
Creatine & Ribose:
Muscle Cell
Energizers and
Volumizers
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Creatine Monohydrate—Technically Speaking

by Daniel Gwartney, M.D.

Competitive and recreational athletes use creatine monohydrate for its performance-enhancing, or ergogenic, properties. It's been shown in numerous studies to be beneficial in activities that are dependent on the anaerobic energy system, which includes such sports as powerlifting, sprinting, swimming and field events. Such sports typically involve high-intensity, short-duration movements with short rest breaks during training. The energy for them comes primarily from stored skeletal muscle ATP and ATP regenerated from phosphocreatine stores. Anaerobic glycolysis is another potential energy source, though its relatively slow rate of ATP production prevents it from contributing to short-duration activities; that is, those of less than 30 seconds.

Studies show that oral creatine supplementation increases total muscle creatine stores. Increases in creatine and phosphocreatine have been demonstrated by muscle biopsy, and those results correlate well with studies that measure anaerobic work performance.

To date, there have been no serious adverse effects associated with creatine supplementation; however, an undetermined percentage of creatine users has reported stomach upset, diarrhea and cramping, which suggests poor intestinal absorption. Anecdotal reports of muscle and tendon injuries appear to be related to inappropriate training and supervision during the initial period of creatine supplementation. Athletes may be susceptible to overtraining, or they may develop or exacerbate an imbalance between muscle groups during periods of accelerated strength and performance improvements.

Creatine monohydrate is typically found in powder form, and manufacturer directions recommend consuming it in eight to 16 ounces of water, juice or isotonic sports drink. They also recommend a loading phase at the beginning of a creatine cycle that consists of four to six five-gram servings a day for four to six days. A maintenance phase then follows, with the recommended dose being five to 20 grams a day. There are some deviations from the recommendations, but there's little evidence to support alternative modes of creatine use.

The majority of problems associated with creatine monohydrate occur during the loading phase. People complain of poor intestinal tolerance, as evidenced by cramps or diarrhea. Commonly, increased fluid consumption resolves the complaints, which are rarely mentioned during the maintenance phase.

There are numerous creatine monohydrate products around. One that has been shown to be beneficial is the combination of creatine and high-glycemic carbohydrates. Studies have shown that creatine uptake into muscle is enhanced in the presence of insulin with those products, which leads to increased muscle creatine stores over what subjects got with straight-creatine supplementation. There are other formula additions to creatine, but none have been shown to be of much benefit. One possible exception is inorganic phosphate salts, which may aid in maintaining the creatine-to-phosphocreatine ratio in the muscle cell.

The addition of carbohydrates has improved the ergogenic value of creatine; however, there's still a barrier keeping people from realizing the complete ergogenic value of creatine. That barrier is poor intestinal absorption. Creatine uptake is mediated by an active sodium dependent transporter, and there's extremely little passive absorption of creatine in the intestine due to the substance's poor solubility in water and the ionic nature in the intestinal environment. Compounding the problem is the supposed downregulation of the creatine transporter that occurs during supplementation. The absorption problem has been clearly demonstrated even during the relatively short loading period. That's consistent with the findings regarding other guanido compounds, such as taurine, in which the intestinal receptor is shown to downreg-

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ulate following oral supplementation.

Overcoming that barrier should effect a significant improvement in creatine's ergogenic profile, both in the acute loading phase and the maintenance phase. Before the introduction of effervescent delivery, that just wasn't possible. The only recourse was to bypass the oral route in favor of intravenous administration. While there may be a place for that in therapeutic environments—for example, where there are patients with certain mitochondrial conditions—it's an unacceptable option for athletic enhancement or recreational use.

Effervescence occurs when weak acids and bases are combined to create a buffered solution at a stable pH. It typically involves the use of bicarbonate salts, which form carbon dioxide gas upon activation. The appearance of the carbon dioxide gas gives the bubbling, or fizzing, effect that you get with popular over-the-counter indigestion and allergy remedies.

Effervescence is a useful and applicable delivery device for creatine for many reasons. First, and possibly most important, is the buffering effect. Stabilizing the pH of the creatine-containing solution at the pI, or isoelectric point, promotes an electrically balanced, or neutral, creatine molecule known as a zwitterion. The net electrical charge of the zwitterion is zero. As creatine is a small molecule, it's now theoretically available for passive absorption—in addition to the active transport that has been shown to downregulate. That's important for two reasons. It provides an alternate and less restricted means of accessing the mesenteric venous system—the transport system can be quickly saturated even during the initial dose. Second, it allows for the continued absorption even during the maintenance phase.

An additional benefit of the buffering effect is the so-called dumping effect. Creatine is of maximum benefit at select times of the day; in the morning after the nighttime fast, for instance, or right after training. These windows of opportunity are short. Studies suggest that a 200-milliliter volume is held in the stomach for 40 minutes to one hour. If you drink more or a meal high in fat or protein is present, that period may extend for hours. The problem is, very little absorption takes place in the stomach by design.

The stomach's role is mostly to grind up and break down the food by acid digestion. Its musosal lining is nearly impermeable, which protects it from the destructive effect of the stomach acids.

The duodenum and the remainder of the small intestine are the sites of greatest absorption. The effervescent delivery of creatine causes a pH shift in the stomach, which the body senses as a signal to dump the stomach contents into the duodenum. Once the creatine passes into the duodenum, the greater surface area and absorptive function of the intestinal lining quickly absorb the creatine zwitterions. What's more, the creatine transporters are located in the jejunum and ileum, two other sections of the small intestine.

As the effervescently delivered creatine is almost completely absorbed, you don't have the stomach problems inherent in creatine use. Noneffervescently delivered creatine, particularly after transporter downregulation, is typically passed down the small intestine, drawing water into the lumen of the bowel in an attempt to dilute and dissolve the crystals. The creatine crystals act as an irritant and have a high osmotic pull. Unfortunately, the majority of water transfer takes place in the large intestine, which has very little absorptive capacity. That leaves the creatine in the colon, along with the attendant water load, and it's the water efflux and the presence of the colonic creatine that lead to diarrhea, cramps and dehydration. The greater absorption with effervescent delivery should remove that curse.

Bear in mind that creatine is designed to augment anaerobic work performance. That means a working muscle to near maximal exertion is highly dependent on the amount of available ATP during the period of exertion. Long-distance races and low-intensity-load exercise aren't significantly affected by creatine supplementation. Therefore, in terms of research it's more appropriate to measure the supplement's effects on repetitive sprints, isotonic, isometric or timed recovery resistance training than on marathon running or long-distance cycling.

One study that's been done in the exercise science labortory is the measure of anaerobic work performed on a cycle ergometer. That measures maximal energy output, which is dependent on ATP and the phosphocreatine shuttle. The study showed an increase in anaerobic work performance (AWP) of 10 percent following a creatine loading phase. Adding carbohydrates increased the AWP to 20 percent over the control group. That was the standard by which creatine products were gauged for the past three years—that is, until effervescent creatine with carbohydrate showed a significant improvement in AWP to 30 percent over the control subjects.

Marketing groups present the findings—and the figures—in confusing terms. Here are the basic facts shown by the research:

- Creatine provides a positive ergogenic effect when used and measured correctly.
- The addition of a high-glycemic carbohydrate enhances the muscle uptake of creatine.
- Thyroid hormone and vitamin E also seem to play a role in mus-

Effervescently delivered creatine with carbohydrate causes a 30 percent increase over the anaerobic work performance (AWP) of control subjects; that is, it's three times, or 300 percent, as effective and 150 percent as effective as creatine and carbohydrate.

Effervescent creatine represents a novel and effective use of a pharmaceutical delivery system that enhances the positive benefits of creatine and negates the adverse effects.

cle uptake of creatine.

•Creatine's greatest drawbacks are its ionic nature and osmotic pull.

•Creatine's effects are further impeded by the use of active transport and the supposed downregulation of intestinal creatine receptors.

•Transit time may cause a variable delay in creatine delivery to the intestine for absorption.

•Effervescent delivery buffers creatine at its pI, which allows it to exist as a zwitterion.

•Effervescence also decreases transit time, providing a quicker and more reliable delivery to the intestine.

•Creatine as a zwitterion may be available for both active and passive transport, bypassing the reduced availability from receptor downgrading.

•Creatine causes a 10 percent increase over the AWP of control subjects.

•Creatine with carbohydrate causes a 20 percent increase over the AWP of control subjects; that is, it's twice as effective.

•Effervescently delivered creatine with carbohydrate causes a 30 percent increase over the AWP of control subjects; that is, it's three times, or 300 percent, as effective and 150 percent as effective as creatine and carbohydrate.

One further benefit of the effervescent creatine is that it is dose-metered in the individual packages, which means that each ingredient is added to each package individually to ensure that each serving contains the amount of each ingredient it's supposed to contain. That's in contrast to the large tubs of batched products, like the creatine-and-carbohydrate blends. The mixing process is imprecise, and settling occurs during both manufacturing and shipping. Creatine may be nearly nonexistent in one portion of the batch and over the stated amount in another. The effervescent system also requires a foil-sealed pack, which provides for a longer shelf life and fewer storage-related changes, and the individual serving packs make it more convenient to use.

Effervescent creatine represents a novel and effective use of a pharmaceutical delivery system that enhances the positive benefits of creatine and negates the adverse effects.

Editor's note: *Daniel Gwartney, M.D., is a clinical pathologist and a graduate of the University of Nebraska College of Medicine. He's been bodybuilding for more than 18 years.*

Effervescent Creatine: How It Ignites Size and Strength

by Steve Holman

Effervescent Creatine Elite is a natural, legal compound that can increase your work capacity for building muscle by almost 200 percent over what you get with powdered creatine monohydrate. It uses the same effervescent technology that enhances the delivery of many oral medicines, a technology that's rapidly becoming the standard in bodybuilding supplementation. This revolutionary method of getting nutrients and/or drugs into the bloodstream produces startling results, as the latest creatine research shows.

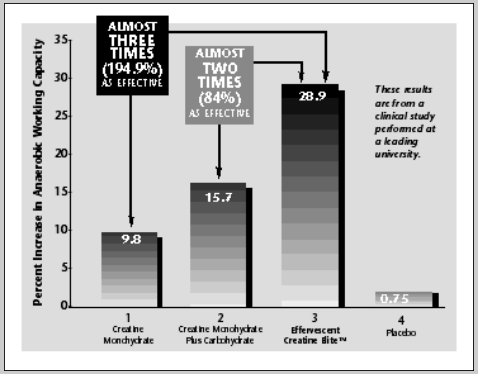
Jeffery Stout, Ph.D., a renowned strength researcher, performed a study involving effervescent creatine at Creighton University's Exercise Science Research Laboratory in Omaha, Nebraska. Using a test that simulates weight training, he compared anaerobic work capacity of subjects taking the following:

1) Creatine monohydrate

2) Creatine monohydrate plus carbohydrates, which, based on other studies, has been the premier creatine transport solution for years

3) The new effervescent creatine

4) A placebo



The preliminary findings are stunning. The effervescent creatine didn't just produce a slight increase; it ramped up work capacity by an unbelievable 194.9 percent over creatine monohydrate and 84 percent over creatine plus carbs. In other words, powdered creatine plus carbs will have to give up its crown as the ultimate transport system. The reason effervescent creatine is almost two times as effective as the current creatine-transport champ is its amazing 100 percent absorption.

For many people standard creatine can cause severe gastrointestinal distress, including painful cramps and diarrhea, a direct result of poor absorption. Even if you don't get cramps, you're probably not absorbing more than one or two grams, according to recent research. Powdered creatine isn't soluble in water, so efficient absorption of a powdered form is impossible for most people. Effervescence solves the problem.

Effervescent Creatine Elite is a combination of creatine monohydrate, potassium bicarbonate and citric acid powders. Once that combination hits water, the reaction between the bicarbonate and the citric acid produces the effervescent effect. That disassociates the creatine from its salt—the monohydrate—so what you get is a powerful free-ionized creatine ready to flood your bloodstream and infuse your muscle structures with the ability to generate new power.

Free-ionized creatine is soluble and dissolves completely in water. That means no grit. Once you drink it, it goes to the stomach, where the solution manipulates the pH, or acidity level. That has two effects: 1) It strips the creatine molecule of its ionic co-electrical charge so it's able to pass through the intestinal cell membrane, and 2) it causes the stomach to "dump" the creatine into the small intestine, where absorption actually occurs. Without the pH manipulation creatine is trapped in the stomach for as long as four hours, which can cause cramps. With pH manipulation, however, the absorption rate is pushed to almost 100 percent, a far cry from the meager 30 percent absorption most people get with powdered creatine. Imagine the kind of gains you can achieve when all of the creatine you take is actually absorbed and is readily available for your muscle structures.

Other advantages of effervescence include the fact that its buffering action reduces the possibility of stomach distress and masks the harsh taste that's prevalent in standard powdered creatine products. With no harsh taste to deal with, the manufacturer only adds a small amount of orange flavoring—and it tastes delicious. It also has 18 grams of dextrose to further speed creatine transport to the muscles.

Effervescent Creatine Elite comes in individual foil pouches, five grams of creatine in each, so you can't make a mistake on dose. All you do is tear open the packet, pour the contents into 16 ounces of water, watch it fizz for 15 seconds and drink it down. The creatine enters your bloodstream in a matter of minutes—not just 20 to 30 percent of the muscle-cell volumizer but almost 100 percent. There's absolutely no waste. That means you get much more size and power output from every dose. The manufacturer does recommend that you load with 20 grams for five consecutive days, as studies indicate that loading can increase total muscle creatine by more than 20 percent. The five-gram daily dose after the loading phase maintains the high concentration in your muscles.

According to Daniel Gwartney, M.D., "Effervescent creatine provides the majority of its creatine load through passive transport as well as by using creatine-specific receptors. That means it gives you a greater loading effect and can provide greater performance benefits for longer periods."

If you're looking for a true muscle-volumizing supercompound, try Effervescent Creatine Elite. It's a serious breakthrough for serious gains—in size, strength and power.

Breaking Barriers

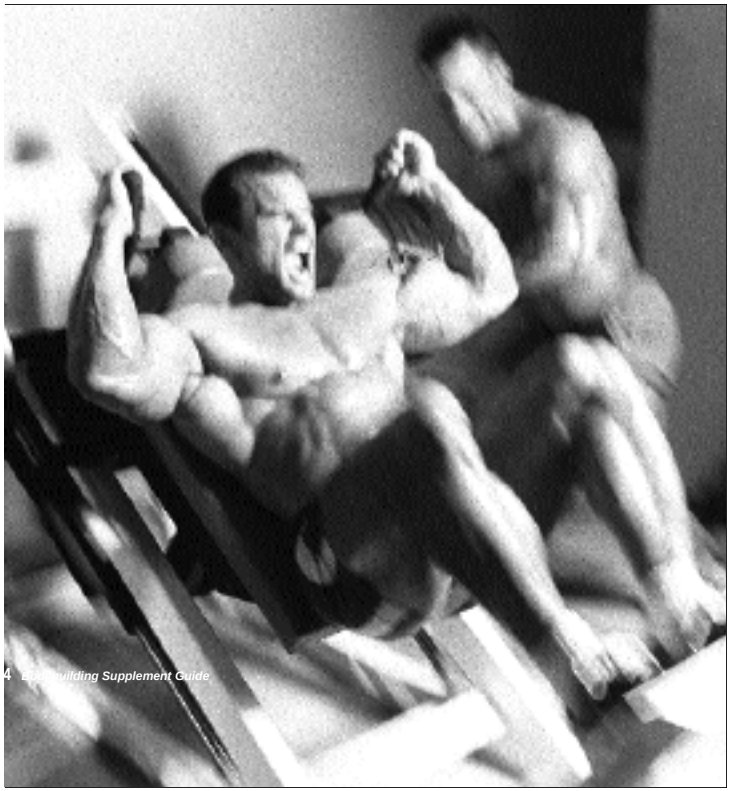
by Daniel Gwartney, M.D.

Creatine monohydrate is clearly the most effective strength- and performance-enhancing supplement ever developed. So, why has it been getting such a bad rap? That's easy. It's the same reason that so much of it gets left in your glass: Creatine doesn't dissolve well in water, and that can cause a number of problems.

Many athletic trainers and strength coaches don't allow their athletes to use creatine at all because of the associated cramping, diarrhea and dehydration that have been reported. I, along with several colleagues, have consulted and advised many athletes and teams. Sometimes these problems go away after hydration is forced on the athletes. Reducing the dose has also helped—four five-gram servings a day for five days, then one five-gram serving per day after that. We've also found that it helps to take creatine first thing in the morning rather than within an hour of an intense practice.

For some people the above may provide the full benefit of creatine supplementation; however, there are other problems. The cramping, diarrhea and dehydration are typically due to the creatine's being retained in the intestines. That causes the body to flush water through the intestines, drawing it away from the bloodstream and muscle. As you can imagine, all that water rushing into the intestines usually leads to its rushing out again. So merely providing extra water doesn't solve the problem, as many people still experience diarrhea due to the excess water in the gastrointestinal tract.

Could the addition of carbohydrates, phosphates, ATP and/or insulin mimickers help? No. Some of those agents are useful when the creatine reaches the muscle, but they do nothing to alleviate the first and worst problem—lack of absorption.



The reasons that creatine doesn't dissolve in water have to do with the biochemical nature of the creatine molecule, the environment in the digestive tract and the transit time, meaning the time it takes for creatine to pass to certain parts of the G.I. tract. You can see for yourself that it doesn't dissolve. Fill a clear glass with water and dump in your five grams of creatine. Let it sit for a minute or five minutes or an hour. What do you see at the bottom? About 3.5 grams of creatine. If you think sugar helps, put a tablespoon or two in the same glass. The white mountain at the bottom of the glass will grow. Go ahead and shake it like one of those Christmas globes with the snow scenes. The creatine won't dissolve.

After that experiment you should realize the consequences of taking this supplement. As mentioned above, when the creatine sits in your gut undissolved, water floods the area in an attempt to break up the particles that are irritating the intestines. That may seem like a small problem—until you realize that it can pull in nearly two quarts of water. I don't know about you, but if I'm going for a record squat, I don't want two quarts of water in my bowels.

Even if the creatine does eventually get enough water to dissolve, that will probably occur too late. The majority of creatine absorption takes place in the first part of the intestine, the duodenum, immediately after passing through the stomach. That area is designed for maximal absorption. Unfortunately, the water gets to the intestines much farther down the G.I. tract, in your colon, right before the exit chute and far from the area of maximum absorption.

It's important for the creatine to be dissolved because only dissolved creatine can be absorbed. The absorption can take place either by active transport, which requires energy and a creatine-specific receptor, or by passive transport, which doesn't. To put it another way, creatine can either float through the gut into the bloodstream or be picked up and dragged across the gut into the bloodstream.

Traditional creatine is only about 30 percent dissolved when you swill it down, so at most only about 1.5 grams are available for delivery. Contrast that with the new effervescent creatine, which is nearly 100 percent dissolved when you drink it, and you see the obvious superiority. With effervescent creatine all five grams are available for delivery. That means no more creatine-associated dehydration, diarrhea or cramping.

Effervescent creatine is also far superior when it comes to transport across the intestinal cell membranes. Creatine has ionic regions. Parts of the molecule have electric charges, like static electricity, and those ionic regions prevent creatine from passing through the intestine without the use of energy to counteract the electrical repulsion. If the creatine molecule is electrically balanced, or neutral, it's called a zwitterion and it can pass through the membranes of the intestine without having to use the receptors for extra energy. That's exactly what effervescent creatine accomplishes. It stabilizes the gastric environment, meaning the stomach and intestines, so the creatine molecules exist as zwitterions.

In traditionally delivered creatine the ionic regions are intact. They create an electrical charge, which requires the use of the creatine-spe-

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Effervescence decreases gastric transit time, so the creatine doesn't sit in your stomach and get chewed up by the acid there. It passes quickly to the duodenum for rapid availability.

cific receptors. If the receptors were available in unlimited supply and never downregulated, there wouldn't be a problem. (Downregulation occurs when an excess of a hormone or other agent causes fewer receptors to be available.) Unfortunately, there's a limited supply of creatine receptors and they're downregulated during creatine supplementation. So, if creatine is delivered via active transport, as traditional creatine is, it becomes less efficiently absorbed over time. Less and less creatine is available for the muscles, which means a decrease in performance. The only options available for maintaining increased bioavailability are intravenous administration—yes, needles—or creatine delivered through passive transport. Effervescent creatine provides the majority of its creatine load through passive transport as well as by using the creatine-specific receptors. That means it gives you a greater loading effect and can provide greater performance benefits for longer periods.

Transit time is another very important issue. Effervescence decreases gastric transit time, so the creatine doesn't sit in your stomach and get chewed up by the acid there. It passes quickly to the duodenum for rapid availability.

Effervescent Creatine Elite recently proved its superiority in a study performed by Jeff Stout, Ph.D., an assistant professor of exercise science at Creighton University in Nebraska. I know Jeff, and I've read many of his published studies. He's one of the best researchers in the field and has a wealth of knowledge.

Jeff's study analyzed anaerobic work capacity, or AWC, in several groups of athletes. AWC is a measure of how much high-intensity work a muscle can perform without rest, and that's the type of performance creatine enhances. The groups in the study included a placebo, or control, group; a powdered-creatine group; a creatine-carbohydrate-blend group and an effervescent-creatine-and-carbohydrate-blend group. The results were significant—and not just by some mathematical formula.

The placebo group had no change, as would be expected, since the subjects received no active supplement. The subjects in the powdered-creatine group increased their AWCs by 10 percent, those in the creatine-plus-carbs group increased by 20 percent, and the effervescent-creatine-and-carbs group showed an almost 30 percent increase—that's like getting three extra reps on your 10-rep bench press. Based on those results, effervescent creatine provides nearly 300 percent of the benefits of powdered creatine and 150 percent of the creatine-carb blends, and its performance-enhancing effects should also last much longer due to less downregulation of the creatine receptors.

I hate to be the one to break the news to the old guard, but while creatine is still king, it's riding higher on the shoulders of effervescent delivery. Effervescent creatine is truly a breakthrough bodybuilding supplement.

Creatine Q&A

Q: Do I have to load effervescent creatine the way I do other creatine products?

A: Yes, you should perform a standard loading phase, using 20 grams of creatine a day for five days, and spread that dosage throughout the day so you get five grams at four different times. If you're using Muscle-Link's Effervescent Creatine Elite, that's four packets a day, which means one 20-packet box will take you through your five-day loading phase.

Q: I eat six meals a day, so how do I load if every dose has to be taken on an empty stomach?

A: Take your effervescent creatine about 30 minutes before a meal. Also, it's best to use effervescent creatine 1 1/2 hours or more after a meal—preferably a protein drink rather than solid food, as protein drinks tend to leave your stomach faster.

Q: Why does my stomach have to be empty?

A: Effervescent creatine manipulates the pH of your stomach so that it immediately dumps the solution into your small intestine for maximum absorption. If food is present, the pH of your stomach will be impossible to manipulate due to stomach acid, and the creatine solution could remain in your stomach for hours, severely diminishing absorption. When your stomach is empty, on the other hand, it perceives the effervescent creatine as digested food and immediately moves it to the small intestine, where it's almost 100 percent absorbed in about 20 minutes. Compare that to the inefficient 30 percent absorption you get with standard creatine, and you see why effervescent creatine has been shown to produce almost three times the results.

Q: Can I get complete absorption with standard powdered creatine products if I use them on an empty stomach?

A: No. The primary problem with standard creatine is its inability to dissolve. That's why you see it settle at the bottom of a glass. It does the same thing in your gut, even if your stomach is empty. According to Daniel Gwartney, M.D., what happens after you swallow powdered creatine can be a painful experience: "Cramping, diarrhea and dehydration are typical due to the creatine's being retained in the digestive tract. When the creatine sits in your gut undissolved, water floods the area in an attempt to break up the particles that are irritating the intestines. That may seem like a small problem—until you realize that it can pull in nearly two quarts of water. I don't know about you, but if I'm going for a record squat, I don't want two quarts of water in my bowels."

Q: Can't I just mix powdered creatine with Alka-Seltzer and get the same effervescent effect?

A: That may sound like a plausible plan, but, unfortunately, it doesn't work. Effervescent delivery is specific to the compound or medication that's being administered. In fact, Fortress Systems has a patent on creatine delivery in an effervescent form. That should tell you that the effervescence for delivering creatine is different from the effervescence that delivers the medications in Alka-Seltzer. The delivery system designed for creatine separates the monohydrate, or salt, from the creatine, creating a highly absorbable zwitterion. If you take powdered creatine with Alka-Seltzer, you may get somewhat less stomach distress, but the absorption of the creatine will still be low—probably around 30 percent—because it's still plain old powdered creatine monohydrate, and your intestines will no doubt still react unfavorably to the undissolved granules that irritate its lining.

Q: Can effervescent creatine help improve my weak bodyparts?

A: Yes, in fact, many bodybuilders are using an extra packet of effervescent creatine immediately before training a weak bodypart so they get rapid creatine uptake by that specific muscle group. Remember, effervescent creatine enters your bloodstream fast, in about 10 minutes, so if you take it right before you train a bodypart, as you work and deplete the muscle, it should immediately suck up any creatine that's pumped into it via the circulatory system and repetitious exercise.

For example, say your chest is your lagging bodypart. On chest day simply use an extra packet of Effervescent Creatine Elite about 10 minutes before your first warmup set. As your chest workout progresses,

A number of athletes have reported increases of as much as 30 pounds on their bench press one-rep maxes after only five days and bodyweight gains of 10 pounds in four weeks.

so does absorption of the effervescent creatine, and as your pecs are engorged with each successive set, much of the newly available creatine goes right where you need it, into the muscle cells of the pec major and minor.

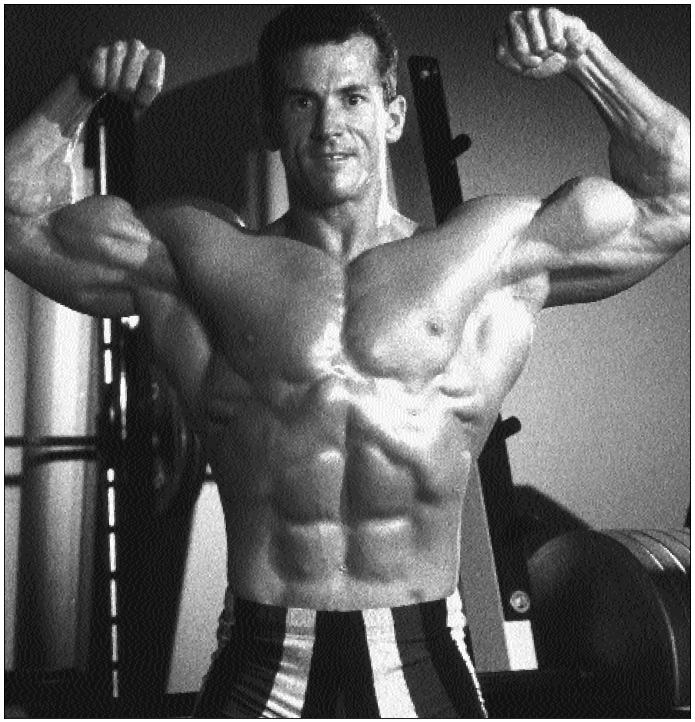
Q: What kind of results can I expect with effervescent creatine?

A: If you use a proven brand, such as Muscle-Link's Effervescent Creatine Elite, you should get an immediate increase in size and strength after the loading phase, even if you've been using standard creatine. A number of athletes have reported increases of as much as 30 pounds on their bench press one-rep maxes after only five days and bodyweight gains of 10 pounds in four weeks.

Q: If I'm using standard creatine with no problems and I'm getting decent gains, should I still try effervescent creatine?

A: If you were driving around in a backfiring '74 Volkswagen Rabbit, would you spend a few extra pennies to move up to a precision-tuned Porsche? You'd be riding in greater comfort and getting to where you were going a lot faster. Remember, most people only get about 30 percent absorption with standard creatine, even when using the creatine transports. With effervescent creatine, however, you get almost 100 percent absorption. Imagine how much better your gains will be when you're getting an entire five-gram dose into your bloodstream as opposed to a meager gram or two. Once you try it, it will be obvious that effervescent creatine is the Porsche Carrera of creatine products.

—Steve Holman, editor in chief, IRONMAN



Q: Are there any study results on Effervescent Creatine Elite vs. liquid creatine? I've read many reports on effervescent creatine vs. creatine monohydrate, creatine monohydrate plus carbohydrate and a placebo, but nothing about studies comparing it to liquid creatine.

A: The studies that have been completed, as well as the studies that are in progress, compare effervescent delivery of creatine to the unaided absorption of creatine, either with or without a carbohydrate source. The effervescent delivery has been shown to aid in tolerance, compliance, reduction of adverse effects and improved performance enhancement.

Powdered creatine monohydrate as well as creatine-and-carbohydrate blends have been used as the reference groups for two primary reasons:

1) Both creatine monohydrate and creatine-carbohydrate blends have been extensively studied, and the effects, proper testing methods and reliability have been well established.

2) Creatine monohydrate powder and creatine-carbohydrate blends represent a very high percentage of the creatine market share.

So-called liquid creatine preparations are not dissolved creatine. They're suspensions of creatine in a gel, typically aloe vera or a glycol base. Suspension is a word that describes particles floating in liquid, whether it be water, glycol, aloe vera or any other fluid. Placing the creatine in liquids other than water doesn't benefit the delivery of creatine because the body will only absorb creatine in the water-soluble form. Failure to split the hydrate salt to free the creatine does nothing for the delivery of the creatine. It's because the creatine is present as a suspension that the directions call for vigorous shaking. In addition, there's concern about the possibility of bacterial growth in many of the liquid creatine preparations.

In a pilot study performed for one of the liquid creatine companies, the liquid creatine preparation was shown to be less effective in terms of performance benefits than powdered creatine (without carbohydrate). Obviously, the company chose not to use the results of that study in any marketing literature. As liquid creatine doesn't represent any benefit over powdered creatine and does not hold a significant market share, there was no justification for including any liquid creatine preparation in any of the studies.

—Daniel Gwartney, M.D.

Q: I just heard about an effervescent creatine with a lot more simple carbs in it than Effervescent Creatine Elite. The company says the sugar makes its effervescent creatine better because you get more insulin in your system, and insulin forces more creatine into the mus-

Placing the creatine in liquids other than water doesn't benefit the delivery of creatine because the body will only absorb creatine in the water-soluble form. Failure to split the hydrate salt to free the creatine does nothing for the delivery of the creatine.

Is there a way o take greater advantage of insulin's creatine-uptake-increasing ability using Effervescent Creatine Elite without derailing the reaction and absorption? You bet! Try chasing Effervescent Creatine Elite with a high-glycemic-index juice about 20 minutes after you take it.

cles. Is that true?

A: The first thing to realize is that it's probably not real effervescent creatine. A lot of simple carbs will diffuse the reaction and derail absorption. If you're using real effervescent creatine and you want the best effects, you have to take it on an empty stomach so that the solution can shift from the stomach to the intestinal tract immediately and be 100 percent absorbed. A lot of sugar can prevent that from happening, which is the very reason Effervescent Creatine Elite has 18 grams of dextrose, enough to provide insulin output but not enough to derail the effects of effervescence.

The company you're referring to is no doubt selling regular powdered creatine in a fizzy sugar solution and trying to pass it off as effervescent creatine. It's essentially a bubbling creatine transport concoction. In the study done by Jeff Stout, Ph.D., effervescent creatine proved to be almost 100 percent more effective than creatine transports. Keep in mind that with a creatine transport, you're just getting plain old creatine, which is only about 30 to 40 percent absorbed. With Effervescent Creatine Elite you get free-ionized creatine that's almost 100 percent absorbed.

Also, Stout and Dr. Dan Gwartney believe that with powdered creatine, whether it's in a transport mix or not, the compound peaks at about 90 minutes. It takes that long because the creatine granules sit in your stomach as your system attempts to dissolve them—most not getting absorbed. Insulin, on the other hand, peaks at 10 to 20 minutes, so the two peaks miss each other by more than an hour.

If the creatine and insulin peaks miss each other, why do creatine transports, with their insulin-triggering capabilities, work better than standard powdered creatine? Because although you're past the insulin peak when you reach your creatine peak, a bit of insulin remains, so you do get somewhat more creatine into the muscle thanks to its nutrient-shunting ability.

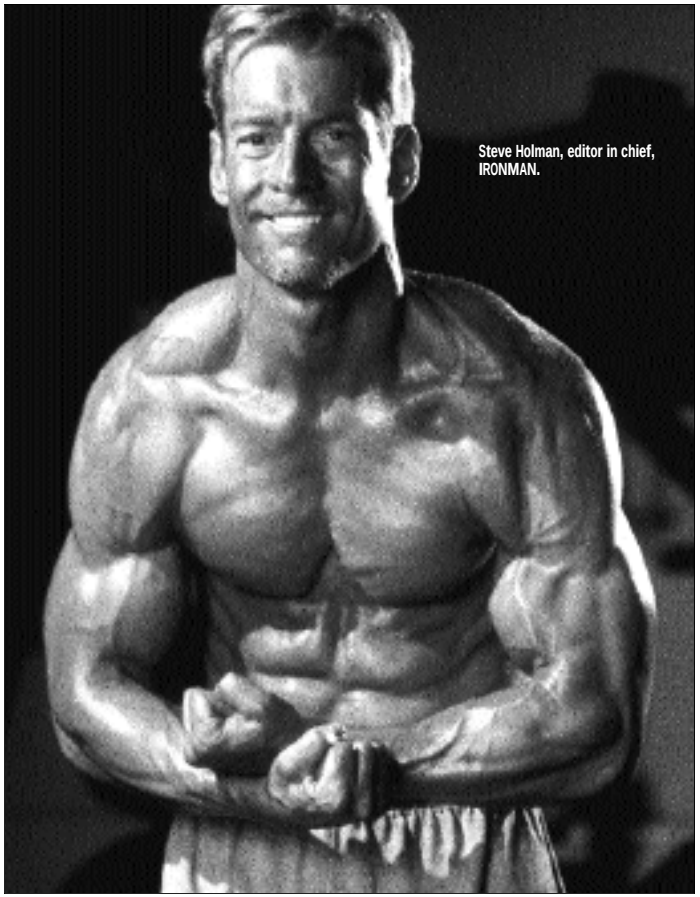
Is there a way to take greater advantage of insulin's creatine-uptake-increasing ability and the awesome power of Effervescent Creatine Elite without derailing the reaction and absorption? You bet! Try chasing Effervescent Creatine Elite with a high-glycemic-index juice about 20 minutes after you take it.

Here's why it works: Once you take Effervescent Creatine Elite, 100 percent of the creatine will be available for absorption at the 20-minute mark. At that point the high-glycemic drink, such as 12 to 16 ounces of grape juice, won't interfere with the reaction or absorption; however, it will give you an insulin surge and peak after another 20 minutes—while all of the creatine is still coursing through your bloodstream and starting to enter your muscle structures. The peaks coincide almost exactly.

Will the extra insulin force more of the free-ionized creatine into your muscles? Insulin does seem to help the creatine transports work a little better than standard powdered creatine, so based on that, the answer appears to be yes. Perhaps if the subjects who were taking Effervescent Creatine Elite in Stout's study had used the above procedure, they would have gotten even more spectacular results. By precisely timing your effervescent creatine and insulin-triggering solution, you can create the perfect environment for heightened size and strength gains—better than any other creatine supplement on the market, bar none.

By the way, all the effervescent creatines on the market were just tested, and FSI's product, which is marketed by Muscle-Link as Effervescent Creatine Elite, is the only one that produced free-ionized creatine, the key to optimal absorption. It's the real deal, unlike the other knock-off products out there. Don't be fooled.

—*Steve Holman, editor in chief,* IRONMAN



Steve Holman, editor in chief, IRONMAN.

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Ribose: The Key to Cellular Energy

by Jerry Brainum

On an elemental level, all the size and strength gains you can possibly make come down to one thing: energy. While it's obvious that you won't be able to train with maximum intensity if you don't feel energetic, you'll also make less bodybuilding progress because of the lack of cellular energy available. Your body needs cellular energy to power such essential reactions as glycogen and protein synthesis within muscle, as well as innumerable other biochemical recovery reactions that occur after exercise.

The most elemental energy source in the body is a compound called adenosine triphosphate, or ATP. The adenosine portion is made up of one molecule each of adenine and a five-carbon sugar, or pentose, known as ribose. As the name implies, the triphosphate portion of ATP consists of three phosphate molecules. When one of those phosphates is broken off from ATP, energy is released and the compound becomes adenosine diphosphate (ADP), which consists of adenosine (including its ribose base) and two phosphate molecules.

All sources of food energy—carbohydrates, fats and proteins—are eventually converted into ATP in the parts of the cell called the mitochondria. Every move you make and every chemical reaction that occurs in your body is powered by ATP.

Nevertheless, the body's stores of ATP are quite limited—about three ounces, or 90 grams. That's enough to supply maximum energy for all of 10 seconds. The body works around the limited ATP storage by using various recycling mechanisms. For example, after a phosphate bond is split from ATP, releasing tremendous energy and leaving ADP, the body, through a series of quick enzymatic reactions, adds a phosphate to the ADP to re-form ATP. That process works efficiently in the presence of oxygen, or aerobic metabolism, using fats and glucose as substrates, or starting molecules.

The situation changes during periods of decreased oxygen availability, or anaerobic metabolism, which is the type of energy cycle used in high-intensity training, such as bodybuilding workouts. Under those conditions the cells get their donated phosphate for re-forming ATP from creatine phosphate stored in muscle. That explains the primary ergogenic effect of creatine as a food supplement. It acts as a second battery in cells to help reconvert ATP by passing over a phosphate molecule. Even though the system sounds efficient, however, the ATP-creatine energy cycle can only supply about 30 seconds of maximum energy, as the creatine is rapidly used up under such conditions.

When that happens, the body relies on still another energy pathway to help resurrect ATP, a system called the myokinase reaction after the enzyme that catalyzes it. It involves using two molecules of ADP and one molecule of AMP, or adenosine monophosphate, which contains just one phosphate molecule, to form one molecule of ATP. The myokinase reaction helps supply necessary ATP when the creatine stores aren't sufficient. The reaction also balances ATP and ADP levels in the cell.

While the myokinase reaction helps to keep the cellular motor running, a problem arises because of the buildup of AMP in the cell. The body deals with it by turning on other enzymatic reactions that downgrade the AMP, which is then eliminated from the body. The problem is AMP's role as a substrate in the recirculation of ATP. If it's eliminated, the existing ATP stores may not be sufficient to supply maximum energy.

Once again, the body has ways of dealing with the problem. Two primary pathways exist to help use AMP in the creation of ATP. One is called the salvage pathway, a system in which the body tries to salvage AMP breakdown products. The good news is that when it works, it works well in helping to maintain ATP stores. That's where ribose enters the picture. Ribose promotes this more efficient salvage pathway, thus allowing better ATP recycling and consequent increased muscular recovery after training.

If the body doesn't use the salvage pathway—for example, when ribose is insufficient—it must

make ATP from scratch in a pathway called the de novo, or new, pathway. That occurs when the body has excreted too much of the metabolic by-products of AMP that serve as precursors for ATP. While having enough ribose available favors the more efficient salvage pathway, the fact is that ribose is also required for the de novo pathway.

Both processes begin when ribose is converted into a molecule called 5-phosphoribosyl-1-pyrophosphate (PRPP). The cells make the conversion whenever PRPP is needed, but, once again, under conditions of strenuous exercise or poor blood circulation (as in cardiovascular disease) the PRPP stores are used up in the salvage or de novo pathways. Using supplemental ribose maintains PRPP, which in turn maintains the ATP salvage pathway. So the real limitation is the availability of ribose.

In truth, the body can synthesize PRPP from glucose, but it's a long, slow process that may take several days. In the meantime the existing muscle ATP stores aren't sufficient to support maximal energy for high-intensity exercise or sports. Ribose is made from glucose in a process called the pentose phosphate pathway, which metabolizes glucose into ribose-5-phosphate. That, in turn, is converted into the active PRPP. Taking supplemental ribose bypasses the two rate-limiting enzymes in the pentose phosphate pathway, leading to quicker production of PRPP, which helps to conserve nucleotides, or AMP metabolites, essential for ATP synthesis.

Another vital use of ribose is in the formation of nucleotides, which, in turn, are needed for energy production; for synthesis of protein, glycogen and nucleic acids; and for the formation of cyclic nucleotides, such as cyclic AMP, a substance that needed for fat oxidation and hormone-cell interactions.

Taking supplemental ribose increases ATP manufacture in skeletal muscle by 340 to 430 percent. In the ATP salvage process supplemental ribose increases the cell's ability to reuse ADP and AMP by up to 700 percent.

The enzyme that controls the conversion of glucose into ribose is glucose-6-phosphate dehydrogenase (G-6-PDH). The problem is that the supply of it in both skeletal and heart muscle is low. Even so, using supplemental ribose bypasses the enzymatic process, enabling the ribose to take an express route directly to the active substance that promotes ATP recovery, PRPP. The bottom line is faster and more efficient restoration of ATP stores in the body.

Since the body only contains about 1.6 milligrams of ribose for every 100 milliliters of blood and since most foods, such as meat products, contain barely discernable amounts of it, you can clearly see the necessity of taking extra ribose.

The body uses ribose in several important ways. It's used to make glucose, the most elemental sugar in the body, which circulates in the blood. Ribose may also be enzymatically converted into pyruvate, which enters the cell in an energy-producing process using oxygen that's called the Kreb's, or citric acid, energy cycle. Still another vital use of ribose is in the formation of nucleotides, which, in turn, are needed for energy production; for synthesis of protein (i.e., messenger RNA), glycogen and nucleic acids (RNA and DNA); for enzymatic control of electrolyte metabolism; and for the formation of cyclic nucleotides, such as cyclic AMP, a substance that's needed for fat oxidation and hormone-cell interactions.

Ribose is used in the manufacture of the B-complex vitamin riboflavin, or vitamin B_2, which among other things makes your urine bright yellow. Ribose is also used in the manufacture of several antiviral drugs, such as Ribaviran, which prevents virus replication by inhibiting RNA and DNA synthesis.

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Although scientists have been aware of ribose metabolism since 1930, its importance didn't become apparent until the 1950s. Since then ribose research has burgeoned, having mostly to do with the effect of ribose protection against cardiovascular problems. When the heart doesn't get enough blood flow, a condition called ischemia, or when it's under low oxygen conditions, or anoxia, ATP stores in the heart are rapidly degraded. The heart's inability to rapidly restore the ATP loss leads to a buildup of AMP in the heart. Many studies have shown that supplying supplemental ribose restores ATP in the heart. A forthcoming study from the University of Maryland uses ribose to treat cardiac ischemia, which is typically manifested as the pain of angina pectoris in people suffering from coronary artery disease.

In fact, any disease that results in decreased blood flow to tissues and subsequent lowered oxygen delivery can lead to a depletion of ATP. That can cause symptoms of severe pain, cramping, stiffness and soreness. In one genetic enzyme deficiency called myoadenylate meaminase deficiency (MADD), muscle cells cannot conserve nucleotides. When that happens, AMP is degraded to inosine and hypoxanthine and leaves the body. The lack of ATP substrates makes a person suffering from MADD very weak, with stiff, sore muscles.

The same lack of adequate blood flow and oxygen can temporarily occur during intense muscular contractions, again leading to a loss of the nucleotides needed to rebuild ATP in the cells. When that happens, you won't feel fully recovered from workout to workout, and your strength gains will suffer. Research shows that the loss of vital nucleotides during intensive exercise can be as high as 20 to 28 percent. Most of such loss occurs during anaerobic exercise, since the high oxygen levels typical of aerobic exercise conserve nucleotides.

At present more than 150 peer-reviewed published studies attest to the fact that ribose effectively increases ATP and total nucleotide (TAN) recovery while improving performance in heart and muscle cells during periods of lowered blood flow or low oxygen. Those conditions can occur in the heart with coronary artery disease or during certain surgical procedures. As noted above, ischemia can also occur during intense anaerobic exercise.

Several studies have illustrated the severity of nucleotide loss during either intense exercise or ischemia. A Swedish study focused on two groups of exercising men, in which 11 healthy men performed high-intensity exercise three times a week for six weeks, followed by another week of twice-daily sessions. Another group of nine men rested for the first six weeks, then trained twice a day with the first group during the final week.

Muscle biopsies, which are small bits of muscle tissue taken for analysis, showed that ATP levels in the thigh muscles of the first group

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Ribose supplements are particularly synergistic with creatine, which works by supplying a phosphate molecule after ATP is broken down to ADP to release energy.

dropped 13 percent during six weeks of training but did not decrease further during the final week of twice-daily sessions. Even after three days of rest ATP still hadn't returned to pretraining levels in the muscles of the first group and was 10 percent lower than the pretraining levels.

In the second group ATP levels dropped 25 percent right after the final workout. Even after three days of rest those men still showed ATP levels that were 19.5 percent less than when they started. This study showed that ATP levels dropped considerably with exercise and were not restored in the trained muscles even after three days of rest. Another study showed a 19 percent drop in muscle ATP levels after seven weeks of sprint training.[1]

Still another study showed that perfusion, or supersaturation, of skeletal muscle with ribose for 30 minutes increased de novo synthesis of nucleotides by 340 to 430 percent, depending on which type of muscle fiber was tested.[2] A more recent study done by scientists from the University of Missouri is being presented at the 1999 meeting of the American College of Sports Medicine. It examined the role of ribose in the adenine nucleotide salvage pathway and involved mixed plantaris, or leg, muscles in rats. The results showed that providing ribose to the exercising rats—who did anaerobic exercise, which leads to the greatest breakdown and loss of nucleotides needed for ATP synthesis—led to a significant increase in nucleotide salvage. For example, the dose that some rats received, which translates to a human dose of 2.5 grams of ribose, led to a 244 percent increase in nucleotide salvage over baseline, and an amount that translated to a human dose of 15 grams led to a whopping 639 percent increase.

Another new, unpublished study from Ball State University in Indiana investigated the use of supplemental ribose on performance and recovery during and after high-intensity exercise. As noted above, previous reports showed that it takes as long as 72 hours to significantly restore ATP and TAN after intensive exercise.

In the new study two subjects took ribose and another two took a placebo, or inactive substance, in this case glucose, for three days before doing sprint cycling for three days of two sessions daily. Each session consisted of 15 10-second sprints with resistance at 7 percent of body mass, with 50 seconds' rest between sprints. Both the ribose and placebo were given in three 10-gram doses.

The results showed that peak power was 9.9 percent higher and mean, or average, power was 9 percent higher in the subjects who took the actual ribose supplement. Muscle biopsies of the subjects showed that those taking the ribose more effectively used their energy stores and recovered quicker after exercise. They also showed greater recovery after 48 hours than the placebo group. The researchers believe that occurred because of increased de novo synthesis of adenine nucleotides in the ribose group. As you'll recall, ribose supplementation allows the body to bypass various slower enzymatic conversion processes.

The authors noted that while subjects took 30-gram doses of ribose, that amount is in excess of what's required to maintain optimal ATP and TAN levels. While the amount needed relates to activity and intensity of exercise, doses greater than or equal to 2.2 grams a day of ribose should maintain peak ATP and TAN levels. One researcher found that ribose may increase the salvage of nucleic acids by up to 700 percent!

These studies show that ribose can benefit anyone engaged in intensive exercise. A good daily dose is around three to five grams, and the more you train, the more you should take. Ribose is slightly sweet (it is, after all, a sugar) and can be taken in various forms. You should avoid using it in hot protein drinks, however, since ribose, when heated, may react with the amino acids in protein and lose effectiveness.

Ribose supplements are particularly synergistic with creatine, which works by supplying a phosphate molecule after ATP is broken down to ADP to release energy. But creatine doesn't replace the ATP that's lost during intense exercise. When there isn't sufficient ATP in the cell, creatine throws the phosphate ball, but there's no one to catch it. Adding ribose will help to conserve the vital adenine nucleotides needed to replenish ATP through both the more efficient salvage system and the slower de novo pathway. The net effect is that when you use creatine and ribose, you maximize cellular energy production.

Ribose should also increase the effectiveness of other supplements that require an optimal supply of ATP, such as pyruvate and carnitine, among others.

In terms of safety, doses of up to 60 grams of ribose have led to few complications. Some people who take in more than 25 grams per dose may get diarrhea, while others in rare cases experience mild, transient hypoglycemia, perhaps due to an insulin reaction. Most excess ribose, however, is simply excreted in the urine.

In the past the manufacture of ribose was an expensive process, which explains why it wasn't sold commercially. Now, however, a new company has developed a bacterial fermentation process involving the conversion of corn syrup, a form of glucose, that makes mass production of ribose simpler, so it can be sold at a reasonable price. Some types of ribose, though, may contain impurities in the form of contaminating sugars, such as arabinose or glucose, and other metabolites.

Based on its established metabolic attributes, ribose may well prove to be the next supplement superstar. Who knows—ribose may turn out to be the nutrient of the millennium!

These studies show that ribose can benefit anyone engaged in intensive exercise. A good daily dose is around three to five grams, and the more you train, the more you should take.

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Ribose:
Super Recovery and More Muscle Energy Through Creatine Synergy

It seems as if every time a new compound is released in the supplement marketplace, it's touted as the greatest breakthrough of all time. That can be a good thing, as it makes us all somewhat skeptical, but it can be a bad thing in that when a true breakthrough does come along, we miss it. "Yeah, yeah," we mutter as we turn the page, "another breakthrough."

If you said something similar when you saw the article on ribose by Jerry Brainum in this book, you may have glossed over a true supplement breakthrough that could change your workouts and recovery ability forever. Ribose may be the greatest supplement innovation since creatine—and that's not hype but fact backed by more than 150 peer-reviewed studies.

As you may or may not know, creatine works because it fortifies ATP, the compound your muscles use for energy. When you do a set, ATP is broken down rapidly, but creatine regenerates it by donating a phosphate to the depleted ATP (now ADP). The result is you get re-formed ATP and more anaerobic work capacity, which can result in more muscle growth stimulation. That's why creatine works.

Ribose also fortifies muscle ATP but through a different pathway—and perhaps even more critical, it bolsters muscle recovery after you train. Here's the way Brainum explained it: "Two primary pathways exist to help use AMP [adenosine monophosphate] in the creation of ATP. One is called the salvage pathway, a system in which the body tries to salvage AMP breakdown products. The good news is that when it works, it works well in helping to maintain ATP stores. That's where ribose enters the picture. Ribose promotes this more efficient salvage pathway, thus allowing better ATP recycling and consequent increased muscular recovery after training. If the body doesn't use the salvage pathway—for example, when ribose is insufficient—it must make ATP from scratch."

Making ATP from scratch is not a very efficient process and can compromise gains, so you don't want to be ribose deficient. Unfortunately, most hard-training bodybuilders are deficient because they don't get enough recovery time to regenerate ribose, which means they eventually run out of gas, plateau and more than likely fall victim to overtraining. One study showed almost a 20 percent drop in muscle ATP after only seven weeks of sprint training. Now imagine what happens to overall muscle ATP in bodybuilders after a few weeks of training all of their muscle groups. It's no wonder overtraining is so prevalent and the sport is filled with so-called hardgainers. (Perhaps hardgainers are simply not recovering due to ribose depletion.) Ribose supplementation could prevent that, or at least significantly slow the onset of overtraining by speeding the recovery process and ATP formation. Muscle biopsies of subjects taking ribose showed that they used their energy stores more effectively and recovered quicker after exercise. The hard numbers say that supplemental ribose increases ATP manufacture in skeletal muscle by 340 to 430 percent. In the ATP-salvage process supplemental ribose increases the cell's ability to reuse ADP and AMP by up to 700 percent. We're talking major muscle energetic upticks here along with a significant boost in muscle recovery between training sessions.

Brainum also discussed ribose's vital role in the formation of nucleotides, which are "needed for energy production; synthesis of protein (i.e., messenger RNA), glycogen and nucleic acids (RNA and DNA); enzymatic control of electrolyte metabolism; formation of cyclic nucleotides, such as the cyclic AMP needed for fat oxidation and hormone-cell interactions." Are you beginning to see the ribose-breakthrough connection?

Could ribose be the missing link that speeds recovery and puts an end to the hardgainer tag forever? Possibly. One thing is certain, however: All bodybuilders can benefit from better recovery and more efficient muscle energetics during a workout, and ribose is proving to be the new breakthrough in muscle regeneration supplementation as well as ATP-creatine synergy for more workout intensity.

—Steve Holman

Ribose Q&A
by Jerry Brainum

Ribose could potentially be the most significant new food supplement since creatine hit the market about six years ago. Until now, ribose was only meaningful to biochemists and medical researchers. While it plays a pivotal role in the synthesis of adenosine triphosphate (ATP), the most elemental form of energy produced in cellular metabolism, and thus could have important effects on energy and exercise recovery, until recently the only research on ribose had to do with its use in treating cardiovascular diseases.

Now, however, a new process of ribose production makes it more readily available to consumers. While I covered the basics about how ribose works in the body and why it could have a significant effect in active people, such as athletes and bodybuilders, in the previous article, I didn't answer all the questions about this substance. To complete the picture about the practical use of ribose, I interviewed a man who is actively engaged in the marketing and research of it.

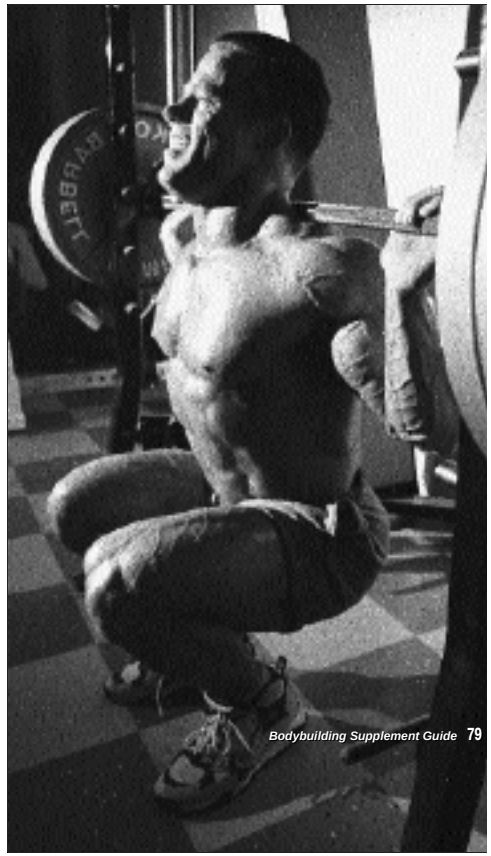
Clarence Johnson is the president and CEO of Bioenergy Inc., a company currently engaged in marketing ribose for public consumption. Besides being a business executive, Johnson has a solid scientific background. He has a master of science degree in microbiology from the University of Minnesota and has completed all but his defense of dissertation toward obtaining a doctorate in nutritional biochemistry.

Q: Since ribose helps the body produce ATP, why not just use direct ATP supplements?

A: ATP is a large and complex molecule not readily absorbed by the body. In addition, even if it could be efficiently absorbed, the ATP would not be shunted to tissues that are deficient in it. When tissues become energy depleted, they are, by and large, required to build their own energy stores.

Certain other adenine-nucleotide-pathway intermediates have been researched. Some are effective in increasing depleted energy stores. Adenosine, adenine, inosine, 5-amino-imidazoicarboximide riboside (AICAR) are some of the ATP precursors that have been marginally useful in increasing ATP regeneration following energy depletion. In fact, my company has a patent on the use of ribose plus adenine for energy production.

Most studies involving these compounds have been of short duration, and only partial ATP recovery occurred. Furthermore, ATP precursors that are relatively distant in terms of the enzymatic steps required to re-form ATP may be less efficient in inducing ATP recovery, while structurally related precursors like adenosine exhibit undesirable side effects, such as vasoconstriction (tightening of blood



Dr. Ronald Terjung and his colleagues showed that single doses as low as 2.2 grams were sufficient to increase nucleotide salvage after energy depletion by 177 percent over baseline. Single doses of 6.4 grams increase salvage by 536 percent of baseline.

vessels) and slowed atrioventricular conduction (a disturbance in normal heart rhythm).

Q: Since ribose is a sugar, wouldn't taking an oral ribose supplement result in its being metabolized directly to glucose?

A: The direct answer is no. Research conducted with 3H-labeled ribose has determined its metabolic route in the body. As quickly as five minutes to one hour following the appearance of ribose in the blood, it begins to appear in the cell nuclei of several tissues, including the liver, kidney, heart, skeletal muscle, smooth muscle and several others. Most of this ribose is directly metabolized to purines and pyrimidines, which are used for nucleic acid synthesis (mostly RNA) and nucleotides, such as ATP. RNA, of course, is required for protein synthesis, and the adenine nucleotides are used to build energy stores via ATP.

Some ribose is metabolized to glycogen in the cell cytoplasm (the space between the cell membrane and the cell nucleus). That's due to a flux of ribose up the pentose phosphate pathway (PPP) to glucose. The amount of ribose directed to this pathway is regulated by the requirements of the purine and pyrimidine pathways. Free ribose is first directed toward nucleotide and nucleotide biosynthesis, or nucleotide salvage, with flux up the PPP if an abundance of ribose is present.

A small amount of ribose is also metabolized to glycoproteins, which exist in many cellular secretions formed in the Golgi apparatus of cells. Those secretions may include pancreatic secretions, mucous and certain lipids, or fats; however, the glycoprotein secretions aren't relevant to the role of ribose in heart and skeletal muscle.

Q: What's the suggested optimum daily dose of ribose for athletic or exercise purposes, and what's that dose based on?

A: Scientists have worked out the dose-response kinetics describing the role of ribose in adenine nucleotide salvage. For example, research conducted by Dr. Ronald Terjung and his colleagues showed that single doses as low as 2.2 grams were sufficient to increase nucleotide salvage after energy depletion by 177 percent over baseline. Single doses of 6.4 grams increase salvage by 536 percent of baseline. In another study, Terjung's group determined that a single dose of 6.4 grams increased the synthesis of new adenine nucleotides in skeletal muscle by 340 to 430 percent, depending on muscle fiber type.

In a pilot study conducted at Ball State University in Indiana, researchers found that doses of 30 grams daily, taken as three doses of 10 grams each, increased total power output, peak power output and mean power output by 9.5 to 9.9 percent. That study also showed two additional and interesting findings. First, total adenine nucleotide levels—that is, the sum of ATP, ADP and AMP—in athletes decreased by up to 39 percent after high-intensity exercise. In short, energy levels dropped significantly following hard training. Second, after 48 hours of rest the athletes given ribose showed an increase in both ATP and adenine nucleotides, and they recovered to 85 percent of preexercise baseline. Athletes not taking the ribose continued to lose both ATP and total adenine nucleotides and, therefore, showed no recovery at all. That result is consistent with the findings of other researchers, who also found little or no recovery in adenine nucleotide pools even after three days of rest following intense exercise.

What, then, is the proper dose of ribose? At this point we don't know. More research is required, and Bioenergy is contracting with universities to continue those studies. We do know, however, that doses as low as 2.2 grams per day can provide beneficial effects, and higher doses may provide additional benefits.

At this point I'd suggest doses of three to five grams a day to maintain high levels of nucleotides in muscle. Higher doses may be taken to boost energy before and after high-intensity workouts or for competition. As a practical matter, though, I don't think it's necessary to take in more than 10 grams per dose. For best results I'd suggest taking a dose an hour or so before training and again 30 minutes after the workout. For maintaining ATP stores, it's best to take a single dose after a workout. More information on this will likely emerge with continuing re-

Mark Berkey | Qube

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Q: What's the maximum safe dose of oral ribose supplements?

A: Research shows that up to 60-gram doses are safe. No one has yet examined doses higher than that. Such doses of ribose are not recommended, however. Dose levels greater than 20 grams may cause gastrointestinal discomfort and possibly diarrhea. That can happen with any carbohydrate consumed in single large doses.

In addition, high-dose ribose can lead to a slight, asymptomatic decrease in blood glucose levels. Some speculate that this is due to a mild insulin reaction that drives glucose out of the blood into tissues. The effect has occurred in studies involving dogs, but the human-based research isn't as clear at this point. Since athletes taking ribose will also likely get other carbohydrates, this effect should be of no particular consequence, since the carb ingestion will maintain blood glucose levels.

My company, Bioenergy, has obtained premarket clearance for sale of ribose as a supplement in doses of up to 20 grams. That would certainly be considered a safe dose.

Q: Are there any long-term studies examining the effects of ingesting oral ribose supplements?

A: Several studies have examined the safety of ribose supplementation and infusion. One involved giving 60 grams a day to a single subject for one year without incident. Bioenergy has conducted laboratory-animal safety studies and found ribose to be safe; however, there aren't any studies that have investigated very long-term ribose ingestion at any dose level.

Bioenergy is engaged in clinical trials using ribose as an injectable drug. They're being conducted under an Investigational New Drug submission with the Food and Drug Administration (FDA) and are about to move into phase-three, or multicenter trials. That means ribose has passed the first two safety hurdles required by FDA standards.

Q: How long should people take supplemental ribose without a break?

A: Again, to maintain adenine nucleotide levels at their peak, I'd suggest taking at least a maintenance dose daily. Clearly, that can be lower with less strenuous activity and increased as exercise intensity goes up.

Q: Recent creatine studies indicate that creatine should be taken in cyclical fashion, due to possible decreased creatine absorption following a downgrade of a creatine-carrier system in the body. Does the same hold true for ribose; that is, should it also be cycled for best results?

A: Since uptake of ribose into cells occurs through facilitated diffusion and thus doesn't require any type of cellular carrier system, it need not be cycled. When a cell needs ribose, it will readily take it up. What must be adjusted is doses, which should be based on level of exercise intensity and frequency.

Q: Since ribose works by helping to preserve vital adenine nucleotides—that is, ATP precursors—why not just supplement them?

A: As I noted earlier in my explanation of why ATP itself isn't a useful supplement, various ATP precursors have been tested and found to be not as effective in helping to regenerate ATP as ribose supplements. The reason is simple: The limiting factor in salvage or synthesis of adenine nucleotides is a ribose compound called 5-phosphoribosyl-1-pyrophosphate, or PRPP, which must be present in sufficient amounts to drive the salvage and synthesis reactions. PRPP is essentially a ribose molecule with three phosphate groups attached. Supplemental ribose is the most direct route to production of PRPP in the cell.

Q: Are there any known medical contraindications to using oral ribose supplements, such as possible allergies or worsening of existing diseases? In short, are there some people who should not use this supplement?

A: Again, the only known side effects that have appeared thus far involved gastrointestinal problems such as diarrhea when large single doses of ribose were taken. However, anyone with hypoglycemia or a tendency to rapid changes in blood glucose levels should consult a physician before using ribose supplements.

Q: Some articles have warned against combining ribose with protein supplements. Is that correct?

A: There's confusion on that point. In a short book recently published about ribose, Edmund Burke, Ph.D., suggests that ribose not be taken with protein-containing compounds, such as various types of supplements. The reason Burke suggests that is simple: Ribose is known as a reducing sugar, which means that when it mixes with certain other compounds, it creates reactions that convert it into something else.

For example, when ribose is mixed with protein and heated, it forms

Since uptake of ribose into cells occurs through facilitated diffusion and thus doesn't require any type of cellular carrier system, it need not be cycled. What must be adjusted is doses, which should be based on level of exercise intensity and frequency.

Cardiac research involving ribose shows that it improves performance when taken before and after stress. For long-term aerobic events, though, it may also be beneficial to use ribose during the event.

what's called the Milliard reaction with amino acids contained in the protein. That's the same process that turns meat brown when cooked and provides the typical aroma of cooked beef. In this case the functional benefits of ribose are lost. If the protein isn't heated or cooked, however, the Milliard reaction doesn't occur.

So, if you keep a protein mixture cold, no problems occur in reaction to ribose. If, however, ribose is mixed with protein and warmed up, such as what happens when you leave a protein drink in the hot sun or a hot car, a Milliard reaction may occur, and the functional benefit of ribose may be lost.

Q: What's the best way to take ribose supplements? With carbs, with meals or on an empty stomach?

A: The best way to take ribose is probably with other carbohydrates or alone on an empty stomach. That would ensure maximum absorption. However, I'd suggest taking ribose an hour or so before and/or about 30 minutes after exercise. Cardiac research involving ribose shows that it improves performance when taken before and after stress. For long-term aerobic events, though, it may also be beneficial to use ribose during the event. Note that if used in this manner, a low dose is advisable to avoid an embarrassing side effect, such as diarrhea.

Q: How long does it take to feel the effects of a ribose supplement?

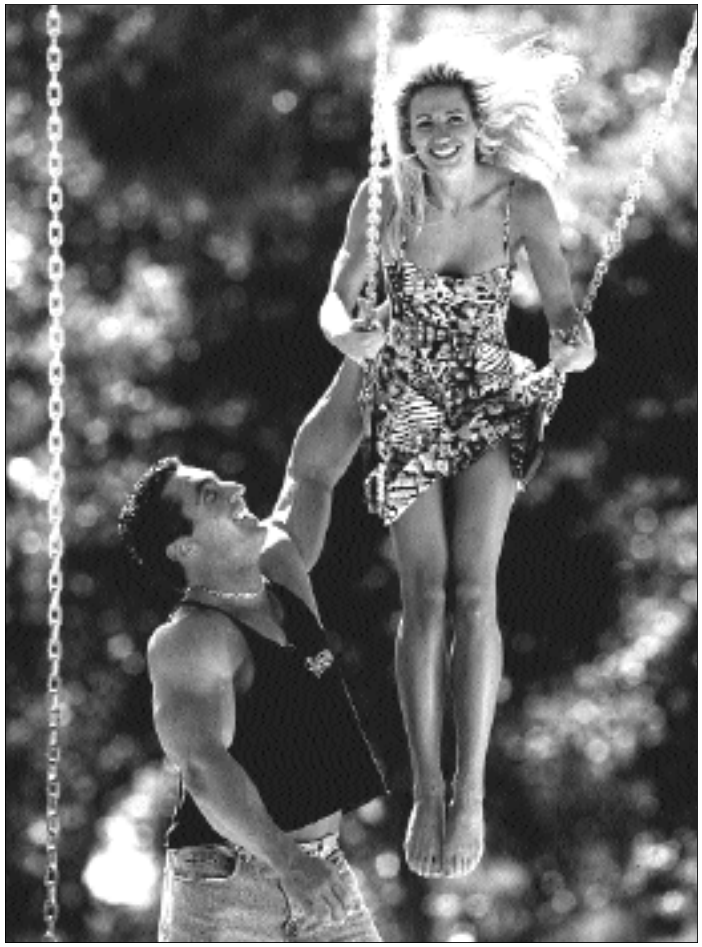
A: In our experience about 60 percent of the people who've taken ribose supplements actually feel an effect. Some say they just have more energy. Others believe they can train harder and longer. It usually takes about three or four days to get those feelings. I would emphasize, however, that the research suggests that everyone taking ribose will get a beneficial effect if he or she exercises hard enough to deplete adenine nucleotide pools. Users may not feel it, but ribose is still working to enhance their energy and recovery.

The biochemistry about this is quite clear. Adenine nucleotides decrease in all strenuous exercise under both aerobic and anaerobic conditions. If an athlete exercises hard enough to lower cellular energy charge, then ribose will assist in recovery. It's like a rapid recharge on a rechargeable battery.

Q: What beneficial effects can a person using ribose supplements expect? Do they include increased energy? Added strength? Increased exercise recovery?

A: There's absolutely no question that ribose supplementation will positively affect heart and muscle cell recovery following high-intensity exercise, and in most cases users will feel more energetic.

The body requires ribose to form adenine nucleotides, such as adenosine triphosphate (ATP). Research has shown, however, that the metabolic pathway leading to ribose production in heart and skeletal muscle isn't efficient, due to a lack of a specific enzyme called glucose-6-phosphate dehydrogenase (G-6-PDH) that regulates the pentose phosphate pathway in cells. In other tissues, such as liver and kidneys, the pathway isn't rate-limited by the enzyme. Consequently, the kidneys and liver can make as much ribose as they need, although that source of ribose isn't available to other organs and tissues. Each cell must maintain its own supply of ribose for nucleotide and RNA production. As energy-producing substrates are used up and lost, they must be replenished. That's where ribose comes in.



There is absolutely no question that ribose will positively affect heart and muscle cell recovery following high-intensity exercise, and in most cases the user will feel more energetic.

Does it add up to increased strength levels? I don't know. It's often suggested, however, that the key to increased muscle strength is increased muscle recovery. Muscles—including the heart—must have the highest amount of energy possible to perform at maximum load. To the extent that ribose improves recovery, it's reasonable to expect that it will help increase strength over time. That's evidenced by the Ball State study discussed above, in which subjects taking ribose were able to perform more work, as measured by higher total, peak and mean power

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Q: Are any existing food supplements synergistic with ribose, and, conversely, should some supplements be avoided when people take ribose?

A: The metabolic actions of common food supplements are unique. Creatine, for example, increases energy by providing an increased pool of creatine phosphate to drive the passing of a donated phosphate in the recycling of ADP (adenosine diphosphate) to ATP. Carnitine helps to ferry fatty acids across the mitochondrial membrane, which enhances energy production from fatty acid metabolism. Pyruvate enhances the TCA, or Krebs, cycle that drives the electron transport system in cells, leading to enhanced ATP cycling from ADP. Those nutrients are all unique, but they're all interrelated. They do have one thing in common though: They don't work well without a sufficiently high pool of adenine nucleotides to recycle.

Strenuous, high-intensity exercise decreases the pool of adenine nucleotides in heart and skeletal muscle. That point is beyond debate; it's an established fact. Ribose effectively increases those pools, and as such, it's synergistic with all the compounds that increase the available pool of adenine nucleotides for the above compounds to work with. Thus, while the metabolic mechanisms of the different nutrients are unique, they're also interrelated.

Q: Does ribose also interact with creatine supplements in terms of increasing the effectiveness of creatine in the body?

A: While ribose doesn't directly interact with creatine supplements, it does directly affect the adenine nucleotide pool and so enables creatine to work more effectively. In that sense, ribose does increase the effectiveness of most creatine supplements.

Q: Can people take ribose and creatine at the same time, or should the supplements be used at different times?

A: Ribose is definitely compatible with creatine and can be used at the same time.

Q: Since the average single dose of creatine is five grams, or one teaspoon, what would constitute an average dose of ribose?

A: Ribose is a fairly expensive supplement, due to relatively high production costs, so users may want to experiment with ribose doses. I suggest taking 2.2 grams before and after your workout. That's consistent with the research.

Q: I understand that ribose hasn't been commercially available until now because in the past it was prohibitively expensive to manufacture. Why is the current process more economical?

A: That's a complicated question. There are two basic ways to produce ribose. The expensive technique involves growing yeast cells to high biomass, breaking them apart, collecting the contained nucleic acids (DNA and RNA) and, finally, breaking apart the nucleic acids to collect the ribose. Plenty of steps and expense are involved.

We make ribose by direct fermentation from corn sugar (glucose), a process that's similar to making cheese or other fermented foods. Bacteria in the fermentation eat glucose and produce ribose through their metabolism. We collect, purify and crystallize the ribose. Since the process contains fewer steps, it's less expensive.

Q: What specific adenine nucleotides are lost during intense exercise?

A: An excellent question! The adenine nucleotides include adenosine triphosphate, adenosine diphosphate and adenosine monophosphate (AMP), which collectively supply the vast majority of cellular energy and fuel such activities as muscle contraction. Energy is provided to the cell each time one phosphate group is broken down into another (ATP to ADP to AMP). Under normal conditions, with abundant oxygen available, the recycling of ADP to ATP occurs instantaneously and energy is recycled. When oxygen is depleted, as occurs during high-intensity exercise, though, the recycling process cannot keep up.

When there isn't sufficient oxygen, ADP further degrades. Two molecules of ADP combine to form one molecule of ATP and one molecule of AMP, and the ATP helps the cell perform work. As the process continues, however, the cell suffers an increase in AMP concentration, which it cannot tolerate. Cells need to maintain a careful balance between ATP, ADP and AMP concentrations to maintain normal work and stay healthy. When AMP levels rise, the ratio is pushed out of whack, and the cell must do something to decrease the rising AMP levels.

Skeletal muscles have a few options to correct the imbalance. Notable among them is a process for releasing AMP metabolites from the cell to lower overall AMP concentration; however, that leads to a reduced total adenine nucleotide pool, and it can be a significant reduction. For instance, 50 percent decreases in adenine nucleotide pools have been observed in the heart, and published reports show that the pool can drop 32 percent or more in skeletal muscles. Again, fewer adenine nucleotides mean less ATP, which equals less cellular energy.

Q: Since some rare cases of hypoglycemia, or low blood sugar, can occur with higher doses of ribose, should people who have a tendency to blood sugar fluctuations or diabetes be wary of using ribose?

A: High doses of ribose do decrease blood glucose levels. That's the bad news. The good news is that the blood sugar drops aren't usually noticed and are often transient, meaning that they don't last too long. Still, people who have hypoglycemia or diabetes should consult with their physician before using ribose supplements.

Q: Is supplemental ribose just aimed at active people engaged in sports or exercise, or can it also be used to advantage by sedentary people seeking increased energy?

A: The answer is a resounding yes. Anyone who feels he or she needs more energy can take ribose. While we haven't yet conducted specific trials to document that, my company has supplied ribose supplements

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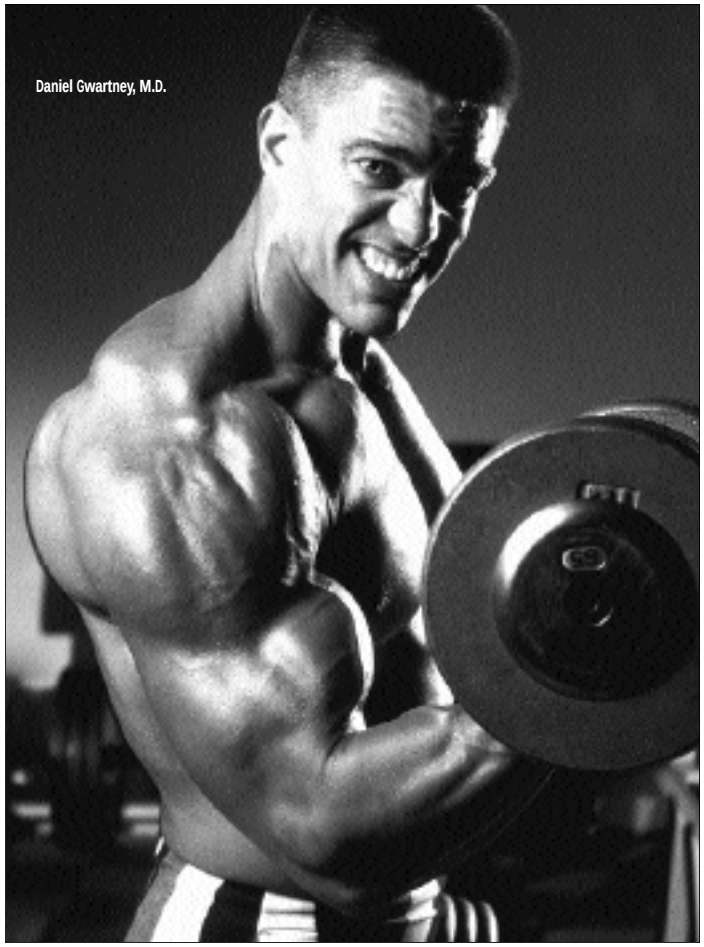


to several people who are sedentary or who exercise lightly. They have generally reported feeling more energetic while taking ribose. While I admit that's entirely anecdotal, it does point to some benefits from ribose for such people.

Q: Is ribose safe for pregnant or lactating women? Is it safe for children?

A: To my knowledge, there's never been a study that specifically looked at the safety of ribose in pregnant or lactating women. Even so, ribose is an all-natural and easily metabolized simple carbohydrate, so there's no reason to suspect that it wouldn't be safe for pregnant or lactating women—or children—if taken in moderate doses.

Q: Are some forms of ribose superior to others?

A: The key to how good ribose is lies with its purity. Several impurities can be found in ribose. Virtually all of them are other sugars, such as glucose or arabinose, or sugar alcohols such as sorbitol. The impurities may be hard to find with standard analytical techniques because they're hidden by the ribose. By and large, such impurities aren't toxic, but they also aren't ribose.

Bioenergy supplies highly purified ribose manufactured in the United States. Our plant operates under good manufacturing practices (GMP) as defined by the Food and Drug Administration for food production and is available for inspection at any time. Final purification of our product is done at a plant that also makes pharmaceuticals. Such plants must provide the highest purity possible. Other suppliers of ribose import their products from overseas, and those products may come from plants that don't meet GMPs and aren't available for ready inspection. Purity does matter.

Q: Do you anticipate that ribose will be an expensive supplement in comparison to creatine supplements?

A: Unfortunately, I do. The manufacturing process for ribose is much more complicated than that of creatine, which will keep the price higher. As production volume and efficiency increase, however, the possibility exists that ribose prices will become more moderate.

Q: Will ribose work better for a world-class athlete than it will for the average gym jockey?

A: That's a tough question, as there are lots of factors at play. World-class athletes are different from the rest of us. They're often genetically gifted and through years of training have conditioned their muscles to react more efficiently and effectively. Being human, though, they still lose adenine nucleotides after intense athletic or exercise activity.

Anyone who exercises at high intensity will lose those nucleotides and will benefit from using ribose supplements. The degree to which people lose nucleotides and the speed of recovery may vary, but all will benefit. In that respect I don't expect a world-class athlete to react more favorably to ribose than the average gym jockey, assuming that the gym jockey works out to his or her fullest capacity.

Q: How can ribose be used to treat various medical conditions?

A: My company is currently conducting clinical research involving the use of ribose in treating ischemic heart conditions. A large volume of other research from labs in the U.S., Europe and Japan has been conducted over the past several decades and has shown considerable efficacy for ribose in the treatment of energy-deficient hearts.

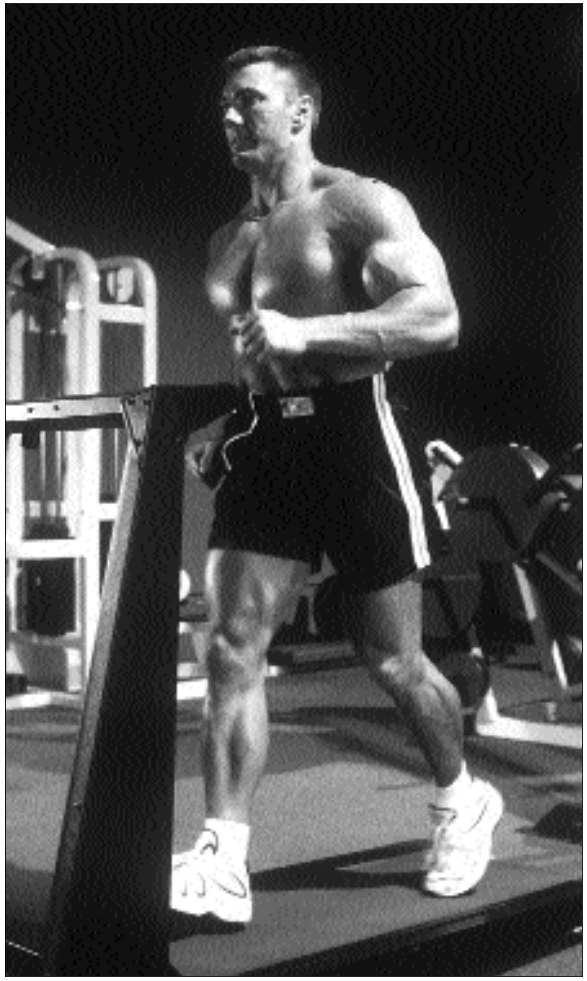
Ribose is also useful in treating other medical conditions. Any pathology involving a deficiency of ribose-producing enzymes may be improved with supplemental ribose.

Q: Do you anticipate ribose supplements eventually becoming as popular as or even more popular than creatine supplements?

A: I must say that I really do. While ribose is more expensive than creatine, it's an incredibly effective nutrient for energy recovery. Only ribose can maintain the body's adenine nucleotide pools, which are the

Anyone who exercises at high intensity will lose those nucleotides and will benefit from using ribose supplements. The degree to which people lose nucleotides and the speed of recovery may vary, but all will benefit.

Only ribose can maintain the body's adenine nucleotide pools, which are the cornerstone of all energy production. The biochemistry and physiology behind ribose use are beyond question. Ribose works, period.



cornerstone of all energy production. Certainly, we need further research, as there are still several unanswered questions. Nevertheless, the biochemistry and physiology behind ribose use are beyond question. Ribose works, period, and has broad application for athletes and anyone interested in maintaining good cardiovascular health.

Anavolics: The Science Behind Cell Volumization

by Daniel Gwartney, M.D.

Anavolics is a term I coined that's derived from two words, *anabolic* and *volume*. Perhaps it makes some sense that as a tissue, specifically muscle, grows (anabolic), it will take up more space (volume). As a review of the published studies indicates, however, that may be putting the cart before the horse. It appears that an increase in volume occurs first, and the anabolic process follows.

Very few supplements are anabolic. Frankly, the only ones that have shown any mass-building properties are creatine, certain amino acids (in various concentrations), high-protein formulas and insulin-based high-glycemic formulas. Some products used in animal feed are promoted as anabolic but aren't effective as performance supplements. The fact is, nothing currently available is as effective as anabolic steroids. Creatine is close for the first-time user, being comparable in effect to a light cycle of an oral steroid like Anavar. That's not surprising, as many of the oral steroids cause an increase in hepatic, or liver, production of creatine.

Most of the other supplements that have an effect are used to increase energy production or availability or act as stimulants. A select few have been shown to modify the catabolic response, decreasing muscle breakdown during exercise or fasting.

The bottom line is that most lifters and many athletes want to find a natural, nonbanned supplement that has an anabolic effect. Despite what many of the recreational, fad-oriented fitness gurus say, we all want more muscle. At every bodybuilding show I attend or judge, I hear statements like, "Next year I'm going to come in 10 pounds heavier," or, "If I could just pack on some more size." Even the three-times-a-week, color-coordinated, minivan-driving lifter is looking for an extra inch or two of arm mass—just some indication that all the work isn't being wasted. Gyms lose roughly half of their clients every year. Many quit because they see no progress; others because they're lazy. If people see progress, they get excited and stay involved.

That's the real purpose of all the dietary supplements—to support effort and allow people to see

That's the real purpose of all the dietary supplements—to support effort and allow people to see results. I don't think any of us expect a miracle. The new product AnaVol-R™ is designed to support effort and facilitate growth. Its formula is based on data and conclusions from scientific studies, hypotheses drawn from other sources and some ideas that come from experience and observation.

Is there any evidence that the idea of increasing cell volume to create an anabolic response is based in reality? The answer is yes. Cell volume increase occurs prior to the biochemical events related to protein or glycogen synthesis.

results. I don't think any of us expect a miracle.

The new product AnaVol-R™ is designed to support effort and facilitate growth. Its formula is based on data and conclusions from scientific studies, hypotheses drawn from other sources and some ideas that come from experience and observation. As consumers respond and give us feedback on this compound, each generation may be modified to include the best and newest information.

Is there any evidence that the idea of increasing cell volume to create an anabolic response is based in reality? The answer is an emphatic yes. Cell volume increase is a common, meaning shared, event seen in cells that are exposed to hormones or nutrients that cause an anabolic response. In fact, the cell volume increase occurs prior to the biochemical events related to protein or glycogen synthesis. A German researcher by the name of Haussinger has published a large number of studies investigating the role cell volume changes play in cellular metabolism. I'm not implying that he supports, endorses or is even aware of this product. I mention him only so readers who wish to do their own review will have a starting point.

If volume changes are actually responsible for the metabolism of a cell, why haven't others written about it in the many fine (and less-than-fine) strength magazines? Frankly, the material isn't easy to find. The easy stuff is already exploited to nearly unrecognizable states. Ephedrine, creatine, protein and caffeine have all been included in many products because the information base is easily accessed and widely distributed; however, there's a huge amount of scientific material that is not available on databases like Medline. Much of it is what's called basic research, meaning that it's been performed in a test tube, cell plate or tissue culture or on animal models. Basic science represents the frontier of science, as it challenges researchers to prove or disprove something that's as yet unknown. Once it's proven, then it can be applied, meaning that it's put to use. Studies in applied science validate questions that have been raised and investigated in basic science.

Cell volume increases signal anabolic functions. That was demonstrated when researchers exposed cells to anabolic hormones and measured the cellular response. In an identical set of cells they induced an increase in volume by changing the osmolarity, or salt content, of the solution surrounding the cell. The cells that were exposed to anabolic hormones swelled, much like a sponge when exposed to water. Surprisingly, the researchers noted the same cellular response in the second set of cells, even though no anabolic hormone was used. Later studies showed that shrinking the cells caused an opposite effect—the same effect that occured when cells were exposed to catabolic hormones! So let's make this first and critical point clear:

Cell volume increase (swelling) creates an anabolic response.

Cell volume decrease (shrinking) creates a catabolic response.

Imagine living in a small one-bedroom apartment. You fill it up with furniture, stopping when the rooms are full. Life is wonderful, and soon you're able to afford a two-bedroom house with a basement. What do you need or want as soon as you move? More stuff to fill the rooms. Soon you have an office set (instead of a card table), a washer and dryer, a coffee table and a serious entertainment center. Your space (volume) gets bigger, so you get more stuff. Later, life bites and you return to the one-bedroom apartment. Many of the things disappear—either to Dad's basement or to the repo man. Your space (volume) gets smaller,

A German researcher by the name of Haussinger has published a large number of studies investigating the role cell volume changes play in cellular metabolism.

There are a number of different cellular solutes that can enter a cell and cause it to swell. They typically pull water into the cell, causing a volume increase.

and you lose stuff. Think of your muscle cells as the living space and your possessions as muscle cell protein and cell contents. Bigger place, more stuff; bigger cell, anabolic growth.

The application to bodybuilding is obvious. Let's swell those muscle cells until they explode. Can they explode? That might be cool to watch, but it sounds painful and may affect your bench press. Actually, the cells can't explode and in fact can only have a moderate degree of swelling. There are regulatory mechanisms in place to prevent the occurrence of unlimited swelling. When a cell dies, however, the mechanisms are gone, and it may shrivel into a dead shell.

So, as exciting as unlimited growth would be, the best we can get is slow progressive growth after repeated exposure to agents that cause cellular swelling. That brings us to supplements.

There are a number of cellular solutes that can enter a cell and make it swell. They typically pull water into the cell, causing a volume increase. What's more, some of the agents will have hormonal responses in addition to the cell volume effect.

The following are the ingredients in AnaVol-R™. I have included a few references just to prove that it's all not just flying out of my lower sphincter, as has been known to happen in this industry.

•***Creatine monohydrate, five grams.*** When creatine was first introduced into the market, one of the main effects touted was cell volumizing. That point was quickly dropped because nobody knew how to make it a selling point, and the supposed effects of creatine were so easily felt that it didn't matter whether there was any real science behind it. Recently, a study by Ziegenfuss, Lowery and Lemon was published online in the *Journal of Exercise Physiology* (October 1998) that showed a 3 percent increase in water inside the cell after a three-day loading routine. That's consistent with the results most of us see with creatine loading: a gain of about 2 to 3 percent of bodyweight during loading (four to six pounds for a 200-pound person). Remember, the purpose of AnaVol-R is not only to provide a performance-enhancement effect but also to induce an increase in cell volume. What about creatine solubility? AnaVol-R is titrated, or balanced, at a pH of approximately 4.5. That's the pH at which creatine is soluble, just as occurs in the effervescent formulas. Five grams of creatine, delivered at a pH of 4.5, should be absorbed well and tolerated well.

•***D-ribose, two grams.*** D-ribose (the *R* in AnaVol-R) is a newcomer to sports nutrition. That's not because we didn't know about it but because it couldn't be manufactured cost-effectively until recently. Numerous studies are looking at the use of D-ribose for low-cellular-energy states in disease and ischemic conditions. They've all shown a positive effect of D-ribose supplementation on adenosine triphosphate (ATP) and total adenine nucleotides (TAN). The benefit of adding D-ribose to AnaVol-R is twofold. First, by maintaining cellular ATP, it ensures that cellular energetics are favorable toward the anabolic processes. Second, if the high turnover in ATP required by exercising muscle affects cellular ATP, it may also affect other nucleotides. What does that mean exactly? We've all heard of DNA and RNA. The acronyms stand for deoxyribonucleic acid and ribonucleic acid. If you look carefully, you'll see the prefix *ribo-*. Ribo- as in ribose, or D-ribose. DNA and RNA are the genetic molecules that determine the structure and function of all human cells. If we are robbing the cell energy nucleotide pool, we may be affecting the nuclear, or genetic, nucleotide pool, which is not a good thing. D-ribose, at the very least, will support the formation of new ATP and repair or salvage existing ATP (Brault, J.J., and Terjung, R.L., 1999). Possibly, it may aid in promoting the cell's ability to respond to stimuli such as training or volume changes (Bernofsky, 1980; Coffey, et al., 1965; Hellsten-Westing, et al., 1993). What's more, D-ribose also aids in the insulin response of AnaVol-R (Goodman, C., and Goetz, F.C., 1970; Malaisse, W., and Malaisse-Lagae, F., 1969).

•***Pinitol, 50 milligrams.*** Here's something completely new. Pinitol is a methylated sugar (3-O-methyl-1,2,4 cis-3,5,6 trans hexahydroxycyclohexanol) that has two effects of significant value: increased glucose uptake by the muscle cell and increased glycogen synthesis. Pinitol is an isomer, or type, of inositol. It's extracted from soy and sugar pine heartwood. It was first discovered to have hypoglycemic effects—that is, it lowers blood sugar—in 1987 (Narayanan, C., 1987) and later found to enhance insulin function as well.

Pinitol was first discovered in the methanol fraction of *Bougainvillea spectabilis*, a botanical used in traditional healing for many purposes, including diabetic-associated conditions. It was later found to be a component of pH 2.0 D-chiro-inositol glycan insulin putative mediator (Fonteles, M.C., et al., 1996). Infusion of pinitol leads to an insulinlike action without causing hypoglycemia. Therapeutically, that's very important, as it demonstrates some means of regulatory control to prevent the negative consequences of hypoglycemia. To the athlete it means not getting sluggish, drained and losing it. It's not yet clear how that happens, but it may be due to selective action at the muscle to increase glycogen synthesis.

Ongoing research at St. Johns University has demonstrated both glucose uptake and glycogen synthesis in muscle tissue culture, and further research that should clarify pinitol's role in cell volume and cell metabolism is under way. It's definitely one product we'll be hearing more about in the future.

Of all the proposed so-called insulin mimickers and insulin co-factors, pinitol is the one with the most promise. Insulin hits a receptor and then is done. It's a big protein, so you can't see it passing through the cell membrane. Rather, it acts through secondary messengers, or insulin mediators. One of the first mediators is a pseudo-disaccharide of pinitol and galactosamine chelated to manganese, which may activate rate-limiting enzymes for both oxidative (used for energy) and nonoxidative (stored as glycogen) glucose metabolism. Research has shown that levels of the mediator are reduced by 50 percent in the muscles and urine

If we're robbing the cell energy nucleotide pool, we may be affecting the nuclear, or genetic, nucleotide pool—which is not a good thing. D-ribose at the very least, will support the formation of new ATP and repair or salvage existing ATP used during exercise.

Pinitol is a methylated sugar that has two effects of significant value: increased glucose uptake by the muscle cell and increased glycogen synthesis. Of all the proposed so-called insulin mimickers and insulin co-factors, it's the one with the most promise.

of type II diabetics (Asplin, L., et al., 1993). There are some other exciting properties of pinitol, but I'm not at liberty to disclose them at this time. Trust me. There will be knockoff products using pinitol in no time. Just remember where you heard it first, folks.

•***Maltose-and-dextrose blend, 24 grams.*** Dextrose is a sugar found in nearly every powder, bar and candy, and like other sugars it has four calories per gram. It's used in creatine delivery to prompt an insulin spike. Using a lot of it will give a greater insulin spike, but it will also give you a big tummy. If you want to look eight months pregnant, go for the high-dextrose-content formulas. What's more, if you take a large amount of sugar at once, the sugar will go to your liver for storage rather than the muscle (Charrington, A., Vanderbilt University Medical Center). It has to do with the amount of sugar in the portal blood, the blood that delivers nutrients from the intestines to the liver, compared to what's in the peripheral bloodstream, the circulating blood supply to the body. Too much sugar, and it doesn't do the job. I wouldn't recommend driving heavy equipment after you take a high-dextrose-formula supplement either.

Maltose is a type of sugar, a disaccharide, that has a higher glycemic index than dextrose and is well tolerated. It's not so potent a signal for insulin release that it will trigger hypoglycemia, but it will aid in promoting the insulin signal without adding a large number of carbs. Consequently, the sugar blend is designed to promote an adequate insulin response to enhance the cell volume effect of the nutrients without making you fat. A maltose-and-dextrose blend of 24 grams, added to the two grams of D-ribose, provides 26 grams of sugar, stimulating insulin release.

•***Chromium GTF, 100 micrograms.*** Chromium doesn't do much and is really too weak to be considered as a single-ingredient product. Whenever insulin function is a factor in product action, however, there's a place for chromium. Chromium picolinate has received all of the attention in the supplement market, and it's given in doses as high as 500 micrograms (that's micrograms, not milligrams). High doses may have potential for adverse long-term effects. Picolinate may be fine, or it may be linked to negative cellular events. I'm not certain that it's entirely safe and don't feel it's worth the risk.

Chromium GTF acts as a co-factor to insulin. That means the insulin is actually doing the work, but the chromium GTF performs a function or functions that allow insulin to do its job better. It's like having a great chef in a restaurant. He'll prepare a fantastic meal, but if there aren't enough waiters, the food will arrive cold and won't please you as it should. The chef (insulin) is doing the work, but he needs a co-worker (chromium GTF) to enable him to do his best.

•***Proprietary blend of amino acids, dipeptides and tripeptides.*** Muscle cells, like all cells, have class-specific amino acid carriers. By class, I mean that certain types of amino acids use one carrier, while other types use another. That's true for the intestinal membrane as well. It's based on such factors as size, charge and side chains. Amino acids are limited by the number of transporters present on the intestinal membrane as to how much may be absorbed; however, one method of getting around that limitation is to provide not only free-form amino acids but dipeptides and tripeptides as well.

Dipeptides and tripeptides are carried across the intestinal membrane by separate carriers, which allows a greater concentration of amino acids to reach the bloodstream. It doesn't take a great concentration of certain amino acids to cause a muscle cell to swell—and swelling equals anabolic growth.

There's a small number of amino acid transporter classes on the muscle cell. There's also a small number of amino acids that have been shown to have a cell-volume-increasing effect on muscle cells. So, by using the specific amino acids to react with the specific transporters, you should be able to get a volumizing effect. You won't be changing wardrobes overnight, but remember that you're after the long-term effect of increased cell volume. The good news is that the volumizing effect of the amino acids is enhanced in the presence of insulin. Now you can see why the pinitol, sugars and chromium GTF play such vital roles in the formula.

In a nutshell, then, AnaVol-R is a formula designed to promote cell volume increases to support an anabolic phase of metabolism. It has the potential to trigger growth. It's not a 300-calorie creatine-and-carb blend that will plump you up like a Thanksgiving turkey, and it's not a hormone. It's based on the way the body reacts to the signals that lead you to grow. It's designed to allow—even force—your body to grow.

AnaVol-R is designed to draw fluid into the muscle in order to generate an anabolic response. The following recommendations involve a little intelligence and some common sense. I haven't determined whether or not loading would be beneficial.

There is a small number of amino acids that have been shown to have a cell-volume-increasing effect on muscle cells. So, by using the specific amino acids to react with the specific transporters, you should be able to get a volumizing effect.

•Take one serving of AnaVol-R in one liter of water immediately upon awakening. That's a lot of water, but after sleeping for eight hours, your body needs it anyhow.

•Wait at least 45 minutes before eating, which will allow the AnaVol-R to be absorbed without the interference of a meal.

•Eat at least 40 grams of protein with your first meal to provide amino acids for the volume-mediated anabolic response.

•Continue to drink sufficient fluids throughout the day to avoid dehydration, which may lead to fluid and volume loss from the cells. Studies have shown that hyperhydration increases the loss of total bodyfat stores.

•Eat every three hours, if possible, monitoring calories to meet your physique and performance goals, and include at least 25 grams of protein with each meal.

•If you want, have another serving of AnaVol-R before going to sleep; however, keep in mind that you'll be getting up to urinate if you

In a nutshell, then, AnaVol-R™ is a formula designed to promote cell-volume increases to support an anabolic phase of metabolism. Its potential is for growth, plain and simple.

do.

AnaVol-R is a first-generation product that will evolve into a giant maker. In fact, I believe the current formula is already a giant maker. There's only one way to find out: Try it.

Editor's note: *AnaVol-R™ was developed by Ergogenix, LLC, a private research and development company working in the specialty nutrition industry.*