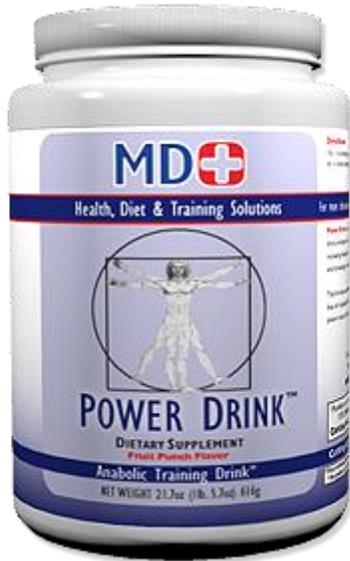


MD+ Power Drink **version III**

The Revolutionary, Research-Driven, Anabolic, Anti-Catabolic, Fat-burning, Training Drink



Power Drink fills a gap that's been mostly overlooked by most other supplement companies. While they're absorbed in what to use before and after training, and rightly so, they're missing one of the most important opportunities for maximizing the results you get from training. The right mix of ingredients to use **WHILE** you're training.

<https://metabolicdiet.com/product/power-drink/>

All my nutritional supplement products are at <https://metabolicdiet.com/shop/>

Power Drink information updated October 6, 2021, by Mauro Di Pasquale, B.Sc. (Hons); M.D.

Power Drink is manufacture in a GMP and NSF certified pharmaceutical grade facility.

The information below on the new Power Drink version III is in a constant draft form as revisions are made as new information becomes available. This latest information will give you the flavor of just what Power Drink will do for you in helping you achieve your health, body composition, and physical and mental performance goals.

Taking supplements in and around training is one of the most efficient and productive ways to use nutritional supplements. That's because the body is most receptive to these supplements under the stress of exercise. So, it makes good sense to be fully prepared to maximize the anabolic, body composition and fat burning effects of exercise, and by using the right nutritional supplement array before, during and after exercise.

I formulated [MD+ Exersol](#) to be the complete exercise solution and as such, to take the guesswork out of what supplements to use before, during and after training. [Resolve](#) to get your body ready and able to train, Power Drink to sustain and support your energy and metabolism while you work out, and [Amino](#) to maximize protein synthesis and make use of the post workout anabolic period.

While all three formulations are cutting edge, and make Exersol unique, it's Power Drink that fills a glaring gap in training supplements. And I'll explain why.

The idea behind Power Drink was born almost five decades ago. During my many years as an elite athlete in several sports, and especially in Powerlifting, I used a protein-based drink during my training and competitions. At the time and until I brought Power Drink to the market two decades ago, the concept of nutrition while training was based on water, carbs, and electrolytes ala Gatorade.

In the mid to late 1960s I was heavily into resistance training and competing on a University level in wrestling and gymnastics. I realized even before the time that Gatorade was a rather simple formulation (1965) that the ingredients used in the Gatorade formulation, (as mentioned - water, sugar, and electrolytes) wouldn't fulfill most of the requirements of a true supplement that would be significantly useful while training.

During my competitive years, which spanned two decades, realizing the major shortcomings of Gatorade, mainly that it didn't contain protein, I made up my own exercise drink which at the beginning contained water, electrolytes, and skim milk powder (which contained milk proteins). Over time several other ingredients were added that I felt were necessary for anyone who was seriously into exercise and sports.

Today there are other companies supplying products to be used while exercising. However, none come even close to the complexity and efficacy of Power Drink.

You Don't Have to Break Down to Build Up

We all know that during training muscle is broken down. Most people believe that this breakdown is a necessary part of training. After all you have to break muscle tissue down before you can build it up. Don't you? Unfortunately, that's one of the most stubborn of training myths.

Muscle breakdown, the actual breaking down of muscle protein into amino acids – termed muscle catabolism, isn't what provides the adaptation stimulus for increasing muscle size. It's the microscopic damage done to the muscle cell structure and the subsequent adaptation to that damage that determines the muscle building response.

You don't have to break down the muscle at all to get this response in full force. In fact, doing so is counter-productive. The more muscle you keep from breaking down, and the more you increase protein synthesis, the better the results from your training. Taking Power Drink while you're training will put your miles ahead of everyone else who just uses water or at best a drink along the lines of Gatorade even if that drink contains a smidgeon of protein and/or amino acids.

Power Drink, because of its effects on increasing protein synthesis and decreasing protein breakdown, is a powerful anabolic and anticatabolic product. As well, Power Drink increases cellular hydration and the utilization of amino acids and creatine by working muscle.

There are few studies showing the powerful effects of ingesting the right mix of proteins and other ingredients while training. However, a recent study looked at the co-ingestion of protein and carbohydrate during exercise. They found that the ingestion of protein **stimulates whole body and muscle protein synthesis rates during resistance-type exercise.**¹

As if that wasn't enough, Power Drink, because of its positive effects on the fat burning hormones and mechanisms allows you to burn more body fat while you're training.

And with the other ingredients included in Power Drink, such as the dipeptide carnosine and beta-alanine, which among other things are efficient buffering agents, you can train harder and longer and know that you have a powerful ally that will help you make good use of all that hard work.

Besides a hefty dose of high-quality protein, Power Drink also contains several anabolic and cytoprotective amino acids and peptides, electrolytes and other ingredients that help maximize the anabolic and fat burning potential of training, and much more.

The formula contains no carbohydrates or fat except for glycerol, which does not raise either glucose or insulin levels appreciably, and ribose, which is a resource for the reformation of ATP and other important cellular compounds. The glycerol, along with the taurine, plays a vital part in keeping the muscles hydrated and thus in an anabolic state.

The bottom line is that Power Drink is a research driven training drink that provides the nutrients necessary to increase muscle size and decrease body fat. And by providing all the necessary ingredients to feed working muscles and shift the use of body fat as the energy source for training, Power Drink dramatically increases the positive effects of training, allows you train longer and harder, and increases recovery.

Dealing with Muscle Cramps

Muscle cramps are common in athletes during training and recovery, at night, before and during competitions, and at any other time. Although we're not completely sure what causes them, and there are various reasons for cramps, especially in those with arterial disease and those taking certain medications such as diuretics and some beta agonists, in general, and especially in athletes, it's thought that they're due to an imbalance in electrolytes and hydration.

Muscle cramps can be so severe that oral administration of quinine, quinidine, and/or botulinum toxin treatment of the calf muscles are sometimes used. However, in athletes the remedies for cramps usually include stretching the cramping muscles in various ways for immediate relief, and in tandem increasing your intake of one or more compounds the commonest being **sodium, potassium,**

calcium, magnesium, and phosphorus. I've also recommended the use of other ingredients including **glycerol, taurine and carnosine** for the relief of cramps. All are in Power Drink.

I formulated Power Drink primarily as a drink to be used while exercising to maximize the body composition and performance enhancing effects of exercise. However, when formulating Power Drink I kept in mind the problem of muscle cramps.

I had muscle cramp problems during my elite Powerlifting career as a result of trying to make weight. In the early years of my two decade run as a world class powerlifter I had to devise a way of dealing with muscle cramps or quit lifting. What I came up with to solve my cramping problems was used to help me formulate Power Drink.

Power Drink version III Nutritional Supplement Panel

Power Drink™ III <small>VERSION</small>		Net Weight: 24.2 ounces (686 grams)
Directions: Mix to taste 2 heaping scoops of dry powder with 14 to 24 ounces of water, stir or shake to dissolve. Drink the mix during your training session.		
Supplement Facts:		Serving Size 2 Heaping Scoops (49 grams) Number of Servings 14
	Amount Per Serving	% Daily Value
Calories	195	
Calories from Fat	11	
Total Fat	1.20 grams	2%
Saturated Fat	0.30 grams	2%
Cholesterol	25 mg	10%
Total Carbohydrate	2.2 grams	1%
Sugars	1.2 grams	
Whole Protein (as Whey Isolate and Concentrate)	28 grams	50%
Calcium (as Lactate and Phosphate)	135 mg	15%
Phosphorus	130 mg	13%
Magnesium (as Aspartate)	160 mg	30%
Sodium (as Chloride and Bicarbonate)	150 mg	4%
Potassium (as Phosphate and Succinate)	280 mg	8%
L-Leucine	2250 mg	**
Glutamine Peptides (from Casein)	2000 mg	**
Creatine (as Monohydrate and Propionate)	1200 mg	**
L-Arginine (as AKG and Aspartate)	1050 mg	**
L-Taurine	1000 mg	**
L- Glutamine	800 mg	**
Beta Alanine	800 mg	**
L-Isoleucine	600 mg	**
L-Valine	600 mg	**
L-Histidine	500 mg	**
HydroMax Glycerol	300 mg	**
D- Ribose	200 mg	**
Caffeine Anhydrous	120 mg	**
Power Drink Proprietary Complex 2460 mg		
Betaine, L-Alanine, L-Glycine, Gamma-Amino Butyric acid (GABA), L-Carnosine (as Zinc Carnosine), Phosphatidic acid, Resveratrol, Pycnogenol.		
Other Ingredients: Beet Root Powder, Inulin, Xylitol, Citric Acid, Natural Flavors and White Stevia Powder.		
* Daily values are based on a 2000 calorie diet ** Daily value not established		

Ingredients in Power Drink and Their Effects

Power Drink contains many ergogenic and modulatory ingredients that maximize the training effect. I've listed some of them below, along with a brief explanation of what they do.

While Power Drink has a comprehensive mix of proteins and amino acids, which will be detailed below, Power Drink also contains several other ingredients that improve not only aerobic and anaerobic exercise and sports performance, but also improve both mental and physical health.

Protein and Amino Acids

The protein and amino acid composition in Power Drink is unique and the resulting amino acid array maximizes protein synthesis and minimizes muscle catabolism.

Whey Protein

One serving of Power Drink (44 grams) contains over 30 grams of whey protein (mostly in the form of whey isolate but also with a smaller percentage of whey protein concentrate) a "fast" protein that results in high systemic amino acid levels. The same properties that make whey protein a bad choice as a nighttime protein make it an excellent choice as a training protein since it can be taken continuously all through the training session. And the whey protein isolate concentrate combo gives the benefits of both without causing any bloating during training.

The whey protein combo has a direct effect on increasing protein synthesis, and at the same time increases systemic levels of the potent anabolic hormones and growth factors, including insulin, testosterone, growth hormone and insulin-like growth factor I (IGF-I).

As well the whey protein in Power Drink encourages the formation of the glutathione and increases the body's antioxidant and immune capacity, which in turn translates to increases in training efficiency and recovery.

When training, whey protein acts differently than when you're not training. When you're not training, the amino acids in whey protein are partially converted to glucose through gluconeogenesis, the amount that's converted depends on how much whey protein you take. This can be a problem as excess whey can then also be directly or indirectly converted to body fat.

Because of its rapid conversion into glucose in the non-training state, whey protein is a poor protein to use prior to training, especially as I don't recommend carbs before training because of its counter-productive effects on the breakdown and oxidation of body fat and on growth hormone levels.

However, whey used during training prevents the breakdown of muscle protein which would normally occur while training. The use of whey protein while training mainly prevents the breakdown of muscle protein and increases protein synthesis.

Branched Chain Amino Acids

The protein formulation contains over 10 grams of branched chain amino acids per serving – the whey in Power Drink is approximately 25% BCAAs, the glutamine peptides contain over 11%, and there's an extra 2250 mg of leucine (which has been shown to be an important regulator of protein synthesis) and 600 mg each of isoleucine and valine.

High amounts of branched-chain amino acids (BCAA), which have been shown to stimulate protein synthesis before and after training. BCAA have also been shown to increase resistance to fatigue and enhance lipid oxidation (fat burning) during exercise in those who are glycogen-depleted.²

This means that Power Drink is especially useful for those who follow my phase shift diets in which pre-exercise glycogen depletion exists in the low carb phase. Studies have also recently shown that glycogen depletion prior to exercise enhances fat metabolism, speed and endurance.^{3,4,5} It's also my view that glycogen depletion before training, if you're on my phase shift diets, also enhances the effects of training on body composition and strength.

Also, while of the BCAAs leucine seems the most important in improving body composition and muscle mass, especially in older people,^{6,7,8,9} it's also paramount that the other two BCAAs also be present in the formulation since supplementation with leucine alone may have side effects due to impairment in the availability of valine and isoleucine. This is because the activity of the rate-limiting enzymatic complex in BCAA degradation, i.e., branched-chain alpha-keto acid dehydrogenase, is markedly stimulated by the presence of leucine or its keto acid, alpha-ketoisocaproate, which in turn decreases the availability of endogenous valine and isoleucine if they're not included in the formulation.^{10,11,12}

Glutamine, Glutamate, and Alpha-Ketoglutarate

Power Drink contains significant amounts of glutamine and glutamate, as L-glutamine, glutamine peptides, and as part of the amino acid makeup of whey protein.

L-Glutamine (glutamine), the most abundant free amino acid in the body, is involved in multiple aspects of metabolism and signal transduction pathways. While some glutamine comes from dietary sources, most of the systemic glutamine is produced by skeletal muscle from alpha-ketoglutarate/glutamate and ammonia, and has several important effects in the body including its use as an energy substrate since the alpha-ketoglutarate (AKG) is a substrate of the Krebs/TCA/Citric Acid Cycle (the three are used interchangeably) and its formation increases TCA cycle flux and ATP formation.

As well AKG, either directly through the TCA cycle intermediates or indirectly through the formation of alanine formed in muscle via the alanine transaminase reaction. The alanine is then transported out of the muscle and to the liver to undergo gluconeogenesis and thus increase glucose availability.

The ammonia for these processes eventually comes from deamination of the branched chain amino acids (BCAAs – leucine, valine, and isoleucine) and under conditions of stress when more of the BCAAs are used to produce needed alanine and glutamine, the result is a decrease in protein synthesis and the anabolic effects of exercise.

Glutamine has significant effects on body composition and performance as it favorably affects insulin sensitivity, growth hormone, IGF-1 and cortisol levels, protein synthesis, cell volume, muscle catabolism (inhibits it) and gastrointestinal and immune function.¹³¹⁴¹⁵¹⁶¹⁷ Oral glutamine supplements have been shown to reduce obesity, waist circumference and, pro-inflammatory markers.¹⁸ Glutamine's effects on insulin sensitivity and resistance varies with the tissues involved. For example, while glutamine enhances insulin sensitivity in muscle, which is beneficial for gaining muscle mass, it enhances insulin resistance in adipose tissue, which is beneficial for reduced body fat. The Jekyll and Hyde effect markedly improves body composition.

Glutamine is used for energy by most cells in the body but especially by the GI tract, liver, kidney and the immune system. The process for energy production is by successive deamination of glutamine to glutamate, then to alpha-ketoglutarate that enters the TCA/Krebs cycle and through the oxidative phosphorylation forms ATP, the main energy source on which the body functions.

Glutamine is also used as a basis for the synthesis of the ATP molecule itself, nucleic acids (DNA and RNA synthesis and repair), other amino acids and proteins, glucose through gluconeogenic pathways, carbamoylphosphate, and other metabolites. As well glutamine increases glutathione, a powerful endogenous antioxidant that mitigates the counter-productive effects of exercise on excessive muscle damage without affecting the positive effects of exercise.

The interconversions, reactions, pathways and signaling that glutamine is involved in are complex and impacts many metabolic processes that are beyond the means of this information piece. As an example, glutamate can be used (besides conversion to glutamine) in an alanine aminotransferase reaction to produce alpha-ketoglutarate (AKG) and alanine or by the reverse reaction alpha-ketoglutarate can be aminated by ammonia or via a transamination reaction from other amino acids to form glutamate and pyruvate. The resulting alanine and pyruvate are involved in complex interactions and so the complexity of how glutamine affects metabolism soon increases exponentially.

For now, we'll simply cover some of the basics on glutamine dynamics, benefits, and what many people consider potential adverse effects from glutamine supplementation. I'll be writing a more detailed article on glutamine in the near future, including the importance of amino acid transporters that have been shown to be key components of the mTORC1-mediated amino acid sensing pathway that in turn has anabolic effects on skeletal muscle.

I'll also cover the dual effects of the amino acid transporters, and the transporters involved in glutamine transport into cells (mediated by solute carrier (SLC) family protein SLC1A5/ASCT2) and the transporter complex that regulates the simultaneous transport of glutamine out of cells and the transport of leucine into cells (complex SLC7A5/SLC3A2 (LAT1/CD98) and the implications of glutamine supplementation on this transporter complex and leucine levels in the body including in skeletal muscle.

While normal levels of endogenous glutamine are sufficient under most conditions, at times, such as when the body is under stress, it's not enough. Depending on endogenous glutamine to supply the glutamine that the body needs under special circumstances including exercise, is like robbing Peter to pay Paul – using up needed carbon skeletons and amino acid precursors from muscle to make glutamine, thus impoverishing muscle tissue, because glutamine is more importantly needed elsewhere in the body for energy, to bolster immunity, and other purposes.

At times when endogenous glutamine resources are stretched beyond what's needed, a time when glutamine becomes an essential amino acid since not enough can be formed endogenously, glutamine supplementation becomes a necessity.

Supplementation with glutamine, optimally as a free amino acid, or as glutamine peptides for quick access when needed, and from whole proteins that contain high levels of glutamine to keep glutamine levels optimized for normal times, has many beneficial effects by allowing other tissues access to the glutamine they need to function optimally, and by increasing health, body composition (fat loss and muscle hypertrophy), and physical and mental performance.

Glutamine has both direct and indirect anabolic effects. Glutamine directly increases energy metabolism and protein synthesis. Indirect effects include decreasing the deamination of the BCAAs and other amino acids and thus keeping their levels higher in skeletal muscle. Increased levels of leucine, for example, has stimulatory effects on protein synthesis and inhibitory effects on protein degradation/muscle catabolism. Also, transitory increases in ammonia, by providing amine groups for the formation of various amino acids, has an inhibiting effect on skeletal muscle proteolysis/breakdown.

A study published in 2016 found that glutamine supplementation improves some parameters of sport and exercise performance, and chronic supplementation appears to be of special importance for increasing tolerance to intermittent exercise, lowering feelings of fatigue, and optimizing recovery from muscle damage.¹⁹ The study also suggested that glutamine also acts as a relevant resource for rehydration during strenuous and prolonged physical activity.

Insulin and Glutamine

I've been interested in the metabolism and effects of insulin for over five decades. While at the University of Toronto I often attended classes at the Banting Building, the main building making up the complex now called The Banting and Best Department of Medical Research. Banting and Best were the first to discover and commercialize insulin and as I was a competitive athlete throughout my seven years at the University of Toronto, insulin and its effects were of great interest to me and has remained so to this day.

My definition of the phenotype is the NOW state of the organism as a result of the NOW interactions. These interactions are in constant flux - an uninterrupted flow that is constantly changing. You never step into the same river twice is a good analogy of a continuum of changes that occur in the body in response to the environment.

Insulin Resistance and Sensitivity – both are much more complex phenomenon than is almost universally accepted - that insulin resistance is bad and insulin sensitivity is good. In fact, it can be the other way around depending on how specific tissues respond to insulin and the state of the individual as far the interaction of their genome, transgenerational epigenome, the person specific epigenome, and environment. The effects of increasing or decreasing insulin resistance or insulin sensitivity is only meaningful when taken in context to the interaction of these three influences.

But then those three influences are what runs the living world, and especially humans, the dominant species. I consider the genome, the raw DNA, as a resource with its potential to be used or not depending on transgenerational epigenetic and non-DNA elements that are inherited from the sperm and egg when they fuse to form the one celled blastocyst. From that time on, intrauterine influences

and then after birth to the time of death, the environment makes or breaks how the resources inherent in the raw DNA plus transgenerational epigenetic effects as well as the transmission of other elements when conception occurs, are actuated or partially actuated, or not actuated.

Because of the complexity of insulin and its effects, I never believed, or stated in my writings, that insulin exerts its effects evenly in the body. I've always believed, at least for the last four decades and in a contrarian way, that the effects of insulin vary depending on the tissues involved, lifestyle, environmental influences, and the presence or absence of disease.

Regardless, it's widely felt that increasing insulin resistance is bad for health, body composition and mental and physical performance, and insulin sensitivity good for all these factors. As well, it's also the consensus that whatever influence insulin has, whether resistance or sensitivity, that this is the case for the whole body. However, both concepts are flawed.

However, this is not the place for detailed information on insulin since I'll be soon devoting an extensive article on how and why insulin doesn't act like almost everyone thinks. On the other hand, I did want to mention a paper published in 2019 on glutamine and insulin that lends some credence to my views.

This study investigated whether chronic oral glutamine (Gln) supplementation may alter metabolic parameters and the inflammatory profile in overweight and obese humans as well as whether Gln may modulate molecular pathways in key tissues linked to the insulin action in rats.²⁰

What they found was that in the obese group, Gln supplementation reduced waist circumference and serum insulin. In the rats Gln supplementation reduced adiposity, improved insulin action and signaling, and reversed both defects in glucose metabolism in the liver and muscle.

They concluded that **"In summary, our data showed that glutamine supplementation could reduce the insulin action and glucose uptake in fat and adipose mass, which improves the insulin action and signaling in the liver and muscle of rats."**

So, what we're seeing here is insulin resistance (in fat – the increased lipolysis and use of fat for fuel which resulted in fat loss) and insulin sensitivity (in muscle and liver resulting in an anabolic effect) resulting in an improvement in body composition. The authors data suggests that Gln supplementation leads to insulin resistance in adipose tissue via the hexosamine pathway, thus reducing adipose mass.

An interesting fact is that they suppose that this results in an improvement in systemic insulin action, which in turn results in insulin sensitivity in muscle and liver. But I don't believe that it's that simple as there's involvement of epigenetic changes to different tissues and subsequent nutrient and energy sensing and core metabolic pathways that need to be factored in when discussing variations in insulin signaling in different tissues in the same organism.

Glutamine and Ammonia

Ammonia is produced in the body from several processes including amino acid (mostly from glutamine and BCAAs) and purine deamination.

As far as adverse effects, there are none from the use of several grams of glutamine before and after exercise. However, there is a long-standing misconception that glutamine supplementation increases ammonia to the point that it has a negative effect physically and mentally on exercise performance.

The basis of this often-repeated belief is that glutamine acts as an important energy source for various tissues, including the gastrointestinal tract, the liver and skeletal muscle. The successive deaminations from glutamine to alpha-ketoglutarate results in the formation of 2 molecules of ammonia (NH₃) and it's the potential ammonia accumulation that many feel may make glutamine supplementation counter-productive by increasing physical and mental fatigue.

The ammonia-fatigue theory is almost a century old (a paper published in 1922 first suggested the correlation between ammonia accumulation and fatigue²¹) and based on the link between exercise and muscle derived ammonia production with the results of studies where ammonia production was correlated with fatigue under pathological conditions in which increases in ammonia resulted in neuromuscular dysfunction.

This association was then falsely extrapolated to suggest that further increases in ammonia during exercise from glutamine supplementation results in fatigue and compromised exercise performance.

This ammonia-fatigue theory, especially involving glutamine supplementation, while hopelessly outdated, persists. But the fact is that a normal person without significant liver or kidney disease or genetic mutations that results in a deficiency of one of the six enzymes in the urea cycle, can keep in check, and even get beneficial effects from any ammonia formed during even the most extreme exercise or sporting event with or without the use of glutamine supplements.

It's been shown that the regular use of glutamine in sports that do not require continuous exertion for long periods of time, because of compensating mechanisms as ammonia levels rise, decreases systemic and skeletal muscle levels of ammonia rather than increasing it.²²

The decrease in ammonia is the result of adaptation responses to the increased glutamine breakdown including the suppression of synthesis of endogenous glutamine (thus sparing skeletal muscle BCAAS, and especially leucine and thus preserving the anabolic effects of intense exercise), elevating the expression of enzymes of the urea cycle, and priming both hepatic and renal systems to increase the disposition of ammonium.

In continuous, prolonged and strenuous exercise ammonium levels rise as exercise progresses but is easily kept in even with the use of glutamine supplements. On the contrary physiological increases in levels of ammonia in healthy people during exercise can have significant ergogenic effects.

The formation of ammonium from ammonia plus H⁺ an acid moiety rather than being counter-productive, has an ergogenic effect as it plays an important role in the regulation of the acid-base balance in the body. The activation of renal production of ammonium from glutamine breakdown and subsequent excretion of ammonium decreases the adverse effects of increasing acidity as exercise progresses, thus further decreasing fatigue and improving exercise performance.

The degree to which ammonia forms the ammonium ion depends on the pH of the solution. If the pH is low, the equilibrium shifts to the right: more ammonia molecules are converted into ammonium ions. If the pH is high (the concentration of hydrogen ions is low), the equilibrium shifts to the left: the hydroxide ion abstracts a proton from the ammonium ion, generating ammonia, which in turn can be

used for the synthesis of amino acids, nucleotides, ATP, etc. or can be converted to urea for excretion, or the ammonium can be directly excreted.

The use of glutamine supplements besides increasing the production of ammonium through the deamination processes leading to glutamate and then alpha-ketoglutarate also has beneficial effects on systemic acid accumulation secondary to prolonged strenuous exercise. After formation of ammonium from glutamine, the alpha-ketoglutarate may be degraded to produce two molecules of bicarbonate, which are then available as buffers for dietary acids, thus adding to the net acid disposition that occurs with ammonium excretion and resulting in a decrease in fatigue and improved exercise/sport performance.

It's also been shown that ammonium regulates mTORC1 and mTORC2 signaling. A recent study concluded that "ammonium triggers the AKT-dependent phosphoinhibition of the TSC complex and of PRAS40, two negative regulators of mTORC1. Consistent with mTORC1 stimulation, ammonium induces the inhibitory phosphorylation of 4EBP1, a negative regulator of protein biogenesis. mTORC1 responds to nutrients, energy levels and growth factors and stimulates translation and anabolic metabolism while inhibiting autophagy. ammonium derived from upregulated glutaminolysis, could turn advantageous for proliferation by triggering key signaling pathways promoting growth."²³

Glutamine and Stress, Injury and Aging

Aging is inevitable, at least for now. And with it comes deterioration of our bodies, increasing disease, and common to it all increased inflammation. The many genetic and epigenetic factors involved that dictate the effect of age on our bodies and minds is beyond the scope of this information piece.

However, one aspect of inflammation and aging involves the heat shock proteins (HSP), especially HSP70, which have anti-inflammatory properties and decrease with aging. HSP also are decreased in couch potatoes and the obese.

It's also been known for several decades that glutamine is involved in modulating levels of heat shock proteins (HSP).²⁴ More recently it's been shown that glutamine's effects on increasing HSP are vital to cell defense and repair under many circumstances including various stressors such as intense exercise, toxins, diseases, and aging.

Oral supplementation with L-glutamine, in free or dipeptide form, can restore the glutamine-glutathione axis, and provide cytoprotection mediated by HSP-27, thus attenuating biomarkers of cell disruption and damage, as shown in rats submitted to high-intensity resistance and endurance exercise training.^{25,26}

A recent review concluded the following, mostly in respect to aging but the information has much wider implications:²⁷

"Glutamine is essential for the maintenance of normal neuronal physiology and skeletal muscle size and function due to its capability of controlling the HS response. Changes in physiological systems (e.g., cardiovascular, endocrine, muscular, nervous) that occurs with aging, along with simultaneous unfavorable changes in body composition (i.e., sarcopenia and visceral/abdominal obesity) may lead to, respectively, lower availability of glutamine and chronic low-grade inflammation. Under these conditions, bodily levels of glutamine may reduce, thus affecting its physiological roles. As glutamine is essential for normal HSF1/HSP70 axis activation, the stress response is likely to be reduced in many elderly people. Exercise is a powerful and low-cost physiological inducer of the HS response,

being capable of reverting age-associated low-HS response states. **Therefore, exercise training associated with glutamine supplementation and heat treatment itself are envisaged as important therapeutic tools able to restore the stress response in the elderly, allowing normal HSP70 synthesis and the maintenance of muscle integrity, size, regeneration, and rapid recovery from injury. In addition, the re-establishment of the HS response by glutamine supplements, under specific and controlled conditions, may also reduce the incidence of neurodegenerative diseases thus increasing longevity with health.**"

Glutamine and Heat Stress/Exhaustion/Stroke

With climate change, there has been and will continue to be more intense waves of drought and heat, usually together, throughout the world. We've seen several examples of extreme climate events over the last few decades, especially prominent were the heatwaves involving large masses of land in Russia in 2010 and in Western and Central Europe in 2003.²⁸ Heat stress, while common under conditions of heat and exercise, will become more prevalent in the coming years.

But regardless of whether you believe in climate change, heat stress is common under conditions of exertion in a hot environment. In most people heat stress results from unaccustomed or over exertion in the heat which leads to dehydration and metabolic changes in the body including deficits in the cardiovascular system and energy metabolism. The result of heat stress includes various symptoms and an inability to continue exercising at any significant level of exertion.

Heat stroke can occur by continuing to push past the symptoms to the point where symptoms become so severe that they often require medical intervention. Taken to the extreme, heat stroke can and has resulted in deaths even among elite athletes. The problem with athletes is that they can be over motivated and along with the misguided motto of no pain, no gain, can ignore the warning signs until they get into real trouble.

As such, it's important to listen to your body and to pick up on signals that you're undergoing heat stress, such as thirst that isn't quenched, being overly hot and not able to cool down, fatigue, nausea, feelings of faintness, and muscle cramps before it becomes a medical problem.

But you can help avoid heat stress by keeping fluid intake above sweating loss, take salt and other electrolytes (also in Power Drink), rest when feeling even the slightest symptoms, and don't continue to exercise until you are free of symptoms.

But there's more to the story of heat stress and the more severe exertional heat stroke. Heat stress is associated with activation of systemic and local inflammatory pathways, involvement of heat shock proteins. and adverse changes in the gastrointestinal tract including increased intestinal permeability.

And since we're covering glutamine, it so happens that supplemental glutamine, along with hydration, cooling and rest, can help to both prevent and overcome heat stress. Heat shock proteins are complex proteins that increase under stress, and particularly under heat stress and are protective to tissues, helping the body cope with systemic inflammation and the increase in gut permeability that are important hallmarks of heat stress.

Several studies have shown that supplemental glutamine positively modulates the heat shock proteins, decreases intestinal permeability, protects body proteins from becoming dysfunctional, and decreases systemic inflammation.²⁹³⁰³¹

As well, whey protein, also in Power Drink, is high in glutamine, and has been shown to reduce the dysfunction of the heat shock proteins, thereby protecting the body's proteins from inflammatory heat stress, and to improve rehydration and restore fluid balance, along with electrolytes (also in Power Drink).³²³³

Enhancing the Beneficial Effects of Glutamine

But there's more to the story since Power Drink contains several other ingredients that have additive and synergistic effects on body composition and performance but also facilitate the benefits of glutamine supplementation.

Glutamine plus Alanine

As an example, L-alanine, which is also in Power Drink, is a non-essential amino acid that has benefits on its own but also works to improve the beneficial effects of other ingredients that are also in Power Drink.

Studies have shown that the combination of glutamine and alanine is an effective non-invasive alternative to increase body L-glutamine pools. And that chronic oral supplementation with L-glutamine, whether in its dipeptide form or in the free form, to a limited extent by itself but better if taken along with L-alanine, represents an effective nutritional method to maintain L-glutamine stores, which attenuate the release of substances indicative of muscle damage and oxidative stress by enhanced glutathione antioxidant system and HSP70 response, thus improving the beneficial effects of high-intensity endurance and resistance exercise training.³⁴³⁵³⁶³⁷³⁸³⁹⁴⁰

The basis as to why glutamine plus alanine is more effective to bring out the benefits of glutamine supplementation on body composition and performance enhancement has not been fully worked out. However, alanine and glutamine metabolic routes often work in parallel, particularly in active muscle as both are transported from muscle to other tissues for various reasons.

The formation of both for transport to other parts of the body, especially the liver, and immune and gastrointestinal systems involves the catabolism of other skeletal muscle amino acids, specifically, leucine, isoleucine, valine, aspartate, glutamate, asparagine, arginine, and proline. Supplementation with both alanine and glutamine spares these amino acids so they can be used to maintain or increase skeletal muscle mass.

During exercise, as systemic glucose levels decrease, both glutamine, mostly in the kidney, and alanine, mostly in the liver, are used for glucose formation by gluconeogenesis. Alanine supplementation decreases the breakdown of muscle tissue to procure both alanine and glutamine so they can be used to replenish systemic glucose. It also decreases the use of muscle pyruvate for the formation of alanine, which is then exported out of skeletal muscle to be used mainly by the liver to make glucose via gluconeogenesis.

The more strenuous the exercise, the more alanine is produced, and less pyruvate is available in skeletal muscle which compromises protein synthesis and skeletal muscle performance. To some extent the degree in which pyruvate is cannibalized to form alanine for glucose formation outside of skeletal muscle can be seen by elevations of the enzyme alanine transaminase (ALT), often elevated with exercise and just as often mistaken as a sign of liver disease when in fact it's more a sign of

alanine formation due to depletion of glucose secondary to exercise. Alanine supplementation with exercise will decrease ALT levels since the transamination reaction to form alanine isn't as active.

As well, alanine plus glutamine together have an increased effect on heat shock proteins and thus on the benefits of maintaining the heat shock response to stress and aging.⁴¹

Other Examples

Glutamine, along with other osmolytes in Power Drink, including betaine, glycerol, creatine, and the amino acids arginine, lysine, taurine, and proline, protect cells from stress and increase protein synthesis secondary to the volumizing effects on muscle cells.

However, excessive amounts of glutamine are not necessary to obtain all the effects of glutamine supplementation since the inclusion of glutamate and alpha-ketoglutarate in Power Drink also contribute to the beneficial effects of Power Drink on health, body composition and performance.

One 44 gram serving of Power Drink contains over 8 grams of glutamine, glutamate, and alpha-ketoglutarate.

Bottom Line

The bottom line is that glutamine's beneficial effects on body composition, performance, and recovery is a consequence of multifactorial cell and systemic mechanisms, including inhibition of inflammatory pathways, accumulation of intracellular osmolytes thus affecting hydration, synthesis of antioxidants especially the potent endogenous antioxidant glutathione, energy metabolism intermediates especially alpha-ketoglutarate, control of global ammonia levels throughout exercise, decreasing acidity secondary to exercise, increased protein synthesis through activations of mTORC1, decreasing excessive muscle damage and the suppression of neutrophil function, working additively and synergistically and affecting the metabolism of other amino acids such as the BCAAs, arginine, citrulline, and alanine, and activation of heat shock response intermediates especially HSF-1 and HSP70.⁴²⁴³⁴⁴⁴⁵⁴⁶

Simply put glutamine supplementation decreases fatigue, increases exercise intensity, decreases exhaustion, improves recovery, and enhances the body composition and performance effects of exercise.

Arginine

Arginine and other ingredients in Power Drink, increase GH, IGF-I and insulin secretion and response, thus providing a synergistic anabolic effect on muscle and canceling out insulin's lipogenic and anti-lipolytic effects. In other words, you get all the good anabolic and fat burning effects from the synergism and none of the bad.

Arginine also increases nitric oxide formation, which is felt to have a beneficial effect on blood flow in muscle and thus enhance nutrient and oxygen delivery, buffering and the clearing of metabolic by products, and increasing protein synthesis.

Power Drink contains over 1200 mg of arginine, 500 mg in free form, 66 mg bound up in peptide form, and 640 mg in the slower release form as part of the whey protein.

Taurine

Taurine ((2-aminoethane-sulfonic acid), a sulfur-containing amino acid is the second most abundant amino acid in the body, the most abundant free amino acid found in skeletal muscle tissue, the heart and brain. It's also one of the most abundant amino acids in most organs in the body.

Taurine has a myriad of beneficial functions in the body, including the musculoskeletal and central nervous system, from development to cytoprotection in all age groups.⁴⁷⁴⁸⁴⁹ As such, it is beneficial for improving body composition and physical and mental performance. Although it's one of the few amino acids not directly used for protein synthesis, it can indirectly increase protein synthesis.

Taurine is often considered a non-essential or hesitantly a conditionally essential amino acid for humans since it can be synthesized by the body from methionine and cysteine. However, the limiting enzyme required for biosynthesis of taurine is very low in humans and biosynthesis may not be adequate for times when the need for taurine are increased.

Because of these limits, and to make sure there's enough taurine available when needed, taurine has been added to infant formulas as well as to intravenous solutions used for various medical conditions.

Because of its many functions and suboptimal levels in most people, I consider taurine an essential amino acids for anyone looking to improve body composition (add muscle and reduce body fat) and/or increase exercise/sports performance.⁵⁰⁵¹

Taurine is highest in meat and seafood and the average person, non vegan, takes in around 60 mg per day. However, over twenty times that amount can be beneficial for improving body composition and performance, increasing health and wellbeing, and as complimentary treatment for prevention and treatment of various diseases, including sarcopenia and musculoskeletal disorders.⁵²⁵³

Vegan intake of taurine is usually much lower than non-vegans and I always recommend taurine supplementation for vegans, especially vegan athletes. As an aside I always recommend other forms of supplementation for vegans, depending on how carefully a vegan structures their diets, including vitamins D, B2, B12, B6, and niacin, zinc, iron, selenium, calcium, L-carnitine, carnosine and/or beta-alanine, omega-3 fatty acids, and creatine.⁵⁴⁵⁵⁵⁶

Effects on Performance

Taurine is a nutrient that enhances the training effect by its many roles in improving skeletal muscle function including increasing growth hormone and IGF-1, and decreasing inflammation, muscle soreness, and injury.⁵⁷⁵⁸⁵⁹⁶⁰⁶¹⁶²⁶³⁶⁴⁶⁵⁶⁶⁶⁷⁶⁸⁶⁹

As well, taurine has immune system benefits, insulin like effects as far as increasing protein synthesis and decreasing muscle breakdown and cell volumizing effects. The volumizing effect on certain nutrients on muscle cells is also felt to lead to an increase in protein synthesis.

Over the years, oral taurine administration has been shown to help muscle cramping in patients with liver cirrhosis and myotonic dystrophy. Several studies have suggested that it may also help to alleviate muscle soreness and cramps occurring during and after exercise.⁷⁰

Studies on mice and rats show that taurine is useful for reducing physical fatigue, muscle damage, and exercise induced muscle injury during exercise training, presumably due to its antioxidant effects and the beneficial effects that taurine has on metabolism and on muscle and cardiac functions.^{71,72} It's also been shown to improve the electrical and contractile properties of skeletal muscle fibers.⁷³

Another study on rats has shown that oral taurine supplementation may increase muscle performance and reduce muscle injury caused by exercise.⁷⁴ The aim of the study was to determine if increasing muscle levels of taurine would decrease free radical damage after exercise-induced injury. The authors found that first of all taurine levels rose in muscle after supplementation, and secondly that running performance was improved by the taurine supplementation. Thus, it appears taurine supplementation may facilitate exercise performance and reduce some of the counterproductive muscle injury caused by exercise.

In humans, taurine supplementation in patients with heart failure increases their exercise capacity.⁷⁵ It's been shown that taurine decreases oxidative stress in skeletal muscle after eccentric exercise⁷⁶ and that taurine may attenuate exercise-induced DNA damage and enhance the capacity of exercise due to its cellular protective properties.^{77,78}

There is some evidence to show that taurine may enhance training further by decreasing training induced fatigue. One study found that Na⁺-K⁺-ATPase activity is depressed with fatigue, regardless of training state, suggesting that this may be an important determinant of fatigue.⁷⁹ Another paper associated fatigue and training with reduced Ca²⁺-ATPase activity.⁸⁰ Previous studies have shown that taurine stimulates Na⁺-K⁺-ATPase activity and also the pumping rate of the Ca²⁺-activated ATPase pump. One study found that taurine increased fat oxidation in endurance trained athletes.⁸¹

Two recent studies in humans found that human endurance performance can be improved by orally ingesting as little as one gram of a single dose of taurine.^{82,83} Another recent study found that taurine supplementation increases lipolysis and contributes to energy systems, exerting its effects on increasing endurance.⁸⁴

One study found that taurine administration increased taurine concentrations in skeletal muscles, reduced the decrease in taurine in skeletal muscles that is seen with exercise, increased physical endurance by increasing the duration of running time in rats, and was considered to reduce exercise-induced muscle fatigue.⁸⁵ Also taurine supplementation has been shown to increase skeletal muscle force production, protect muscle function and reduce oxidative stress.⁸⁶

Taurine is one of the most abundant free amino acids in the testes and is instrumental in the production of testosterone and in fertility. A recent study concluded that taurine plays important roles in male reproduction and that a taurine supplement could stimulate the secretion of LH and T, increase the levels of testicular marker enzymes, elevate testicular antioxidation and improve sperm quality.^{87,88,99,91, 92,93,94,95,96,97,98}

Taurine also plays well with the branched chain amino acids (BCAA) as the combination has been shown to decrease delayed onset muscle soreness and muscle damage.⁹⁹ It's also likely that the beneficial effects of both taurine and the BCAA on skeletal muscle function are enhanced by other nutrients such as beta-alanine and carnosine.¹⁰⁰

Taurine is considered a potent antioxidant and cytoprotective agent that may be useful for combating the adverse effects of physical and psychological stress, and aging.^{101,102,103,104}

In a recent paper taurine was felt to have beneficial effects on periodontal disease, a disease that is wide spread and increases inflammation, which is counterproductive for optimal health and performance.¹⁰⁵¹⁰⁶

Taurine, because of its beneficial effects on skeletal muscle functioning may also be used therapeutically for skeletal muscle disorders.¹⁰⁷¹⁰⁸

For the most current information on taurine see my recent online article at https://metabolicdiet.com/wp-content/uploads/2017/product_pdf/Taurine.pdf.

Body Composition Effects

Taurine has a several effects in the body that contribute to weight and fat loss, and body composition, including beneficial effects on lipid metabolism and protein synthesis.¹⁰⁹

An early study showed that taurine decreases bodyweight in obese mice.¹¹⁰ Another study on 30 Japanese college students found that taurine is effective in reducing body weight and fat mass, possibly due to its beneficial effects on lipid metabolism.¹¹¹ As well it may have an important role in cardiovascular disease prevention in overweight or obese subjects.

More recent studies have found that taurine supplementation can increase energy expenditure and the function of lipolytic enzymes, decrease body fat, decrease catabolism of skeletal muscle, especially visceral body fat, improve performance, and has additive effects with exercise.¹¹²¹¹³¹¹⁴¹¹⁵¹¹⁶

Other recent studies have found that taurine supplementation can increase energy expenditure and the function of lipolytic enzymes, decrease body fat especially visceral body fat,, restore muscle function in overuse of exercised muscle, decrease catabolism of skeletal muscle, improve strength and endurance performance, decrease muscular fatigue, increase enzymatic antioxidants modulate cytokines, improve cognition and physical fitness, and has additive effects with exercise.¹¹⁷¹¹⁸¹¹⁹¹²⁰¹²¹¹²²¹²³¹²⁴

Taurine has also been shown to increase glucose sensitivity and enhance mitochondrial metabolic function.¹²⁵¹²⁶ The data suggest that taurine administration has a marked effect on lipid metabolism and can therefore be beneficial to persons looking to lose body fat. Also, that restoration of plasma taurine level could be critical in preventing or improving obesity-related -cell dysfunction.

As well, the data suggests that taurine depletion causes inadequate β -oxidation due to decreased pH buffering capacity, which consequently leads to metabolic dysfunction.

Besides the effects on fat metabolism and mitochondrial functioning, taurine also has effects on cellular hydration that increases protein synthesis and thus decreases the loss of muscle with weight loss.¹²⁷

Taurine has been shown to be an important amino acid in several tissues in the body, including muscle.¹²⁸ Because of its properties in skeletal muscle it's been suggested as a treatment for various muscle disorders.¹²⁹

Taurine, because of its effects on increasing insulin sensitivity, growth hormone levels, and protein synthesis (secondary to its effects on osmoregulation and cell volumizing^{130, 131, 132}), helps to spare

muscle when dieting, with the result that weight loss is mostly from the loss of body fat. Taurine is also beneficial because of its effects on osmotic regulation of neuronal activity.¹³³

Taurine is also useful in regenerative therapies. A recent study looked at the effects of taurine in chondrogenesis when used with stem cells. However, the use of taurine may well aid in chondrogenesis when used along other ingredients present in Resolve and as such may be useful of increasing the repair of cartilage in joints, including the vertebral column facets in degenerative spinal osteoarthritis.¹³⁴ The same study also looked at the beneficial effects of Taurine on telomerase and for anti-aging.

The bottom line is that taurine supplementation significantly enhances the body composition and performance benefits of exercise as well as improving health and well-being. Because of all these properties, taurine (1000 mg per serving) is an integral part of Power Drink.

For the most current information on taurine see my recent online article at https://metabolicdiet.com/wp-content/uploads/2017/product_pdf/Taurine.pdf.

Other Amino Acids

Several amino acids are present in substantial amounts in the combination of the whey protein isolate and the glutamine peptides (see amino acid arrays of both below).

For example, Power Drink contains over 2200 mg of **proline** per serving. Proline, one of the main components of collagen and thus tendons, ligaments and joints, is important for musculoskeletal health and might be useful in decreasing injury and increasing recovery. As well, proline is important in DNA and protein synthesis, and for the immune system. Decreases in serum proline levels have been noted in prolonged exercise. Part of this is likely due to the gluconeogenic properties of both amino acids.

Alanine is another important amino acid and there's over 1600 mg in Power Drink (both as a free amino acid and as part of the amino acids that make up the whey proteins). During exercise, skeletal muscle releases alanine into the circulation in direct proportion to the intensity of the exercise.¹³⁵ However, although yielding much needed energy, this catabolism of BCAAs and cellular protein (to produce glutamine and alanine) is counterproductive. Any loss of amino acids is detrimental if they could have been used to maintain or increase skeletal muscle mass.

For more info on alanine see the information above under glutamine and the article [Alanine – the Essential, Non-Essential Amino Acid](#).

Power Drink contains almost 3000 mg of **lysine**, an amino acid important for stimulating GH secretion (in concert with other amino acids including arginine and glutamine) and in optimizing protein synthesis.

There's also about 3500 mg of **aspartic acid** per serving. Aspartic acid (aspartate) has been shown to enhance both aerobic and anaerobic muscle capacity. A recent study found that the supplemental use of aspartate and asparagine can decrease exercise fatigue.¹³⁶

Power Drink also has significant amount of other amino acids, including about 1100 mg of each of the neurotransmitter precursors **phenylalanine** and **tyrosine**.

The conditionally and non-essential amino acids present in Power Drink have been shown to be most used for protein synthesis in muscle (serving not only as direct substrates but also sparing the conversion of these amino acids from the essential ones). While the presence of essential amino acids is critical to protein synthesis, there is some evidence that lack of the nonessential amino acids can result in lower plasma levels of these amino acids¹³⁷ which may ultimately compromise protein synthesis.

Citric Acid (Citrate)

Citric acid has several useful functions, such as increasing the absorption and bioavailability of several nutrients, including creatine, calcium and magnesium. As well, it has antioxidant properties and adds some tart flavoring to Power Drink.

However, its most useful function is related to the effects it has on increasing the supply of mitochondrial citric acid thus increasing the flux of the Citric Acid Cycle (also known as the TCA Cycle and Krebs Cycle).

It's important, however, not to take in excessive amounts of citrate, a practice that's becoming more common among bodybuilding and power athletes using several grams a day. Supplemental citric acid or citrate ends up in the cytoplasm of cells and thus its fate depends on the amount present and activity level.

Cytosolic citrate, the citrate that is a result of using oral citrate, differs somewhat from mitochondrial citrate in that mitochondrial citrate, in the right amounts, can increase TCA cycle flux and is an anapleurotic TCA cycle intermediate. Cytosolic citrate, in smaller amounts, can be translated into pyruvate (via the actions of malate dehydrogenase and malic enzyme) and then enter the TCA cycle either as acetyl-coA or oxaloacetate, depending on many circumstances.

However, excessive amounts of cytosolic citrate may be counter-productive as cytoplasmic citrate (via the acetyl-coA and malonyl-coA axis) has antilipolytic and lipogenic properties. As such, if taken in excessive amounts and thus mostly remains in the cytosol as it would overload mitochondrial acetate, it can decrease the breakdown and oxidation of body fat, and acts as a stimulus for increasing fat production. Also, high levels of citric acid and/or citrate commonly cause gastrointestinal upset.

There's 100 mg (0.1 grams) of citric acid in one serving of Power Drink. Just enough to get the useful effects in stimulating TCA flux and increased energy production, but not enough to accumulate in the cytoplasm and produce counter-productive changes in fat metabolism.

Creatine Monohydrate, Phosphorus, Ribose and Sodium

Power Drink contains several ingredients that maximize phosphocreatine (PC) levels in muscle and thus boosts your anaerobic power, helping you to train more intensely. These ingredients include creatine monohydrate, the creatine precursors (arginine, glycine and methionine) and other amino acids that increase the utilization and effectiveness of the creatine in increasing tissue PC levels.

Creatine monohydrate has been shown to enhance athletic performance, and to increase strength and muscle mass,^{138,139,140,141,142,143,144,145} these effects are enhanced in Power Drink by stacking creatine with other ingredients.

For example, by providing some of the raw material that are used in forming ATP, including phosphorus and ribose, and the increased stimulus for ATP formation, Power Drink increases both Aerobic and Anaerobic ATP production and salvage.

Sodium is also important for increasing creatine uptake in muscle and some studies has been found to be important for creatine uptake into relatively insulin insensitive muscles such as the soleus.¹⁴⁶

Carnosine, Beta-Alanine, Phosphorus and Creatine

Acid, or H⁺ ions are produced as you exercise, especially when you push the envelope. The buildup of these ions results in an intracellular proton load that comes from both the formation of lactic acid and its subsequent dissociation, and the production of ATP when there's a lack of oxygen available to the muscle cells - anaerobic ATP production. While generally true, it's also felt that lactic acid is produced locally under situations where there is enough oxygen, that is under aerobic conditions.

Overall, however, the result can be an accumulation of H⁺ ions that is thought to increase muscle fatigue and interfere with muscle contraction. And there is that the use of buffering compounds enhances exercise performance in cases where relative tissue hypoxia is a factor.¹⁴⁷

The intracellular buffers that can contribute to this enhanced buffering capacity are phosphorus, carnosine, and creatine. These ingredients are an integral part of the Power Drink formula.

Both Beta-alanine and Carnosine (a dipeptide beta-alanyly-L-histidine) were added to Power Drink because of their powerful antioxidant, anti-inflammatory, and immune system effects, as well as its beneficial effects on performance, healing and recovery.^{148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167}

Carnosine, a potent antioxidant and buffering agent, is found in the highest concentration in muscle and brain, where it is felt to have an anti-ischemic effect and thus protect and buffer these tissues.

Carnosine has beneficial effects on exercise performance by helping to overcome muscle fatigue, likely due its effectiveness as a buffering agent, and perhaps its antioxidant, chelating, and enzyme regulating effects.¹⁶⁸

Carnosine is also believed to decrease both central and peripheral fatigue. In the brain, it is also used to synthesize neurotransmitters which are involved in fatigue. In muscle, carnosine decreases exercise fatigue and contribute to recovery.

Carnosine also inhibits glycation, a destructive protein/sugar reaction that occurs in the body and which contributes to metabolic dysfunction and aging through several mechanisms including the breakdown of connective tissue, a loss of elasticity, and a decrease in cellular hydration.¹⁶⁹

Carnosine, along with alpha lipoic acid (both in Power Drink) provide protection against glycation, tissue stress, and premature aging.¹⁷⁰

As is known, exercise is a catabolic process. Ordinarily this catabolic process continues even though exercise is stopped. Carnosine has an immediate effect on helping to change the catabolic state to one that's anabolic and aiding recovery in this and other ways. It also has beneficial effects on muscle damage and on increasing blood flow in muscle.¹⁷¹

Carnosine levels tend to be higher in athletes such as sprinters^{172,173} and in bodybuilders¹⁷⁴. For example, one study found that high levels of muscle carnosine increased performance in the latter half of short maximal cycle sprinting.¹⁷⁵ Another study found that beta-alanine supplementation increased muscle carnosine levels¹⁷⁶ and resulted in an improvement in exercise performance.¹⁷⁷

These studies also show that intramuscular carnosine may be an effective physiological H⁺ buffer and that there is a significant relationship between the carnosine concentration in human skeletal muscle and high intensity exercise performance. Studies have shown that beta-alanine supplementation increased muscle carnosine levels¹⁷⁸ and results in an improvement in exercise performance.¹⁷⁹

Since dietary carnosine is absorbed across intestinal epithelial cells, using carnosine itself would seem to be more useful than using beta-alanine. However, a recent study found that using carnosine and beta-alanine together results in a greater effect than using either one alone.¹⁸⁰ As such, I've included both in Power Drink III.

Electrolytes and Minerals

Studies have shown that replacement of water, electrolytes, especially **sodium** and **potassium**, and certain minerals (which also act as electrolytes) while exercising has a beneficial effect on strength, exercise intensity and endurance. Besides replacing various nutrients that are affected by exercise, these substances also have potential beneficial training effects. For example, **magnesium**, **calcium** and **potassium** are important in protein synthesis, muscle contraction, energy production and metabolism.

Glycerol/Glycerine/Glycerin

I added glycerol to the present Power Drink formulation because in lower doses it can have beneficial effects without any adverse effects on low carb dieting. Glycerol has several possible roles in increasing the effects of exercise and exercise efficiency.

Glycerol, and creatine and taurine, are predominantly present in the intracellular space and as such all three have distinct volumizing effects. Increasing intracellular volume is considered to increase protein synthesis and thus to have anabolic effects.

Glycerol also results in an increase in body water that has been theorized to result from a glycerol mediated increase in water reabsorption in the distal tubules and collecting ducts of the kidney. So, in fact the use of glycerol can result in both increased intracellular and extracellular fluid volume. Since both glycerol and creatine have volumizing effects, the use of both compounds together may have an additive anabolic effect on muscle cells.

Besides the above effects, glycerol may also have some beneficial effects on athletic performance due to its osmotic action. Recent research has shown that when a glycerol and water mix is used as a hydration beverage before training or competition aerobic and anaerobic performance improves.¹⁸¹ Thus glycerol-induced hyperhydration by delaying the adverse effects of dehydration and heat stress, reduces the thermal burden of exercise¹⁸²¹⁸³.

The bottom line in all this is that glycerol can be useful and may provide some anabolic effects. Also, by helping to combat dehydration, and by supplying energy either by being converted to glucose or being oxidized along the same pathway as glucose glycerol supplementation may help fight fatigue during periods of intense training.

As well, I use HydroMax Glycerol in Power Drink as it is the only high-yield branded glycerol powder (it has 65% or higher glycerol content - much more per unit than any other glycerol powder) with a pilot in house human study indicating a positive efficacy during exercise.

Xylitol

Xylitol, glycerol, and ribose make up the bulk of the carbohydrate content of Power Drink and increase its palatability. But there are other reasons why these were included in the formulation.

Studies have shown that xylitol affects metabolism in different ways than sugars and most other carbs and as such not impacting on insulin or fatty acid oxidation.^{184 185} As well, other studies have shown that xylitol may improve nitrogen balance, increase fat oxidation and decrease carbohydrate oxidation (likely spares glycogen) as compared to glucose (likely secondary to a decreased insulin response).^{186 187}

Resveratrol

Resveratrol is a potent anti-oxidant with significant anti-aromatase activity.¹⁸⁸¹⁸⁹ Researchers have shown that resveratrol may have significant anti-aging effect and extend lifespan and healthspan.¹⁹⁰

As well, resveratrol has been shown to decrease fatigue, enhance body composition and both physical and mental performance, interact with our microbiome, and improve testicular function.¹⁹¹¹⁹²¹⁹³¹⁹⁴¹⁹⁵¹⁹⁶¹⁹⁷¹⁹⁸¹⁹⁹²⁰⁰²⁰¹²⁰²

Betaine

Besides acting as a precursor for methionine, choline and carnitine, betaine has other useful properties. Betaine has been shown to protect tissues under stress, regulate fatty acid metabolism, reduce body fat in animals, and be useful in the prevention of chronic diseases.²⁰³ Betaine also acts as an important methyl donor.

Methyl donors are important for the methylation reaction, which adds a methyl group (one carbon atom and three hydrogen atoms), on proteins, enzymes, chemicals, DNA, and amino acids like homocysteine. Methylation is important for maintaining many functions in the body including genetic expression, and neurological and musculoskeletal function.

Summary

Power Drink, with its many natural ergogenic ingredients, and for many reasons, is the ideal training drink.

The bottom line is that Power Drink will:

- Maximize the anabolic and fat burning effects of exercise.
- Maximize protein synthesis and decreases muscle breakdown during training and anytime it's used.
- Maximize energy for training through both anaerobic (maximizing ATP and phosphocreatine levels in muscle tissue thus increasing anaerobic stamina and power) and aerobic pathways (maximizing TCA cycle flux by providing anapleurotic amino acids, increasing gluconeogenesis, and maximizing the use of fat as the primary aerobic fuel).
- Decrease both peripheral and central fatigue.
- Replace and replenish nutrients and fluid lost through exercise.
- Prevent muscle cramps.
- Increase training time and efficiency.
- And Enhance recovery.

EXERSOL

A Three-Phase Workout System for The Power and Endurance Athlete



Exersol is the most advanced, three-phase exercise-orientated nutritional support system ever formulated. Exersol gives you the peace of mind that comes with knowing you have everything you could possibly ever need to maximize the anabolic and fat burning effects of exercise. Exersol allows you to train harder and more effectively, making the training you do before, during and after, that much more productive.

Those who want to maximize the anabolic and fat burning effects of exercise should also look at [Exersol](#), the EXERCISE SOLUTION, which includes [Resolve](#), [Power Drink](#) and [Amino](#).

References:

- ¹ Beelen M, Koopman R, Gijsen AP, Vandereydt H, Kies AK, Kuipers H, Saris WH, van Loon LJ. Protein coingestion stimulates muscle protein synthesis during resistance-type exercise. *Am J Physiol Endocrinol Metab*. 2008 Jul;295(1):E70-7.
- ² Gualano AB, Bozza T, Lopes De Campos P, Roschel H, Dos Santos Costa A, Luiz Marquezi M, Benatti F, Herbert Lancha Junior A. Branched-chain amino acids supplementation enhances exercise capacity and lipid oxidation during endurance exercise after muscle glycogen depletion. *J Sports Med Phys Fitness*. 2011 Mar;51(1):82-8.
- ³ Hulston CJ, Venables MC, Mann CH, Martin C, Philp A, Baar K, Jeukendrup AE. Training with low muscle glycogen enhances fat metabolism in well-trained cyclists. *Med Sci Sports Exerc*. 2010 Nov;42(11):2046-55.
- ⁴ Drust B, Morton JP. Promoting Endurance Training Adaptations with Nutritional Interventions: The Potential Benefits of "Low Carbohydrate" Training. *Kinesiology* 2009; 41: 19-24.
- ⁵ Hawley JA, Burke LM. Carbohydrate availability and training adaptation: effects on cell metabolism. *Exerc Sport Sci Rev*. 2010 Oct;38(4):152-60.
- ⁶ Norton LE, Wilson GJ, Moulton CJ, Layman DK (2017) Meal distribution of dietary protein and leucine influences long term muscle mass and body composition in adult rats. *J Nutr* 147:195–201
- ⁷ Katsanos CS, Kobayashi H, Sheffield-Moore M, Aarsland A, Wolfe RR. A high proportion of leucine is required for optimal stimulation of the rate of muscle protein synthesis by essential amino acids in the elderly. *Am J Physiol Endocrinol Metab* 2006;291:E381–7.
- ⁸ Xu ZR, Tan ZJ, Zhang Q, Gui QF, Yang YM. The effectiveness of leucine on muscle protein synthesis, lean body mass and leg lean mass accretion in older people: a systematic review and meta-analysis. *Br J Nutr*. 2015 Jan 14;113(1):25-34.
- ⁹ Xu D, Shimkus KL, Lacko HA, Kutzler L, Jefferson LS, Kimball SR. Evidence for a role for Sestrin1 in mediating leucine-induced activation of mTORC1 in skeletal muscle. *Am J Physiol Endocrinol Metab*. 2019 May 1;316(5):E817-E828.
- ¹⁰ Harris RA, Joshi M, Jeoung NH. Mechanisms responsible for regulation of branched-chain amino acid catabolism. *Biochem Biophys Res Commun* 2004;313:391– 6.
- ¹¹ Shimomura Y, Murakami T, Nakai N, Nagasaki M, Harris RA. Exercise promotes BCAA catabolism: effects of BCAA supplementation on skeletal muscle during exercise. *J Nutr* 2004;134:1583–7.
- ¹² Paxton R, Harris RA. Regulation of branched-chain -ketoacid dehydrogenase kinase. *Arch Biochem Biophys* 1984;231:48 –57.
- ¹³ Laviano A, Molino A, Lacaria MT, Canelli A, De Leo S, Preziosa I, Rossi Fanelli F. Glutamine supplementation favors weight loss in nondieting obese female patients. A pilot study. *Eur J Clin Nutr*. 2014 Nov;68(11):1264-6.
- ¹⁴ Legault Z, Bagnall N, Kimmerly DS. The Influence of Oral L-Glutamine Supplementation on Muscle Strength Recovery and Soreness Following Unilateral Knee Extension Eccentric Exercise. *Int J Sport Nutr Exerc Metab*. 2015 Oct;25(5):417-26.
- ¹⁵ Phillips GC. Glutamine: the nonessential amino acid for performance enhancement. *Curr Sports Med Rep* 2007; 6: 265-8.
- ¹⁶ Koo GH, Woo J, Kang S, Shin KO. Effects of Supplementation with BCAA and L-glutamine on Blood Fatigue Factors and Cytokines in Juvenile Athletes Submitted to Maximal Intensity Rowing Performance. *J Phys Ther Sci*. 2014 Aug;26(8):1241-6.
- ¹⁷ Cruzat VF, Bittencourt A, Scomazzon SP, Leite JS, de Bittencourt PI Jr, Tirapegui J. Oral free and dipeptide forms of glutamine supplementation attenuate oxidative stress and inflammation induced by endotoxemia. *Nutrition*. 2014 May;30(5):602-11.
- ¹⁸ Abboud KY, Reis SK, Martelli ME, Zordão OP, Tannahão F, de Souza AZZ, Assalin HB, Guadagnini D, Rocha GZ, Saad MJA, Prada PO. Oral Glutamine Supplementation Reduces Obesity, Pro-

- Inflammatory Markers, and Improves Insulin Sensitivity in DIO Wistar Rats and Reduces Waist Circumference in Overweight and Obese Humans. *Nutrients*. 2019 Mar 1;11(3). pii: E536.
- ¹⁹ Freitas HR. Glutamine in Sport and Exercise. *International Journal of Medical and Biological Frontiers* Hauppauge 2016; 22.4 :277-291.
- ²⁰ Abboud KY, Reis SK, Martelli ME, Zordão OP, Tannah F, de Souza AZZ, Assalin HB, Guadagnini D, Rocha GZ, Saad MJA, Prada PO. Oral Glutamine Supplementation Reduces Obesity, Pro-Inflammatory Markers, and Improves Insulin Sensitivity in DIO Wistar Rats and Reduces Waist Circumference in Overweight and Obese Humans. *Nutrients*. 2019 Mar 1;11(3). pii: E536.
- ²¹ Tashiro S, Ammonia production in the nerve fiber during excitation. *Am. J. Physiol*; 1922:60, 519–543.
- ²² Bassini-Cameron, A., Monteiro, A., Gomes, A., Werneck-de-Castro, J., & Cameron, L. Glutamine protects against increases in blood ammonia in football players in an exercise intensity-dependent way. *British Journal of Sports Medicine* 2008; 42(4):260-266.
- ²³ Merhi A, Delrée P, Marini AM. The metabolic waste ammonium regulates mTORC2 and mTORC1 signaling. *Sci Rep*. 2017 Mar 17;7:44602.
- ²⁴ Lanks KW. Metabolite regulation of heat shock protein levels. *Proc Natl Acad Sci U S A*. 1983 Sep;80(17):5325-9.
- ²⁵ Petry ER, Cruzat VF, Heck TG, Homem de Bittencourt PI Jr, Tirapegui J. L-glutamine supplementations enhance liver glutamine-glutathione axis and heat shock factor-1 expression in endurance-exercise trained rats. *Int J Sport Nutr Exerc Metab*. 2015 Apr;25(2):188-97.
- ²⁶ Petry ER, Cruzat VF, Heck TG, Homem de Bittencourt PI Jr, Tirapegui J. L-glutamine supplementations enhance liver glutamine-glutathione axis and heat shock factor-1 expression in endurance-exercise trained rats. *Int J Sport Nutr Exerc Metab*. 2015 Apr;25(2):188-97.
- ²⁷ Leite, J.S.M., Cruzat, V.F., Krause, M. et al. *Nutrire* (2016) 41: 17. doi:10.1186/s41110-016-0021-y
- ²⁸ Zscheischler J, Seneviratne S. Dependence of drivers affects risks associated with compound events. *Science Advances*, 2017; 3:e1700263 DOI: 10.1126/sciadv.1700263
- ²⁹ Zuhl MN, Lanphere KR, Kravitz L, Mermier CM, Schneider S, Dokladny K, Moseley PL. Effects of oral glutamine supplementation on exercise-induced gastrointestinal permeability and tight junction protein expression. *J Appl Physiol* (1985). 2014 Jan 15;116(2):183-91.
- ³⁰ Zuhl M, Dokladny K, Mermier C, Schneider S, Salgado R, Moseley P. The effects of acute oral glutamine supplementation on exercise-induced gastrointestinal permeability and heat shock protein expression in peripheral blood mononuclear cells. *Cell Stress Chaperones*. 2015 Jan;20(1):85-93.
- ³¹ Moura CS, Lollo PCB, Morato PN, Amaya-Farfan J. Dietary Nutrients and Bioactive Substances Modulate Heat Shock Protein (HSP) Expression: A Review. *Nutrients*. 2018 May 28;10(6).
- ³² James L. Milk protein and the restoration of fluid balance after exercise. *Med Sport Sci*. 2012;59:120-6.
- ³³ de Moura CS, Lollo PC, Morato PN, Carneiro EM, Amaya-Farfan J. Whey protein hydrolysate enhances the exercise-induced heat shock protein (HSP70) response in rats. *Food Chem*. 2013 Feb 15;136(3-4):1350-7.
- ³⁴ Jang HJ, Kwak JH, Cho EY, We YM, Lee YH, Kim SC, Han DJ. Glutamine induces heat-shock protein-70 and glutathione expression and attenuates ischemic damage in rat islets. *Transplant Proc*. 2008 Oct;40(8):2581-4.
- ³⁵ Petry ER, Cruzat VF, Heck TG, Leite JS, Homem de Bittencourt PI Jr, Tirapegui J. Alanine-glutamine and glutamine plus alanine supplements improve skeletal redox status in trained rats: involvement of heat shock protein pathways. *Life Sci*. 2014 Jan 17;94(2):130-6.
- ³⁶ Cruzat VF, Pantaleão LC, Donato J Jr, de Bittencourt PI Jr, Tirapegui J. Oral supplementations with free and dipeptide forms of L-glutamine in endotoxemic mice: effects on muscle glutamine-glutathione axis and heat shock proteins. *J Nutr Biochem*. 2014 Mar;25(3):345-52.
- ³⁷ Raizel R, Leite JS, Hypólito TM, Coqueiro AY, Newsholme P, Cruzat VF, Tirapegui J. Determination of the anti-inflammatory and cytoprotective effects of L-glutamine and L-alanine, or

- dipeptide, supplementation in rats submitted to resistance exercise. *Br J Nutr.* 2016 Aug;116(3):470-9.
- ³⁸ Zhang B, Lin M, Yu C, Li J, Zhang L, Zhou P, Yang W, Gao F, Zhou G. Alanyl-glutamine supplementation regulates mTOR and ubiquitin proteasome proteolysis signaling pathways in piglets. *Nutrition.* 2016 Oct;32(10):1123-31.
- ³⁹ Petry ÉR, Cruzat VF, Heck TG, Homem de Bittencourt PI Jr, Tirapegui J. L-glutamine supplementations enhance liver glutamine-glutathione axis and heat shock factor-1 expression in endurance-exercise trained rats. *Int J Sport Nutr Exerc Metab.* 2015 Apr;25(2):188-97.
- ⁴⁰ Leite JS, Raizel R, Hypólito TM, Rosa TD, Cruzat VF, Tirapegui J. L-glutamine and L-alanine supplementation increase glutamine-glutathione axis and muscle HSP-27 in rats trained using a progressive high-intensity resistance exercise. *Appl Physiol Nutr Metab.* 2016 Aug;41(8):842-849.
- ⁴¹ Petry ER, Cruzat VF, Heck TG, Leite JSM, Homem de Bittencourt Jr PI, Tirapegui J. Alanyl-glutamine and glutamine plus alanine supplements improve skeletal redox status in trained rats: involvement of heat shock protein pathways. *Life Sci.* 2014;94(2):130–6.
- ⁴² Girven M, Dugdale HF, Owens DJ, Hughes DC, Stewart CE, Sharples AP. L-glutamine Improves Skeletal Muscle Cell Differentiation and Prevents Myotube Atrophy After Cytokine (TNF- α) Stress Via Reduced p38 MAPK Signal Transduction. *J Cell Physiol.* 2016 Dec;231(12):2720-32.
- ⁴³ Favano A, Santos-Silva PR, Nakano EY, Pedrinelli A, Hernandez AJ, Greve JM. Peptide glutamine supplementation for tolerance of intermittent exercise in soccer players. *Clinics (Sao Paulo).* 2008 Feb;63(1):27-32.
- ⁴⁴ Sasaki E, Umeda T, Takahashi I, Arata K, Yamamoto Y, Tanabe M, Oyamada K, Hashizume E, Nakaji S. Effect of glutamine supplementation on neutrophil function in male judoists. *Luminescence.* 2013 Jul-Aug;28(4):442-9.
- ⁴⁵ Freitas HR, da Silva PA, da Silva RT. (2015). The effects of acute/chronic glutamine and glutamine peptide supplementation on the performance and immune function in young active adult athletes. *Current Nutrition and Food Science*, 11 (4), 315-322.
- ⁴⁶ Freitas HR. Glutamine in Sport and Exercise. *International Journal of Medical and Biological Frontiers* Hauppauge 2016; 22.4 :277-291.
- ⁴⁷ Timbrell JA, Seabra V, Waterfield CJ. The in vivo and in vitro protective properties of taurine. *Gen Pharmacol.* 1995 May;26(3):453-62.
- ⁴⁸ Thirupathi A, Freitas S, Sorato HR, Pedroso GS, Effting PS, Damiani AP, Andrade VM, Nesi RT, Gupta RC, Muller AP, Pinho RA. Modulatory effects of taurine on metabolic and oxidative stress parameters in a mice model of muscle overuse. *Nutrition.* 2018 Oct;54:158-164.
- ⁴⁹ Scicchitano BM, Sica G. The Beneficial Effects of Taurine to Counteract Sarcopenia. *Curr Protein Pept Sci.* 2018;19(7):673-680.
- ⁵⁰ Ripps H, Shen W. Review: taurine: a "very essential" amino acid. *RMol Vis.* 2012;18:2673-86.
- ⁵¹ Murakami S1. Role of taurine in the pathogenesis of obesity. *Mol Nutr Food Res.* 2015 Jul;59(7):1353-63. doi: 10.1002/mnfr.201500067.
- ⁵² Scicchitano BM, Sica G. The Beneficial Effects of Taurine to Counteract Sarcopenia. *Curr Protein Pept Sci.* 2018;19(7):673-680.
- ⁵³ Khalil RM, Abdo WS, Saad A, Khedr EG. Muscle proteolytic system modulation through the effect of taurine on mice bearing muscular atrophy. *Mol Cell Biochem.* 2018 Jul;444(1-2):161-168.
- ⁵⁴ Laidlaw SA, Shultz TD, Cecchino JT, Kopple JD. Plasma and urine taurine levels in vegans. *Am J Clin Nutr.* 1988 Apr;47(4):660-3.
- ⁵⁵ Dwyer JT. Nutritional consequences of vegetarianism. *Annu Rev Nutr.* 1991;11:61-91.
- ⁵⁶ Hunt JR. Bioavailability of iron, zinc, and other trace minerals from vegetarian diets. *Am J Clin Nutr.* 2003 Sep;78(3 Suppl):633S-639S.
- ⁵⁷ Plotnikoff GA. Nutritional assessment in vegetarians and vegans: questions clinicians should ask. *Minn Med.* 2012 Dec;95(12):36-8.

-
- ⁵⁸ Seidel U, Huebbe P, Rimbach G. Taurine: A Regulator of Cellular Redox Homeostasis and Skeletal Muscle Function. *Mol Nutr Food Res*. 2018 Sep 13:e1800569.
- ⁵⁹ Chupel MU, Minuzzi LG, Furtado G, Santos ML, Hogervorst E, Filaire E, Teixeira AM. Exercise and taurine in inflammation, cognition, and peripheral markers of blood-brain barrier integrity in older women. *Appl Physiol Nutr Metab*. 2018 Jul;43(7):733-741.
- ⁶⁰ Rutherford JA, Spriet LL, Stellingwerff T. The effect of acute taurine ingestion on endurance performance and metabolism in well-trained cyclists. *Int J Sport Nutr Exerc Metab*. 2010 Aug;20(4):322-9.
- ⁶¹ Balshaw TG, Bampouras TM, Barry TJ, Sparks SA. The effect of acute taurine ingestion on 3-km running performance in trained middle-distance runners. *Amino Acids*. 2013 Feb;44(2):555-61.
- ⁶² Ahmadian M, Roshan VD, Aslani E, Stannard SR. Taurine supplementation has anti-atherogenic and anti-inflammatory effects before and after incremental exercise in heart failure. *Ther Adv Cardiovasc Dis*. 2017 Jul;11(7):185-194.
- ⁶³ De Carvalho FG, Galan BSM, Santos PC, Pritchett K, Pfrimer K, Ferriolli E, Papoti M, Marchini JS, de Freitas EC. Taurine: A Potential Ergogenic Aid for Preventing Muscle Damage and Protein Catabolism and Decreasing Oxidative Stress Produced by Endurance Exercise. *Front Physiol*. 2017 Sep 20;8:710. doi: 10.3389/fphys.2017.00710. eCollection 2017.
- ⁶⁴ Thirupathi A, Freitas S, Sorato HR, Pedroso GS, Eftting PS, Damiani AP, Andrade VM, Nesi RT, Gupta RC, Muller AP, Pinho RA. Modulatory effects of taurine on metabolic and oxidative stress parameters in a mice model of muscle overuse. *Nutrition*. 2018 Oct;54:158-164.
- ⁶⁵ McLeay Y, Stannard S, Barnes M. The Effect of Taurine on the Recovery from Eccentric Exercise-Induced Muscle Damage in Males. *Antioxidants (Basel)*. 2017 Oct 17;6(4). pii: E79.
- ⁶⁶ Marcinkiewicz J, Kontny E. Taurine and inflammatory diseases. *Amino Acids*. 2014 Jan;46(1):7-20.
- ⁶⁷ Ra SG, Miyazaki T, Ishikura K, Nagayama H, Suzuki T, Maeda S, Ito M, Matsuzaki Y, Ohmori H. Additional effects of taurine on the benefits of BCAA intake for the delayed-onset muscle soreness and muscle damage induced by high-intensity eccentric exercise. *Adv Exp Med Biol*. 2013;776:179-87.
- ⁶⁸ Kato T, Okita S, Wang S, Tsunekawa M, Ma N. The effects of taurine administration against inflammation in heavily exercised skeletal muscle of rats. *Adv Exp Med Biol*. 2015;803:773-84.
- ⁶⁹ De Carvalho FG, Barbieri RA, Carvalho MB, Dato CC, Campos EZ, Gobbi RB, Papoti M, Silva ASR, de Freitas EC. Taurine supplementation can increase lipolysis and affect the contribution of energy systems during front crawl maximal effort. *Amino Acids*. 2018 Jan;50(1):189-198.
- ⁷⁰ Ra SG, Akazawa N, Choi Y, Matsubara T, Oikawa S, Kumagai H, Tanahashi K, Ohmori H, Maeda S. Taurine supplementation reduces eccentric exercise-induced delayed onset muscle soreness in young men. *Adv Exp Med Biol*. 2015;803:765-72.
- ⁷¹ Manabe S, Kurroda I, Okada K, Morishima M, Okamoto M, Harada N, Takahashi A, Sakai K, Nakaya Y. Decreased blood levels of lactic acid and urinary excretion of 3-methylhistidine after exercise by chronic taurine treatment in rats. *J Nutr Sci Vitaminol (Tokyo)*. 2003 Dec;49(6):375-80.
- ⁷² Horvath DM, Murphy RM, Mollica JP, Hayes A, Goodman CA. The effect of taurine and β -alanine supplementation on taurine transporter protein and fatigue resistance in skeletal muscle from mdx mice. *Amino Acids*. 2016 Nov;48(11):2635-2645.
- ⁷³ Pierno S, De Luca A, Camerino C, Huxtable RJ, Camerino DC. Chronic administration of taurine to aged rats improves the electrical and contractile properties of skeletal muscle fibers. *J Pharmacol Exp Ther*. 1998 Sep;286(3):1183-90.
- ⁷⁴ Dawson Jr R, Biasetti M, Messina S, Dominy J. The cytoprotective role of taurine in exercise-induced muscle injury. *Amino Acids* 2002;22(4):309-24.
- ⁷⁵ Beyranvand MR, Kadkhodai Khalafi M, Roshan VD, Choobineh S, Parsa SA, Piranfar MA. Effect of taurine supplementation on exercise capacity of patients with heart failure. *J Cardiol*. 2011 May;57(3):333-7.

- ⁷⁶ Silva LA, Silveira PC, Ronsani MM, Souza PS, Scheffer D, Vieira LC, Benetti M, De Souza CT, Pinho RA. Taurine supplementation decreases oxidative stress in skeletal muscle after eccentric exercise. *Cell Biochem Funct.* 2011 Jan-Feb;29(1):43-9. doi: 10.1002/cbf.1716.
- ⁷⁷ Zhang M, Izumi I, Kagamimori S, Sokejima S, Yamagami T, Liu Z, Qi B. Role of taurine supplementation to prevent exercise-induced oxidative stress in healthy young men. *Amino Acids.* 2004 Mar;26(2):203-7.
- ⁷⁸ Sugiura H, Okita S, Kato T, Naka T, Kawanishi S, Ohnishi S, Oshida Y, Ma N. Protection by taurine against INOS-dependent DNA damage in heavily exercised skeletal muscle by inhibition of the NF- κ B signaling pathway. *Adv Exp Med Biol.* 2013;775:237-46.
- ⁷⁹ Fraser SF, Li JL, Carey MF, Wang XN, Sangkabutra T, Sostaric S, Selig SE, Kjeldsen K, McKenna MJ. Fatigue depresses maximal in vitro skeletal muscle Na(+)-K(+)-ATPase activity in untrained and trained individuals. *J Appl Physiol* 2002 Nov;93(5):1650-9.
- ⁸⁰ Li JL, Wang XN, Fraser SF, Carey MF, Wrigley TV, McKenna MJ. Effects of fatigue and training on sarcoplasmic reticulum Ca(2+) regulation in human skeletal muscle. *J Appl Physiol* 2002;92(3):912-22.
- ⁸¹ Rutherford JA, Spriet LL, Stellingwerff T. The effect of acute taurine ingestion on endurance performance and metabolism in well-trained cyclists. *Int J Sport Nutr Exerc Metab.* 2010 Aug;20(4):322-9.
- ⁸² Waldron M, Patterson SD, Tallent J, Jeffries O. The Effects of an Oral Taurine Dose and Supplementation Period on Endurance Exercise Performance in Humans: A Meta-Analysis. *Sports Med.* 2018 May;48(5):1247-1253.
- ⁸³ Lim ZIX, Singh A, Leow ZZX, Arthur PG, Fournier PA. The Effect of Acute Taurine Ingestion on Human Maximal Voluntary Muscle Contraction. *Med Sci Sports Exerc.* 2018 Feb;50(2):344-352.
- ⁸⁴ De Carvalho FG, Barbieri RA, Carvalho MB, Dato CC, Campos EZ, Gobbi RB, Papoti M, Silva ASR, de Freitas EC. Taurine supplementation can increase lipolysis and affect the contribution of energy systems during front crawl maximal effort. *Amino Acids.* 2018 Jan;50(1):189-198.
- ⁸⁵ Yatabe Y, Miyakawa S, Ohmori H, Mishima H, Adachi T. Effects of taurine administration on exercise. *Adv Exp Med Biol.* 2009;643:245-52.
- ⁸⁶ Goodman CA, Horvath D, Stathis C, Mori T, Croft K, Murphy RM, Hayes A. Taurine supplementation increases skeletal muscle force production and protects muscle function during and after high-frequency in vitro stimulation. *J Appl Physiol.* 2009 Jul;107(1):144-54.
- ⁸⁷ Manna P, Sinha M, Sil PC. Cadmium induced testicular pathophysiology: prophylactic role of taurine. *Reprod Toxicol.* 2008 Nov-Dec;26(3-4):282-91.
- ⁸⁸ Yang J, Wu G, Feng Y, Sun C, Lin S, Hu J. CSD mRNA expression in rat testis and the effect of taurine on testosterone secretion. *Amino Acids.* 2010 Jun;39(1):155-60.
- ⁸⁹ Yang J, Wu G, Feng Y, Lv Q, Lin S, Hu J. Effects of taurine on male reproduction in rats of different ages. *J Biomed Sci.* 2010 Aug 24;17 Suppl 1:S9.
- ⁹⁰ Yang J, Lin S, Feng Y, Wu G, Hu J. Taurine enhances the sexual response and mating ability in aged male rats. *Adv Exp Med Biol.* 2013;776:347-55.
- ⁹¹ Das J, Ghosh J, Manna P, Sil PC. Taurine protects rat testes against doxorubicin-induced oxidative stress as well as p53, Fas and caspase 12-mediated apoptosis. *Amino Acids.* 2012 May;42(5):1839-55.
- ⁹² Manna P, Sinha M, Sil PC. Cadmium induced testicular pathophysiology: prophylactic role of taurine. *Reprod Toxicol.* 2008 Nov-Dec;26(3-4):282-91.
- ⁹³ Yang J, Wu G, Feng Y, Sun C, Lin S, Hu J. CSD mRNA expression in rat testis and the effect of taurine on testosterone secretion. *Amino Acids.* 2010 Jun;39(1):155-60.
- ⁹⁴ Yang J, Wu G, Feng Y, Lv Q, Lin S, Hu J. Effects of taurine on male reproduction in rats of different ages. *J Biomed Sci.* 2010 Aug 24;17 Suppl 1:S9.
- ⁹⁵ Yang J, Lin S, Feng Y, Wu G, Hu J. Taurine enhances the sexual response and mating ability in aged male rats. *Adv Exp Med Biol.* 2013;776:347-55.

- ⁹⁶ Das J, Ghosh J, Manna P, Sil PC. Taurine protects rat testes against doxorubicin-induced oxidative stress as well as p53, Fas and caspase 12-mediated apoptosis. *Amino Acids*. 2012 May;42(5):1839-55.
- ⁹⁷ Yang J, Zong X, Wu G, Lin S, Feng Y, Hu J. Taurine increases testicular function in aged rats by inhibiting oxidative stress and apoptosis. *Amino Acids*. 2015 Aug;47(8):1549-58.
- ⁹⁸ Adedara IA, Olabiyi BF, Ojuade TD, Idris UF, Onibiyo EM, Farombi EO. Taurine reverses sodium fluoride-mediated increase in inflammation, caspase-3 activity, and oxidative damage along the brain-pituitary-gonadal axis in male rats. *Can J Physiol Pharmacol*. 2017 Sep;95(9):1019-1029.
- ⁹⁹ Ra SG, Miyazaki T, Ishikura K, Nagayama H, Suzuki T, Maeda S, Ito M, Matsuzaki Y, Ohmori H. Additional effects of taurine on the benefits of BCAA intake for the delayed-onset muscle soreness and muscle damage induced by high-intensity eccentric exercise. *Adv Exp Med Biol*. 2013;776:179-87.
- ¹⁰⁰ Everaert I, Stegen S, Vanheel B, Taes Y, Derave W. Effect of beta-alanine and carnosine supplementation on muscle contractility in mice. *Med Sci Sports Exerc*. 2013 Jan;45(1):43-51.
- ¹⁰¹ Cozzi R, Ricordy R, Bartolini F, Ramadori L, Perticone P and de Salvia R (). Taurine and ellagic acid: two differently-acting natural antioxidants. *Environmental and Molecular Mutagenesis* 1995; 26:248-254.
- ¹⁰² Lourenco R, Camilo ME. Taurine: a conditionally essential amino acid in humans? An overview in health and disease. *Nutr Hosp*. 2002 Nov-Dec;17(6):262-70.
- ¹⁰³ Schaffer S, Azuma J, Takahashi K, Mozaffari M. Why is taurine cytoprotective? *Adv Exp Med Biol*. 2003;526:307-21.
- ¹⁰⁴ Bidri M, Choay P. Taurine: a particular aminoacid with multiple functions. *Ann Pharm Fr*. 2003 Nov;61(6):385-91.
- ¹⁰⁵ Kinane DF, Stathopoulou PG, Papapanou PN. Periodontal diseases. *Nat Rev Dis Primers*. 2017 Jun 22;3:17038.
- ¹⁰⁶ Chaudhry S, Tandon B, Gupta A, Gupta S. Taurine: A potential mediator for periodontal therapy. *Indian J Dent Res*. 2018 Nov-Dec;29(6):808-811.
- ¹⁰⁷ Pierno S, Liantonio A, Camerino GM, De Bellis M, Cannone M, Gramegna G, Scaramuzzi A, Simonetti S, Nicchia GP, Basco D, Svelto M, Desaphy JF, Camerino DC. Potential benefits of taurine in the prevention of skeletal muscle impairment induced by disuse in the hindlimb-unloaded rat. *Amino Acids*. 2012 Jul;43(1):431-45.
- ¹⁰⁸ De Luca A, Pierno S, Camerino DC. Taurine: the appeal of a safe amino acid for skeletal muscle disorders. *J Transl Med*. 2015 Jul 25;13:243.
- ¹⁰⁹ Schaffer SW, Jong CJ, Ramila KC, Azuma J. Physiological roles of taurine in heart and muscle. *J Biomed Sci*. 2010 Aug 24; 17: Suppl 1:S2.
- ¹¹⁰ Fujihira E, Takahashi H, Nakazawa M () Effect of long-term feeding of taurine in hereditary hyperglycemic obese mice. *Chem Pharm Bull* 1970; 18: 1636–42.
- ¹¹¹ Zhang M, Bi LF, Fang JH, Su XL, Da GL, Kuwamori T, Kagamimori S. Beneficial effects of taurine on serum lipids in overweight or obese non-diabetic subjects. *Amino Acids*. 2004 Jun;26(3):267-71.
- ¹¹² Rosa FT, Freitas EC, Deminice R, Jordão AA, Marchini JS (2014) Oxidative stress and inflammation in obesity after taurine supplementation: a double-blind, placebo-controlled study. *Eur J Nutr* 53(3):823–830.
- ¹¹³ de Almeida Martiniano AC, De Carvalho FG, Marchini JS, Garcia SB, Júnior JE, Mauad FM, da Silva AS, de Moraes C, de Freitas EC. Effects of taurine supplementation on adipose tissue of obese trained rats. *Adv Exp Med Biol*. 2015;803:707-14.
- ¹¹⁴ De Carvalho FG, Galan BSM, Santos PC, Pritchett K, Pfrimer K, Ferriolli E, Papoti M, Marchini JS, de Freitas EC. Taurine: A Potential Ergogenic Aid for Preventing Muscle Damage and Protein Catabolism and Decreasing Oxidative Stress Produced by Endurance Exercise. *Front Physiol*. 2017 Sep 20;8:710.

- ¹¹⁵ De Carvalho FG, Barbieri RA, Carvalho MB, Dato CC, Campos EZ, Gobbi RB, Papoti M, Silva ASR, de Freitas EC. Taurine supplementation can increase lipolysis and affect the contribution of energy systems during front crawl maximal effort. *Amino Acids*. 2018 Jan;50(1):189-198.
- ¹¹⁶ Paulucio D, Costa BM, Santos CGM, Nogueira F, Koch A, Machado M, Velasques B, Ribeiro P, Pompeu FA. Taurine supplementation improves economy of movement in the cycle test independently of the detrimental effects of ethanol. *Biol Sport*. 2017 Dec;34(4):353-359.
- ¹¹⁷ Rosa FT, Freitas EC, Deminice R, Jordão AA, Marchini JS (2014) Oxidative stress and inflammation in obesity after taurine supplementation: a double-blind, placebo-controlled study. *Eur J Nutr* 53(3):823–830.
- ¹¹⁸ de Almeida Martiniano AC, De Carvalho FG, Marchini JS, Garcia SB, Júnior JE, Mauad FM, da Silva AS, de Moraes C, de Freitas EC. Effects of taurine supplementation on adipose tissue of obese trained rats. *Adv Exp Med Biol*. 2015;803:707-14.
- ¹¹⁹ De Carvalho FG, Galan BSM, Santos PC, Pritchett K, Pfrimer K, Ferriolli E, Papoti M, Marchini JS, de Freitas EC. Taurine: A Potential Ergogenic Aid for Preventing Muscle Damage and Protein Catabolism and Decreasing Oxidative Stress Produced by Endurance Exercise. *Front Physiol*. 2017 Sep 20;8:710.
- ¹²⁰ De Carvalho FG, Barbieri RA, Carvalho MB, Dato CC, Campos EZ, Gobbi RB, Papoti M, Silva ASR, de Freitas EC. Taurine supplementation can increase lipolysis and affect the contribution of energy systems during front crawl maximal effort. *Amino Acids*. 2018 Jan;50(1):189-198.
- ¹²¹ Paulucio D, Costa BM, Santos CGM, Nogueira F, Koch A, Machado M, Velasques B, Ribeiro P, Pompeu FA. Taurine supplementation improves economy of movement in the cycle test independently of the detrimental effects of ethanol. *Biol Sport*. 2017 Dec;34(4):353-359.
- ¹²² Chupel MU, Minuzzi LG, Furtado GE, Santos ML, Ferreira JP, Filaire E, Teixeira AM. Taurine supplementation reduces myeloperoxidase and matrix-metalloproteinase-9 levels and improves the effects of exercise in cognition and physical fitness in older women. *Amino Acids*. 2021 Mar;53(3):333-345. doi: 10.1007/s00726-021-02952-6. Epub 2021 Feb 13. PMID: 33586039.
- ¹²³ Chen Q, Li Z, Pinho RA, Gupta RC, Ugbole UC, Thirupathi A, Gu Y. The Dose Response of Taurine on Aerobic and Strength Exercises: A Systematic Review. *Front Physiol*. 2021 Aug 18;12:700352. doi: 10.3389/fphys.2021.700352. PMID: 34497536; PMCID: PMC8419774.
- ¹²⁴ Miyazaki T, Nakamura-Shinya Y, Ebina K, Komine S, Ra SG, Ishikura K, Ohmori H, Honda A. N-acetyltaurine and Acetylcarnitine Production for the Mitochondrial Acetyl-CoA Regulation in Skeletal Muscles during Endurance Exercises. *Metabolites*. 2021 Aug 6;11(8):522. doi: 10.3390/metabo11080522. PMID: 34436463; PMCID: PMC8401229.
- ¹²⁵ Han J, Bae JH, Kim SY, Lee HY, Jang BC, Lee IK, Cho CH, Lim JG, Suh SI, Kwon TK, Park JW, Ryu SY, Ho WK, Earm YE, Song DK. Taurine increases glucose sensitivity of UCP2-overexpressing beta-cells by ameliorating mitochondrial metabolism. *Am J Physiol Endocrinol Metab*. 2004 Nov;287(5):E1008-18.
- ¹²⁶ Hansen SH, Birkedal H, Wibrand F, Grunnet N. Taurine and regulation of mitochondrial metabolism. *Adv Exp Med Biol*. 2015;803:397-405.
- ¹²⁷ Lambert IH: Regulation of the cellular content of the organic osmolyte taurine in mammalian cells. *Neurochem Res* 2004; 29:27–63.
- ¹²⁸ Bouckenoghe T, Remacle C, Reusens B. Is taurine a functional nutrient? *Curr Opin Clin Nutr Metab Care*. 2006 Nov;9(6):728-33.
- ¹²⁹ Conte Camerino D, Tricarico D, Pierno S, Desaphy JF, Liantonio A, Pusch M, Burdi R, Camerino C, Frayssé B, De Luca A. Taurine and skeletal muscle disorders. *Neurochem Res*. 2004 Jan;29(1):135-42.
- ¹³⁰ Haussinger D. Control of protein turnover by the cellular hydration state. *Ital J Gastroenterol* 1993 Jan;25(1):42-8.
- ¹³¹ Waldegger S, Busch GL, Kaba NK, Zempel G, Ling H, Heidland A, Haussinger D, Lang F. Effect of cellular hydration on protein metabolism. *Miner Electrolyte Metab* 1997;23(3-6):201-5.

- ¹³² Pesantes-Morales H, Quesada O, Morán J. Taurine: An osmolyte in mammalian tissues. *Adv. Exp. Med. Biol.* 1998; 442:209–217.
- ¹³³ Hussy N, Deleuze C, Desarménien MG, Moos FC. Osmotic regulation of neuronal activity: a new role for taurine and glial cells in a hypothalamic neuroendocrine structure. *Prog Neurobiol.* 2000 Oct;62(2):113-34.
- ¹³⁴ Mashyakhy M, Alkahtani A, Abumelha AS, Sharroufna RJ, Alkahtany MF, Jamal M, Robaian A, Binalrimal S, Chohan H, Patil VR, Raj AT, Bhandi S, Reda R, Testarelli L, Patil S. Taurine Augments Telomerase Activity and Promotes Chondrogenesis in Dental Pulp Stem Cells. *J Pers Med.* 2021 May 31;11(6):491. doi: 10.3390/jpm11060491. PMID: 34072707.
- ¹³⁵ Felig P, Wahren J. Amino acid metabolism in exercising man. *J Clin Invest.* 1971;50(12):2703-14.
- ¹³⁶ Marquezi ML, Roschel HA, dos Santa Costa A, Sawada LA, Lancha AH Jr. Effect of aspartate and asparagine supplementation on fatigue determinants in intense exercise. *Int J Sport Nutr Exerc Metab.* 2003 Mar;13(1):65-75.
- ¹³⁷ Iapichino G, Ronzoni G, Bonetti G, Corti M, Grugni L, Guarnerio C, Palandi A, Pasetti G, Rotelli S, Savioli M. [Determination of the best amino acid input after orthotopic liver transplantation]. *Minerva Anestesiologica* 1992;58(9):503-8.
- ¹³⁸ Chilibeck PD, Stride D, Farthing JP, Burke DG. Effect of creatine ingestion after exercise on muscle thickness in males and females. *Med Sci Sports Exerc.* 2004 Oct;36(10):1781-8.
- ¹³⁹ Mendes RR, Pires I, Oliveira A, Tirapegui J. Effects of creatine supplementation on the performance and body composition of competitive swimmers. *J Nutr Biochem.* 2004 Aug;15(8):473-8.
- ¹⁴⁰ Volek JS, Rawson ES. Scientific basis and practical aspects of creatine supplementation for athletes. *Nutrition.* 2004 Jul-Aug;20(7-8):609-14.
- ¹⁴¹ Volek JS, Ratamess NA, Rubin MR, Gomez AL, French DN, McGuigan MM, Scheett TP, Sharman MJ, Hakkinen K, Kraemer WJ. The effects of creatine supplementation on muscular performance and body composition responses to short-term resistance training overreaching. *Eur J Appl Physiol.* 2004 May;91(5-6):628-37.
- ¹⁴² Kilduff LP, Pitsiladis YP, Tasker L, Attwood J, Hyslop P, Dailly A, Dickson I, Grant S. Effects of creatine on body composition and strength gains after 4 weeks of resistance training in previously nonresistance-trained humans. *Int J Sport Nutr Exerc Metab.* 2003 Dec;13(4):504-20.
- ¹⁴³ Kocak S, Karli U. Effects of high dose oral creatine supplementation on anaerobic capacity of elite wrestlers. *J Sports Med Phys Fitness.* 2003 Dec;43(4):488-92.
- ¹⁴⁴ Rawson ES, Volek JS. Effects of creatine supplementation and resistance training on muscle strength and weightlifting performance. *J Strength Cond Res.* 2003 Nov;17(4):822-31.
- ¹⁴⁵ Hespel P, Derave W. Ergogenic effects of creatine in sports and rehabilitation. *Subcell Biochem.* 2007;46:245-59.
- ¹⁴⁶ Willott CA, Young ME, Leighton B, Kemp GJ, Boehm EA, Radda GK, Clarke K. Creatine uptake in isolated soleus muscle: kinetics and dependence on sodium, but not on insulin. *Acta Physiol Scand.* 1999 Jun;166(2):99-104.
- ¹⁴⁷ Parkhouse WS, McKenzie DC. Possible contribution of skeletal muscle buffers to enhanced anaerobic performance: a brief review. *Med Sci Sports Exerc* 1984;16(4):328-338.
- ¹⁴⁸ Saunders B, Elliott-Sale K, Artioli GG, Swinton PA, Dolan E, Roschel H, Sale C, Gualano B. β -alanine supplementation to improve exercise capacity and performance: a systematic review and meta-analysis. *Br J Sports Med.* 2017 Apr;51(8):658-669.
- ¹⁴⁹ Saunders B, DE Salles Painelli V, DE Oliveira LF, DA Eira Silva V, DA Silva RP, Riani L, Franchi M, Gonçalves LS, Harris RC, Roschel H, Artioli GG, Sale C, Gualano B. Twenty-four Weeks of β -Alanine Supplementation on Carnosine Content, Related Genes, and Exercise. *Med Sci Sports Exerc.* 2017 May;49(5):896-906.
- ¹⁵⁰ Blancquaert L, Baba SP, Kwiatkowski S, Stautemas J, Stegen S, Barbaresi S, Chung W, Boakye AA, Hoetker JD, Bhatnagar A, Delanghe J, Vanheel B, Veiga-da-Cunha M, Derave W, Everaert I.

- Carnosine and anserine homeostasis in skeletal muscle and heart is controlled by β -alanine transamination. *J Physiol*. 2016 Sep 1;594(17):4849-63.
- ¹⁵¹ Bellinger PM, Minahan CL. The effect of β -alanine supplementation on cycling time trials of different length. *Eur J Sport Sci*. 2016 Oct;16(7):829-36.
- ¹⁵² de Andrade Kratz C, de Salles Painelli V, de Andrade Nemezio KM, da Silva RP, Franchini E, Zagatto AM, Gualano B, Artioli GG. Beta-alanine supplementation enhances judo-related performance in highly-trained athletes. *J Sci Med Sport*. 2017 Apr;20(4):403-408.
- ¹⁵³ Abbasoglu L, Kalaz EB, Soluk-Tekkesin M, Olgaç V, Dogru-Abbasoglu S, Uysal M. Beneficial effects of taurine and carnosine in experimental ischemia/reperfusion injury in testis. *Pediatr Surg Int*. 2012 Nov;28(11):1125-31.
- ¹⁵⁴ Bellia F, Vecchio G, Cuzzocrea S, Calabrese V, Rizzarelli E. Neuroprotective features of carnosine in oxidative driven diseases. *Mol Aspects Med*. 2011 Aug;32(4-6):258-66.
- ¹⁵⁵ Hipkiss AR, Cartwright SP, Bromley C, Gross SR, Bill RM. Carnosine: can understanding its actions on energy metabolism and protein homeostasis inform its therapeutic potential? *Chem Cent J*. 2013 Feb 25;7(1):38.
- ¹⁵⁶ Gross M, Boesch C, Bolliger CS, Norman B, Gustafsson T, Hoppeler H, Vogt M. Effects of beta-alanine supplementation and interval training on physiological determinants of severe exercise performance. *Eur J Appl Physiol*. 2014 Feb;114(2):221-34.
- ¹⁵⁷ Szczesniak D, Budzen S, Kopec W, Rymaszewska J. Anserine and carnosine supplementation in the elderly: Effects on cognitive functioning and physical capacity. *Arch Gerontol Geriatr*. 2014 Sep-Oct;59(2):485-90.
- ¹⁵⁸ Bellia F, Vecchio G, Cuzzocrea S, Calabrese V, Rizzarelli E. Neuroprotective features of carnosine in oxidative driven diseases. *Mol Aspects Med*. 2011 Aug;32(4-6):258-66.
- ¹⁵⁹ Nagai K, Suda T. Immunoregulative effects of carnosine and beta-alanine. *J. Physiol. Soc Jap* 1986;48:564-571.
- ¹⁶⁰ Boldyrev A, Johnson P. Carnosine and related compounds: antioxidant dipeptides. In: P. Johnson and A. Boldyrev, Editors, *Oxidative Stress at Molecular, Cellular and Organ Levels*, Res. Signpost 2002;101-114.
- ¹⁶¹ Hipkiss AR, Cartwright SP, Bromley C, Gross SR, Bill RM. Carnosine: can understanding its actions on energy metabolism and protein homeostasis inform its therapeutic potential? *Chem Cent J*. 2013 Feb 25;7(1):38.
- ¹⁶² Nagai K, Suda T, Kawasaki K, Mathuura S. Action of carnosine and beta-alanine on wound healing. *Surgery*. 1986;100(5):815-21.
- ¹⁶³ Wang AM, Ma C, Xie ZH, et al. Use of carnosine as a natural anti-senescence drug for human beings. *Biochemistry (Mosc)* 2000;65(7):869-71.
- ¹⁶⁴ Zakharchenko MV, Temnov AV, Kondrashova MN. Effect of carnosine on self-organization of mitochondrial assemblies in rat liver homogenate. *Biochemistry (Mosc)*. 2003;68(9):1002-5.
- ¹⁶⁵ Hipkiss AR. On the enigma of carnosine's anti-ageing actions. *Exp Gerontol*. 2009 Apr;44(4):237-42.
- ¹⁶⁶ Jukić I, Kolobarić N, Stupin A, Matić A, Kozina N, Mihaljević Z, Mihalj M, Šušnjara P, Stupin M, Ćurić ŽB, Selthofer-Relatić K, Kibel A, Lukinac A, Kolar L, Kralik G, Kralik Z, Széchenyi A, Jozanović M, Galović O, Medvidović-Kosanović M, Drenjančević I. Carnosine, Small but Mighty-Prospect of Use as Functional Ingredient for Functional Food Formulation. *Antioxidants (Basel)*. 2021 Jun 28;10(7):1037. doi: 10.3390/antiox10071037. PMID: 34203479; PMCID: PMC8300828.
- ¹⁶⁷ Blancquaert L, Everaert I, Baguet A, Bex T, Barbaresi S, de Jager S, Lievens E, Stautemas J, De Smet S, Baron G, Gilardoni E, Regazzoni L, Aldini G, Derave W. Acute preexercise supplementation of combined carnosine and anserine enhances initial maximal power of Wingate tests in humans. *J Appl Physiol (1985)*. 2021 Jun 1;130(6):1868-1878. doi: 10.1152/jappphysiol.00602.2020. Epub 2021 Apr 29. PMID: 33914660.

- ¹⁶⁸ Begum G, Cunliffe A, Leveritt M. Physiological role of carnosine in contracting muscle. *Int J Sport Nutr Exerc Metab.* 2005 Oct;15(5):493-514. Links
- ¹⁶⁹ Aydin F, Kalaz EB, Kucukgergin C, Coban J, Dogru-Abbasoglu S, Uysal M. Carnosine Treatment Diminished Oxidative Stress and Glycation Products in Serum and Tissues of D-Galactose-Treated Rats. *Curr Aging Sci.* 2018;11(1):10-15.
- ¹⁷⁰ Mirjana M, Jelena A, Aleksandra U, Svetlana D, Nevena G, Jelena M, Goran P, Melita V. Alpha-lipoic acid preserves the structural and functional integrity of red blood cells by adjusting the redox disturbance and decreasing O-GlcNAc modifications of antioxidant enzymes and heat shock proteins in diabetic rats. *Eur J Nutr.* 2012 Dec;51(8):975-86.
- ¹⁷¹ Stvolinsky SL, Dobrota D. Anti-ischemic activity of carnosine. *Biochemistry (Mosc).* 2000; 65(7):849-55.
- ¹⁷² Parkhouse WS, McKenzie DC, Hochachka PW, Ovalle WK. Buffering capacity of deproteinized human vastus lateralis muscle. *J Appl Physiol* 1985;58:14–17.
- ¹⁷³ Susuki Y, Ito O, Takahashi H, Takamatsu K (2004) The effect of sprint training on skeletal muscle carnosine in humans. *Int J Sport Health Sci* 2: 105–110.
- ¹⁷⁴ Tallon MJ, Harris RC, Boobis L, Fallowfield J, Wise JA (2005) The carnosine content of vastus lateralis is elevated in resistance trained bodybuilders. *J Strength Condit Res* 19: 725–729.
- ¹⁷⁵ Suzuki Y, Ito O, Mukai N, Takahashi H, Takamatsu K. High level of skeletal muscle carnosine contributes to the latter half of exercise performance during 30-s maximal cycle ergometer sprinting. *Jpn J Physiol.* 2002 Apr; 52(2): 199-205.
- ¹⁷⁶ Harris RC, Tallon MJ, Dunnett M, Boobis L, Coakley J, Kim HJ, Fallowfield JL, Hill CA, Sale C, Wise JA. The absorption of orally supplied beta-alanine and its effect on muscle carnosine synthesis in human vastus lateralis. *Amino Acids.* 2006;30(3):279-89.
- ¹⁷⁷ Hill CA, Harris RC, Kim HJ, Harris BD, Sale C, Boobis LH, Kim CK, Wise JA. Influence of beta-alanine supplementation on skeletal muscle carnosine concentrations and high intensity cycling capacity. *Amino Acids.* 2007;32(2):225-33.
- ¹⁷⁸ Harris RC, Tallon MJ, Dunnett M, Boobis L, Coakley J, Kim HJ, Fallowfield JL, Hill CA, Sale C, Wise JA. The absorption of orally supplied beta-alanine and its effect on muscle carnosine synthesis in human vastus lateralis. *Amino Acids.* 2006;30(3):279-89.
- ¹⁷⁹ Hill CA, Harris RC, Kim HJ, Harris BD, Sale C, Boobis LH, Kim CK, Wise JA. Influence of beta-alanine supplementation on skeletal muscle carnosine concentrations and high intensity cycling capacity. *Amino Acids.* 2007;32(2):225-33.
- ¹⁸⁰ Effects of Acute Carnosine and β -Alanine on Isometric Force and Jumping Performance. Invernizzi PL, Limonta E, Riboli A, Bosio A, Scurati R, Esposito F. *Int J Sports Physiol Perform.* 2016 Apr;11(3):344-9.
- ¹⁸¹ Patlar S, Yalçın H, Boyalı E. The effect of glycerol supplements on aerobic and anaerobic performance of athletes and sedentary subjects. *J Hum Kinet.* 2012 Oct;34:69-79. doi: 10.2478/v10078-012-0065-x. Epub 2012 Oct 23. PMID: 23487412; PMCID: PMC3590833.
- ¹⁸² Lyons TP, Riedesel ML, Meuli LE, Chick TW. Effects of glycerol-induced hyperhydration prior to exercise in the heat on sweating and core temperature. *Med Sci Sports Exerc* 1990; 22(4):477-83.
- ¹⁸³ Desbrow B, Freney EG, Gaskell SK, Hughes D, Irwin C, Jay O, Lalor BJ, Ross MLR, Shaw G, Périard JD, Burke LM. Sports Dietitians Australia Position Statement: Nutrition for Exercise in Hot Environments. *Int J Sport Nutr Exerc Metab.* 2020 Jan 1;30(1):83-98. doi: 10.1123/ijsnem.2019-0300. PMID: 31891914.
- ¹⁸⁴ Natah SS, Hussien KR, Tuominen JA, Koivisto VA. Metabolic response to lactitol and xylitol in healthy men. *Am J Clin Nutr* 1997;65(4):947-950
- ¹⁸⁵ Diabetologia 1982 Jun;22(6):480-482 The effects of xylitol on the secretion of insulin and gastric inhibitory polypeptide in man and rats. Salminen S, Salminen E, Marks V

- ¹⁸⁶ Georgieff M, Pscheidl E, Moldawer LL, Bistran BR, Blackburn GL. Mechanisms of protein conservation during xylitol infusion after burn injury in rats: isotope kinetics and indirect calorimetry. *European Journal of Clinical Investigation* 1991; 21(2):249-58.
- ¹⁸⁷ Hamberg O. Regulation of urea synthesis by diet protein and carbohydrate in normal man and in patients with cirrhosis. Relationship to glucagon and insulin. *Dan Med Bull* 1997;44(3):225-241
- ¹⁸⁸ Wang Y, Lee KW, Chan FL, Chen S, Leung LK. The red wine polyphenol resveratrol displays bilevel inhibition on aromatase in breast cancer cells. *Toxicol Sci.* 2006 Jul;92(1):71-7.
- ¹⁸⁹ Wang Y, Leung LK. Pharmacological concentration of resveratrol suppresses aromatase in JEG-3 cells. *Toxicol Lett.* 2007 Sep 28;173(3):175-80.
- ¹⁹⁰ Valenzano DR, Terzibasi E, Genade T, Cattaneo A, Domenici L, Cellerino A. Resveratrol prolongs lifespan and retards the onset of age-related markers in a short-lived vertebrate. *Curr Biol.* 2006 Feb 7;16(3):296-300.
- ¹⁹¹ Wu R-E, Huang W-C, Liao C-C, et al. Resveratrol protects against physical fatigue and improves exercise performance in mice. *Molecules.* 2013;18(4):4689–702.
- ¹⁹² Myburgh KH. Polyphenol supplementation: benefits for exercise performance or oxidative stress? *Sports Med.* 2014;44(Suppl 1):57–70.
- ¹⁹³ Hart N, Sarga L, Csende Z, et al. Resveratrol enhances exercise training responses in rats selectively bred for high running performance. *Food Chem Toxicol.* 2013;61:53–9.
- ¹⁹⁴ Köbe T1, Witte AV2, Schnelle A1, Tesky VA3, Pantel J3, Schuchardt JP4, Hahn A4, Bohlken J5, Grittner U6, Flöel A7. Impact of Resveratrol on Glucose Control, Hippocampal Structure and Connectivity, and Memory Performance in Patients with Mild Cognitive Impairment. *Front Neurosci.* 2017 Mar 7;11:105. doi: 10.3389/fnins.2017.00105. eCollection 2017.
- ¹⁹⁵ Kan NW, Ho CS, Chiu YS, Huang WC, Chen PY, Tung YT, Huang CC. Effects of Resveratrol Supplementation and Exercise Training on Exercise Performance in Middle-Aged Mice. *Molecules.* 2016 May 18;21(5). pii: E661.
- ¹⁹⁶ Cui X1, Jing X2, Wu X1, Yan M1. Protective effect of resveratrol on spermatozoa function in male infertility induced by excess weight and obesity. *Mol Med Rep.* 2016 Nov;14(5):4659-4665
- ¹⁹⁷ Mankowski RT1, Anton SD, Buford TW, Leeuwenburgh C. Dietary Antioxidants as Modifiers of Physiologic Adaptations to Exercise. *Med Sci Sports Exerc.* 2015 Sep;47(9):1857-68.
- ¹⁹⁸ Wang S, Liang X, Yang Q, Fu X, Rogers CJ, Zhu M, et al. Resveratrol induces brownlike adipocyte formation in white fat through activation of AMP-activated protein kinase (AMPK) alpha1. *Int J Obes (Lond)* 2015;39:967–76.
- ¹⁹⁹ Polley KR1,1, Jenkins N1,1, O'Connor P1,1, McCully K1,1. Influence of exercise training with resveratrol supplementation on skeletal muscle mitochondrial capacity. *Appl Physiol Nutr Metab.* 2016 Jan;41(1):26-32.
- ²⁰⁰ Price N L, Gomes A P, Ling A J, Duarte F V, Martin-Montalvo A, North B J, et al. SIRT1 is required for AMPK activation and the beneficial effects of resveratrol on mitochondrial function. *Cell Metab,* 2012. 15(5):675±90.
- ²⁰¹ McDermott MM, Leeuwenburgh C, Guralnik JM, Tian L, Sufit R, Zhao L, Criqui MH, Kibbe MR, Stein JH, Effect of Resveratrol on Walking Performance in Older People With Peripheral Artery Disease: The RESTORE Randomized Clinical Trial. Lloyd-Jones D, Anton SD, Polonsky TS, Gao Y, de Cabo R, Ferrucci L. *JAMA Cardiol.* 2017 Apr 12.
- ²⁰² Springer M, Moco S. Resveratrol and Its Human Metabolites-Effects on Metabolic Health and Obesity. *Nutrients.* 2019 Jan 11;11(1). pii: E143.
- ²⁰³ Craig SA. Betaine in human nutrition. *Am J Clin Nutr.* 2004 Sep;80(3):539-49.