) is an adaptogenic herb that uses non-specific mechanism of action to improve various physiological functions that fall outside the normal ranges often due to high levels of stress. Modulating these functions therefore improves the physiology on varying levels leading to improved training and performance.

Rhodiola Rosea recent studies

First Endurance continues to lead the industry in evidence-based research and supplementation. New research clearly indicates the benefits associated with the OptygenHP formula. New evidence supports the claims that OptygenHP reduces cortisol, improves performance and improves lactate threshold.

The following studies are just a handful of recent studies proving the benefits of OptygenHP

Panossian A, Wikman G.
Clinical Pharmacology. 2009 Sep;4(3):198-219. Epub 2009 Sep 1.
Evidence-based efficacy of adaptogens in fatigue, and molecular mechanisms related to their stress-protective activity.

This 2009 study's aim to assess the level of scientific evidence presented for the use of Rhodiola as an adaptogen in fatigue. The review concluded that this phytoadaptogen up-regulates the stress-mimetic effects on the "stress-sensor" protein Hsp70. Hsp70 interacts with glucocorticoid receptors which affect the levels of circulating cortisol. The study review concludes that rhodiola's ability to prevent stress-induced increase in Nitric Oxide (NO), results in increased performance and endurance. Adaptogen induced up-regulation of Hsp70 regulates the resistance to stress and results in enhanced mental and physical performance and, possibly, increased longevity.

Noreen EE, Buckley JG, Lewis SL, Brandauer J, Stuempfle KJ.
Journal of Strength and Conditioning. 2012 May 24. [Epub ahead of print]
The Effects of an Acute Dose of Rhodiola Rosea on Endurance Exercise Performance.

The purpose if this 2012 study was to determine the effects of an acute oral dose of 3mg/kg of Rhodiola Rosea on endurance exercise performance, perceived exertion, mood and cognitive function. Subjects warmed up for 10 minutes, followed by a 6-mile Time Trial (TT) on a bicycle ergometer. The Rhodiola group showed a significantly lower HR during warm up, significantly faster TT and significantly lower rate of perceived exertion. The study concluded that an acute dose of Rhodiola Rosea ingestion decreased heart rate response to sub-maximal exercise, and appears to improve endurance exercise performance by decreasing the perception of effort.

Parisi A, Tranchita E, Duranti G, Ciminelli E, Quaranta F, Ceci R, Cerulli C, Borrione P, Sabatini S.
Journal of Sports Medicine and Physical Fitness. 2010 Mar;50(1):57-63.
Effects of chronic Rhodiola Rosea supplementation on sport performance and antioxidant capacity in trained male: preliminary results.

The purpose of this 2010 study was to investigate the effects of Rhodiola Rosea on physical performance as well as on the redox status of chronic Rhodiola Rosea supplementation in a group of competitive athletes during endurance exercise. Following 4 week supplementation athletes underwent a cardio-pulmonary

exhaustion test. The study found athletes had significantly lower blood lactate levels and plasma creatine kinase levels (this is a marker of protein regulation and overtraining). The study concluded that chronic Rhodiola supplementation is able to reduce both lactate levels and parameters of skeletal muscle damage following an exhaustive exercise session.

Beta-Alanine recent studies

Ghiasvand R, Askari G, Malekzadeh J, Hajishafiee M, Daneshvar P, Akbari F, Bahreynian M.

International Journal of Preventive Medicine. 2012 Aug;3(8):559-63.

Effects of Six Weeks of β -alanine Administration on VO₂ max, Time to Exhaustion and Lactate Concentrations in Physical Education Students.

The aim of this 2012 study is to assess the effects of beta alanine supplementation on VO₂max, time to exhaustion and lactate concentrations in physical education male students. Subjects supplemented with Beta Alanine for six weeks. The group using Beta Alanine showed a significant increase in VO₂max, and improvement in time to exhaustion and lactate concentrations. The study concluded that Beta-Alanine supplementation can reduce lactate concentrations during exercise and thus can improve exercise performance in endurance athletes.

Saunders B, Sunderland C, Harris RC, Sale C.

Journal of International Soc Sports Nutrition. 2012 Aug 28;9(1):39. [Epub ahead of print]

β -alanine supplementation improves YoYo intermittent recovery test performance.

The aim of this 2012 study was to investigate the effects of beta-alanine supplementation on YoYo Intermittent Recovery Test. The YoYo test is an intermittent treadmill test of repeated sprints, which have a high rate of aerobic and anaerobic energy turnover. Football players supplemented with Beta-Alanine for 12 weeks. The study concluded that 12 weeks of beta alanine supplementation significantly improved YoYo performance, likely due to an increase in muscle H⁺ buffering capacity resulting in a reduction in intracellular pH during high intensity exercise.

Optygen Studies (original formula)

In a 2007 clinical trial on endurance trained athletes Dr. Andrew Creer of South

Dakota State University showed Optygen to reduce cortisol (the primary stress hormone) by 26%. Cortisol is a catabolic (breakdown) hormone that the body produces when under stress, such as after hours of running. Chronically elevated cortisol levels can prevent an athlete from recovering, increase the risks of overtraining and suppress the immune system. Researchers concluded that Optygen is beneficial for trained athletes undergoing high training volumes because it decreases baseline stress and improves training sessions.

Another study done by Dr. Karlton Larson (2007 Luther College) showed endurance athletes who used Optygen increased the time to lactate threshold by 42%. Results of this study show Optygen is effective in reducing lactic acid production and delaying onset of lactate threshold (the exercise intensity at which lactic acid starts to accumulate in the blood stream), therefore improving endurance.

OptygenHP Prototype Benefits

Discussion: OptygenHP is designed to be a multifaceted formula with a mechanism of action that is directly related to an improvement in key physiological facets of hard training. Each key mechanism of action has been tested on endurance trained human subjects and further supported by studies done on the complete formula. These mechanisms are:

- 1) **Cortisol:** Optygen/Rhodiola reduces the primary stress hormone cortisol. This also relates to improvements in the cortisol/testosterone ratio. With hard training, stress is increased and hence cortisol is increased. Chronically elevated levels of cortisol lead to overtraining syndrome, suppressed testosterone, poor recovery, poor sleep, catabolism of muscle and poor performance. Optygen and Rhodiola have clearly proven significant modulation of cortisol and improvement in cortisol/testosterone ratio in hard training athletes.
- 2) **Glucose Tolerance Factor:** Chromium has been shown in various studies to modulate Glucose Tolerance Factor leading to a modulation in blood glucose. Athletes can experience a more steady supply of energy with no wild sugar swings.
- 3) **Adenosine Tri Phosphate (ATP) production:** Studies on OptyMax (ES, PN, RR) and Rhodiola extract have all shown an improvement in Adenosine Tri-Phosphate production. ATP is the primary energy source of the human body. Reduction in ATP leads to fatigue. This ATP production is further supported

through the Optygen proprietary ATPPro base consisting of the precursors of ATP production, calcium pyruvate, sodium phosphate, potassium phosphate and ribose.

- 4) Recovery/Inflammation: Studies on OptyMax (PN, RR) fruit extract have clearly shown reduction in the key recovery markers measured by MDA analysis, IL-6 and CK. These improved markers mean less soreness, less muscle catabolism and improved recovery from hard training.
- 5) Glycogen Sparing: Studies on Eleutherococcus senticosus extract and Rhodiola Rosea extract have shown a significant reduction in glycogen use during exercise. Athletes can spare glycogen leading to improved endurance and improved substrate utilization.
- 6) Glycogen Re-synthesis: Studies on OptyMax (PN, RR) fruit extract have shown a significant improvement in the replenishing of glycogen following exhaustive exercise. Improved glycogen re-synthesis means faster recovery and improved performance on back-to-back-to-back hard training days. It's also important to note that these benefits are experienced with lower insulin levels.
- 7) Lactate curve: Studies on Optygen, Rhodiola and Beta-Alanine have shown significant improvements in lactate threshold. Beta-Alanine's primary mechanism of action is to increase the limiting rate of lactate synthesis so lactic acid build up does not slow performance. An improved lactate curve means athletes can hold a faster pace before reaching anaerobic threshold.