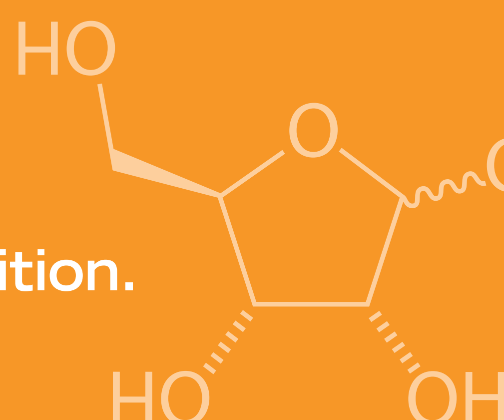
BIOENERGY™ RIBOSE®



Add true energy
that outperforms the competition.

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Increase Performance with BIOENERGY™ RIBOSE®

All Athletes Need Bioenergy RIBOSE

How intense is high-intensity exercise? Only you can define high-intensity exercise. For some, high-intensity exercise may mean daily training for a marathon, 10-K, or triathlon. For others, it may mean walking to the mailbox, climbing a flight of stairs, or a day at the mall. For most of us, though, it simply means stressing our muscles beyond their normal limit.

Regardless how we individually define "high-intensity," the effect on our bodies is the same. Intense exertion taxes our muscles to stay energized. The resulting energy demand/supply mismatch leads to a drain in energy, depleting the cellular energy pool. This loss of cellular energy is a disaster because re-supplying this energy is slow and metabolically costly.

Bioenergy RIBOSE accentuates the body's natural process of energy synthesis. It helps to reduce the loss of energy during stress and accelerates energy and tissue recovery. Through this action, Bioenergy RIBOSE helps muscles regenerate lost energy and potentially minimize any physiological consequences of this energy depletion situation. Whether running a marathon in under three hours or a daily workout session designed to keep your heart and muscles healthy, Bioenergy RIBOSE can help keep your muscles energized and feeling strong.

Energy depletion contributes to a variety of consequences that may negatively impact muscle performance or how we feel after exercise.

The loss of energy in muscles directly contributes to the common symptoms of stiffness, soreness, weakness, and pain. Protein synthesis, of vital importance to athletes, can also be affected.

Exercise Drains Energy From Muscle

High-intensity exercise utilizes and lowers energy in each muscle cell. The cellular mechanisms involved in this energy depletion are complex, but essentially when we exercise beyond the point at which oxygen can be delivered to our muscle, the energy substrates in the cell are consumed and the byproducts of this energy consumption are washed out of the cell. The result is a net loss of energy substrates, known as purines, and an increase in free radical formation (Figure 1).

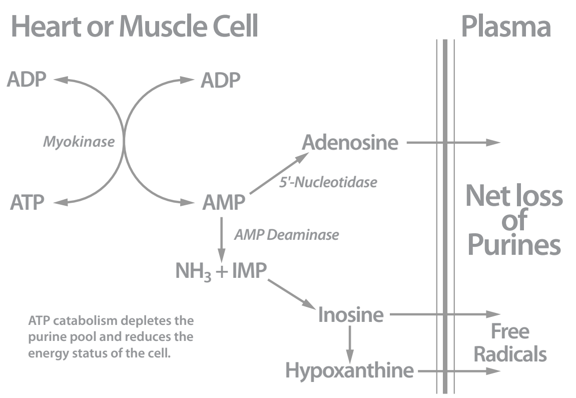

Figure 1 **Energy Catabolism and the Net Loss of Purines**

Using energy faster than it can be supplied through normal cell energy turnover mechanisms triggers enzymes that catabolize the energy molecule. The byproducts of this catabolism are washed from the cell resulting in a loss of energy substrates, depletion of the cellular energy pool, and an increase in free radical formation. Adapted from Tullson PC, RL Terjung.[2]

The longer or more often we exercise at high intensity the more energy we lose. In muscle, repeated bouts of high-intensity exercise can lead to a loss of more than 25% of the energy pool.[1] Tullson and Terjung[2] concluded, "…the plasma concentration of adenine nucleotides [energy substrates] rises during exercise, and increases steeply during maximal exercise consistent with the idea that exercise may cause a net loss of purines from skeletal muscle…Patterns of [energy] catabolism among heart and skeletal muscle fiber types are related to the distribution and kinetic characteristics of the degradative enzymes and the rate of energy expenditure relative to the capacity for aerobic energy production." In other words, if we exercise hard, we don't just burn energy, we lose it. And the longer or more frequently we exercise, the more energy we lose.

This loss of energy is not only confined to skeletal muscle. Because the heart is a muscle, it can be similarly affected. In the heart, chronic oxygen deprivation can lead to an almost complete depletion of cellular energy, eventually leading to cell death (Figure 2).[3]

While athletes seldom deplete cardiac energy reserves to a dangerous level, research shows that amateur high-intensity endurance athletes frequently exercise to a point of cardiac disturbance that may persist for several weeks following an athletic event.[4]

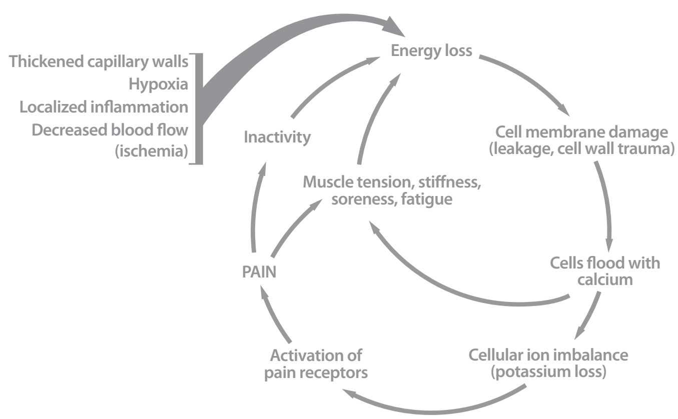

Figure 2 **Muscle Tension, Soreness, and Pain Can Result from Muscle Energy Depletion**

Intense exercise or any other hypoxic condition depriving the muscle of oxygen will deplete the cellular energy pool. This energy loss alters the flux of calcium, causing muscle tension, stiffness, soreness, and fatigue. The increase in intracellular calcium forces potassium to leave the cell, activating pain receptors on the cell membrane. Pain further adds to muscle tension, exacerbating this state. Adapted from Olson NJ, JH Park. Am J Med Sci, 1998;315(6):351-358.

The Pain of Energy Loss

Athletes should be concerned with the metabolic stress placed on their heart as well as their skeletal muscles during prolonged, high-intensity exercise such as triathlons, marathons, or endurance cycling exercise.

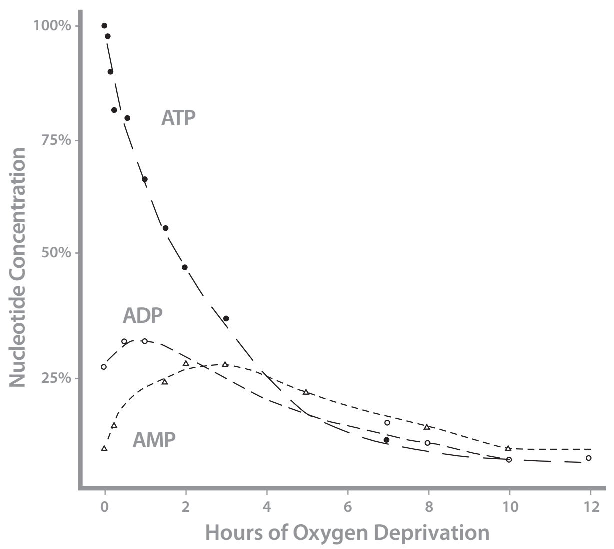

Figure 3 **Energy Depletion Due to Oxygen Deprivation**

Oxygen deprivation triggers reactions that lead to a depletion in the cellular energy pool. This overall reduction in cellular energy can affect tissue function. Adapted from Ingwall JS.[3]

The loss of cellular energy reserves plays a significant role in the physiology of the muscle cell. Energy depletion will first impact the control of ions in the cell, affecting muscle recovery. If sufficiently severe, prolonged, or chronic energy loss can lead to cell wall leakage, edema, and disruption of the electrochemical gradient across the cellular membrane. One example is particularly relevant.[5]

When muscles prepare to contract, calcium from outside the cell rushes to the inside. This calcium binds with the muscle fibers to allow the muscle to contract. Following contraction, this calcium must be physically pumped out of the cell so the muscle can again relax and recover. This calcium pumping comes at a high energetic cost due to the cellular concentration gradient of about 1:10,000. A disruption in this calcium pump function results in increased levels of calcium within the cell, impairing muscle relaxation. Impaired calcium pumping contributes to muscle stiffness, free radical formation, activation of enzymes that attack structural proteins of the cell, and muscle pain known as delayed onset muscle soreness (DOMS) (Figure 3).

It is the frequency and/or severity of exercise that determines the rate and degree of energy loss. In untrained subjects, a single bout of high-intensity exercise may be sufficient to drain energy reserves and contribute to muscle stiffness, soreness, and fatigue. However, in trained muscle repeated bouts of high-intensity exercise over several days may be required. In athletes, energy depletion contributes to an overtraining effect causing muscle pain, weakness, fatigue, and physiological damage to the muscle.

The Impact of Bioenergy RIBOSE in Exercise and Muscle Health

Ribose is a compound used by the body to regulate the synthesis of adenosine triphosphate (ATP), the primary energy molecule of the cell. Ribose also plays a central role in the synthesis of other important cellular constituents, including coenzyme-A, flavin adenine dinucleotide (FAD), nicotinamide adenine dinucleotide (NAD), riboflavin (vitamin B2), DNA, RNA, and others. **Therefore, ribose is a key compound that the body uses to achieve its vital metabolic functions.**

As seen in (Figure 4) ribose plays a central metabolic role in energy synthesis and recovery. Research has shown that ribose administration increases muscle energy synthesis by three- to four-fold, depending on the type of muscle fibers.[2] Ribose also helps keep energy in the cell during periods of stress, with energy salvage rates increasing by three- to eight-fold, depending on the type of muscle fiber and the administered dose of ribose.[6,7] Even very small amounts of ribose (as low as 0.15 mM, or an approximate oral dose of 500 mg) significantly increased energy salvage. Further, high salvage rates were sustained in recovering muscle (Figure 5).

Ribose is produced naturally in every cell in the body, but both the heart and skeletal muscle lack the metabolic capacity to make ribose quick enough to maintain the necessary energy levels in the stressed heart or muscle tissue.[8] Supplementing with Bioenergy RIBOSE allows these muscles to bypass the slow, rate-limited process of making ribose; and therefore, accelerate energy synthesis and recovery.

Several factors influence the degree of energy depletion, the rate of recovery, and whether or not energy molecules or its substrates are lost from the cell. Exercise intensity, duration, frequency of the exercise, and the type of muscle mass recruited all play a role. Frequent, repeated bouts of high-intensity exercise recruiting major muscle mass, such as cycle exercise or running, significantly drains cellular energy levels.[1,9–12]

On the other hand, while infrequent or less intense exercise may, indeed, utilize the available energy in the cell, it may not ultimately drain the energy pool or cause lasting changes in the cell's energy status.[6,13,14] The point is, it varies in each person. A review of the subject is presented in Dodd et al.[15]

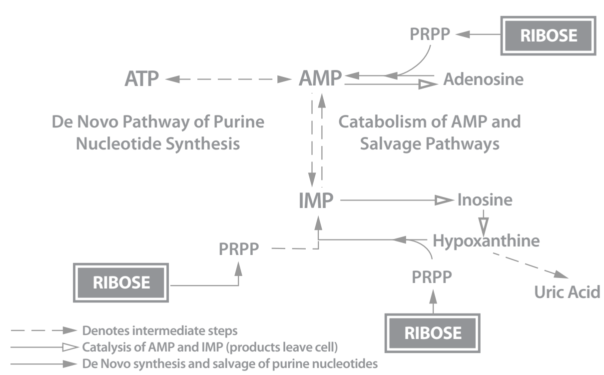

Figure 4 Ribose Availability is Rate Limiting for Energy Synthesis and Salvage

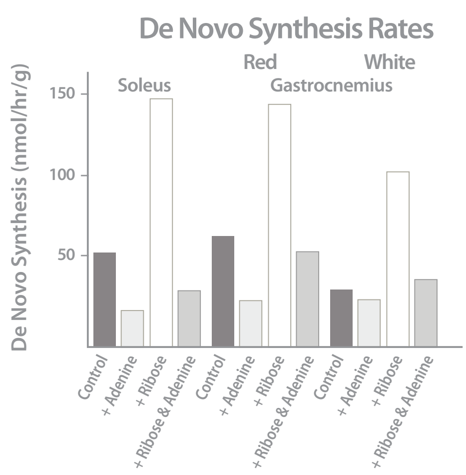

Figure 5 Bioenergy RIBOSE Increases De Novo Energy Synthesis in Muscle

Adapted from Brault JJ, RL Terjung.[6]

The significance of this point is represented in the effect of ribose on exercise recovery or performance. In a double blind, placebo-controlled, crossover study involving eight healthy male subjects, Hellsten et al.[1] determined that one week of high-intensity cycle exercise was sufficient to deplete the muscle energy pool by 25 ± 2%. **After three days of rest, muscle supplemented with ribose was fully recovered while the placebo treated muscle remained significantly below pre-exercise levels** (Figures 6 and 7). These findings are consistent with other published studies investigating energy synthesis and recovery rates.[5,16]

The effect of ribose administration on exercise performance has been examined.[13,14,17–23] In a four-week study involving recreational bodybuilders, ribose was given to determine its effect on body composition and exercise performance.[23] While there was no difference in pre-/post-exercise body composition between the ribose and placebo groups, the ribose group showed significantly greater gains in both muscle strength and endurance. Similar results have been shown in healthy subjects, in patients with myoadenylate deaminase disease, a condition affecting cellular energy metabolism,[18,20,23] and in patients with fibromyalgia.[24,25] **In these patients, ribose administration increased exercise tolerance and performance with decreased muscle stiffness, pain, and fatigue.**

Other striking findings were reported by Wallen et al. Ribose administration to healthy, normal hearts increased the anaerobic threshold and delayed the onset of irreversible ischemic injury by 26%.[26] Seifert et al, using a placebo-controlled crossover design study, reported that ribose administration reduced the heart rate of athletes exercising at a constant workload. Strikingly, they found a maintenance in oxygen-free radical production, which is commonly elevated with high-intensity exercise under hypoxic conditions.[27]

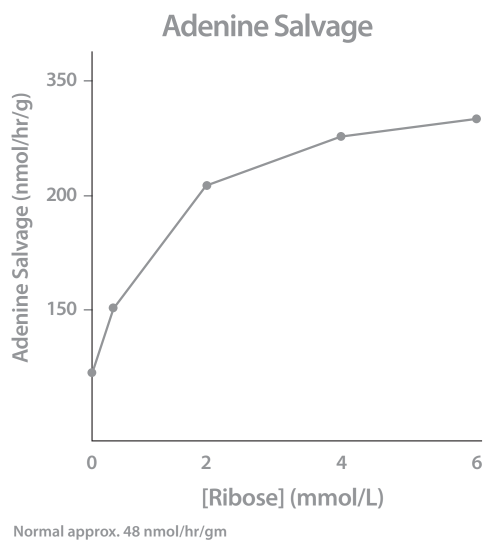

Figure 6 Energy Salvage is Accelerated with Bioenergy RIBOSE

Adapted from Brault JJ, RL Terjung.[6]

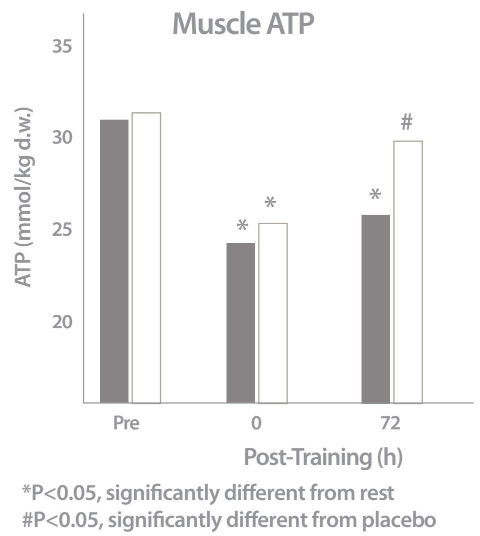

Figure 7 Energy Recovery Following High-Intensity Exercise

Ribose shown in white bars. Adapted from Hellsten Y, et al.[1]

These findings are particularly meaningful for athletes, who place a significant amount of stress on their hearts through repeated, prolonged bouts of high-intensity exercise, commonly found in endurance sport activities. Considering the production of oxygen-free radical production with intense training/competition and exercise recovery, ribose could provide this needed benefit to stressed tissues.

Certain studies have produced neutral[13,17] or negative[14] results. In one study,[17] researchers used eight normal, healthy, male volunteers to assess the affect of ribos e supplementation on exercise performance. They determined that ribose supplementation led to increases in mean and peak power output during repeated anaerobic cycle sprint exercise, but the results were not consistently statistically significant.

Kreider, et al.[13] evaluated the potential ergogenic value of ribose on repetitive exercise using 19 trained male subjects. In this study, subjects performed two 30-second Wingate anaerobic sprint tests separated by three minutes of rest. Subjects were then given ribose or placebo (glucose) twice daily for five days before performing additional post-supplementation tests. Data analyses revealed a significant interaction in work output (p=0.04), showing that work output significantly declined during the post-supplementation sprint in the placebo group (-18 ± 52 J) but was maintained in the ribose group (-0.00 ± 31 J). Even though the work output in the ribose group was maintained in repeated exercise sessions, the researchers unaccountably concluded that ribose supplementation did not affect anaerobic exercise capacity. Unfortunately, while the study was well designed, the exercise session assessment interval was not sufficiently strenuous to deplete the cellular energy pool; therefore, not providing the setting to assess any potential benefit of ribose.

Ribose does not act as a short-term ergogen, but instead works to restore cellular energy lost during and following intense exercise. Adequate energy levels are essential to maintain a muscle's peak physiological state and to maximize one's training. If cells are not stressed enough to deplete energy levels, the potential effect of ribose cannot be fully appreciated.

Op 't Eijnde, et al.[14] measured power output during dynamic knee extension exercise sessions to evaluate the effect of ribose (n=10) or placebo (n=9) on exercise performance and energy recovery. Again, this protocol design was inadequate in addressing intensity, duration, or magnitude of the exercise needed to catabolize nucleotides. The authors stated that the decreases in ATP levels (~25% and 20% following and 24-hours after exercise) did not reflect a energy loss, and the study duration (24-hours) was not sufficient to reveal a meaningful result.

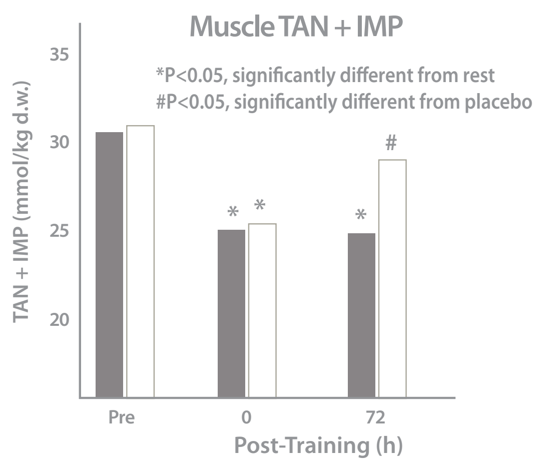

Figure 8 **Total Cellular Energy Following High-Intensity Exercise**

ATP = Adenosine Triphosphate; TAN = Total Adenine Nucleotides (total cellular energy pool); IMP = Inosine Monophosphate (an energy catabolic product). Ribose shown in white bars. Adapted from Hellsten Y, et al.[1]

BIOENERGY™ RIBOSE®

Proven to Energize Muscle, Increase Performance, and Speed Recovery

Ribose administration stimulates energy metabolism and accelerates recovery when muscles face periods of metabolic stress. Depressed cellular energy levels contribute to a myriad of physiological conditions affecting muscular function and performance, which include:

- Muscle stiffness, soreness, weakness and delayed recovery from exercise
- Cell membrane and muscle fiber damage
- Edema and swelling conditions
- Activation of enzymes that attack the cell
- Free radical production
- Delayed onset muscle soreness (DOMS)
- Fatigue
- Delayed macromolecule synthesis

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