



White Paper

TriBsynTM Carnosine Booster

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Carnosine is a dipeptide that plays multiple important physiological roles while beta-alanine (β -ALA), its constituent amino acid, is a non-proteogenic amino acid that serves as the rate-limiting precursor to carnosine synthesis. Due to its unique chemical properties, carnosine provides a variety of health benefits at efficacious dosages and has been clinically proven to improve brain and muscle health, among other health benefits.

TriBsyn™ is a patent-pending formula engineered to maximize the bioavailability of β -ALA and in turn to boost carnosine levels, while eliminating the common side effect of paresthesia, which is often experienced with traditional β -ALA supplements at efficacious doses. This advanced formulation enables absorption through multiple pathways, including direct cellular uptake and traditional gastrointestinal routes, allowing for superior delivery at both the cellular and systemic levels.

This white paper highlights the innovation behind the carnosine booster, TriBsyn™, presenting clinical evidence of its improved bioavailability and providing a summary of the functional benefits of carnosine, while emphasizing the paresthesia elimination and enhanced effectiveness of TriBsyn™.

Clinical Data of TriBsyn™

Conventional β -ALA supplementation often causes paresthesia—a harmless but uncomfortable sensation (e.g., tingling or numbness) due to rapid absorption and resulting peak plasma concentrations. Even small doses can trigger this effect, limiting user compliance and the amount users can tolerate in a single dose, and prolonging treatment periods. Addressing this challenge requires a solution that ensures the performance benefits of β -ALA at efficacious dosages while minimizing paresthesia.

Research shows that the availability of β -ALA is critical for effectively boosting carnosine levels and realizing its associated health benefits. Carnosine, in turn, is metabolized in the blood by carnosinase, which underscores the importance of adequate β -ALA supplementation to achieve optimal carnosine concentrations.

Hydro Oleo Technology for Enhanced β -ALA Delivery and Paresthesia Reduction

TriBsyn™ utilizes proprietary Hydro Oleo technology to enhance the bioavailability of β -ALA while reducing paresthesia. A double-blind, randomized, single-dose, three-treatment, three-way crossover bioavailability study was conducted with 12 healthy older adults under fasting conditions. For the purpose of the study, the innovative formulation combined a low dose (400 mg) of β -ALA with

β -caryophyllene and caffeine encapsulated in phospholipids. Through complexation, β -ALA binds to the hydrophilic side of the phospholipid bilayer, while β -caryophyllene attaches to the hydrophobic side. This structure allows for prolonged absorption and availability, reducing peak plasma concentrations, paresthesia, and associated sensory discomfort.

The formulation is further coated with modified food starch and natural flavoring agents, providing a more enjoyable user experience. By extending the availability of β -ALA in the body, TriBsyn™ allows users to benefit from multiple health advantages without the limitations imposed by conventional dosing.

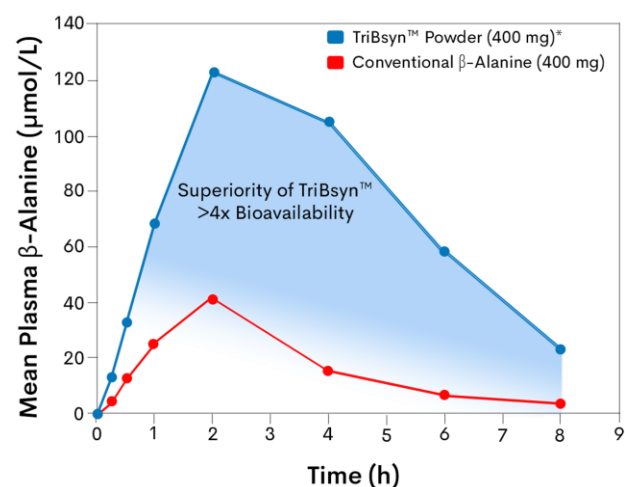
Additionally, the clinical study assessed bioavailability, pharmacokinetics, paresthesia dynamics, and β -ALA excretion. Results demonstrated that TriBsyn™ delivers superior bioavailability at low doses, offering a paresthesia-free alternative to conventional β -ALA.

TriBsyn™ Study Results: Clinically Proven Increased Bioavailability and Paresthesia Elimination

Key Results:

TriBsyn™ delivered over four times β -ALA levels compared to conventional β -ALA (400 mg) and was comparable to that of a high-dose (1200 mg) formulation, confirming a relative bioavailability increase of 445.38% over conventional β -ALA. ($P < 0.001$). Furthermore, TriBsyn™ exhibited a longer half-life (2.36 hours) compared to both conventional formulations (1.72 hours for 400 mg and 1.06 hours for 1200 mg), indicating a different release profile.

Figure 1: Bioavailability Improvement of TriBsyn™



Paresthesia Reduction: Sensory Effects with TriBsyn™

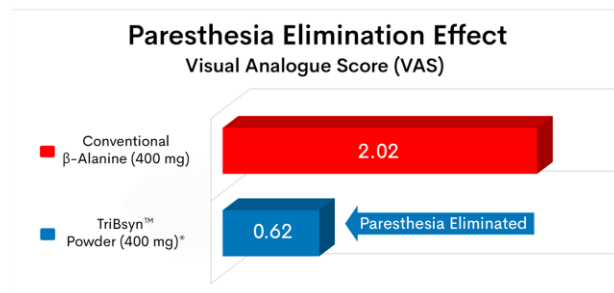
TriBsyn™ not only improves bioavailability but also addresses the common challenge of paresthesia associated with conventional beta-alanine supplements. Using metrics such as the Visual Analogue Score (VAS) and Qualitative Light Symptoms Inventory (QLSI), sensory side effects were assessed.

No paresthesia or adverse effects were reported in the TriBsyn™ group, while the conventional β-ALA groups exhibited increasing paresthesia with dose, as measured by the Visual Analogue Scale (VAS).

Visual Analogue Score (VAS):

TriBsyn™ (400 mg) recorded a VAS score of 0.62 (indicating almost absent symptoms), whereas conventional β-ALA (400 mg) scored 2.02, and the high-dose group (1200 mg) scored 4.01. These results highlight the reduced sensory discomfort in the TriBsyn™ group, despite its higher bioavailability.

Figure 2: Paresthesia elimination effect of TriBsyn™



Qualitative Light Symptoms Inventory (QLSI):

TriBsyn™ registered minimal sensory side effects, with symptoms such as pins and needles, tingling, and numbness largely absent, while both conventional β-ALA groups exhibited mild to moderate symptoms, with the high-dose group showing moderate to strong sensations.

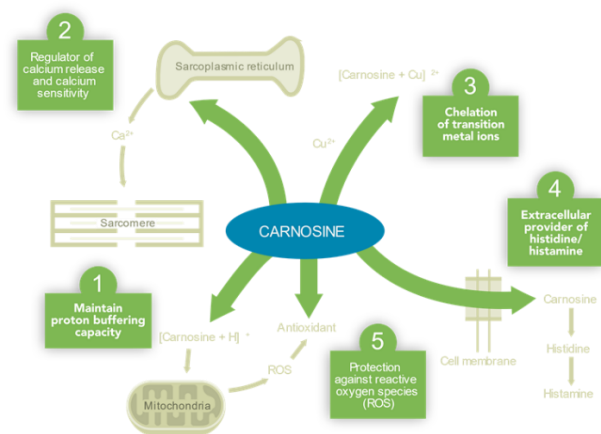
Pain and Mood States:

The Questionnaire de Douleur de Saint-Antoine (QDSA) and the Profile of Mood States (POMS) revealed that TriBsyn™ minimizes sensory discomfort and positively impacts mood and anxiety. TriBsyn™ scored significantly better in pain-related assessments and showed positive effects on mood, with no reported anxiety issues, making it an ideal supplement for maintaining mental and physical well-being.

Key Health Benefits of TriBsyn™

The primary dietary source of β-ALA is animal protein, such as poultry and meat. Animal muscles contain high levels of carnosine, a dipeptide of β-ALA and histidine, which is absorbed into the bloodstream and digested and broken down to β-ALA by the enzyme of carnosinase. β-ALA is then transported into cells, where carnosine synthase combines it with histidine to form carnosine.

Figure 3: Cellular mechanism of action of carnosine.



Carnosine serves as a natural antioxidant and heavy metal chelator. Its chemical structure enables it to detoxify reactive carbonyl species (RCS) generated from lipid peroxidation and glycoxidation, inhibiting the formation of advanced glycation end products (AGEs) and advanced lipoxidation end products (ALEs) (Baye, 2017; Hipkiss, 2006). Consequently, carnosine protects against free radical-generated oxidative damage and AGE-induced cellular toxicity, counteracting numerous harmful biochemical processes associated with aging, stress, and various health conditions (Hipkiss, 2006; Ghodsi, 2018). It supports vital tissues, including the brain, eyes, musculoskeletal system, and cardiovascular system, and may enhance insulin sensitivity while preventing micro- and macrovascular complications. These effects may delay the onset of type 2 diabetes, cardiovascular diseases, and neurodegenerative conditions such as Alzheimer's and Parkinson's disease (Caruso, 2023).

Clinically proven evidence indicates that the availability of β-ALA in plasma is critical for enhancing carnosine production in tissues. TriBsyn™ clinical data support this assertion, demonstrating improved bioavailability in pharmacokinetic studies. Various studies demonstrate that β-ALA supplementation effectively increases carnosine content throughout the body, including the brain and muscles. As the rate-limiting precursor to carnosine

synthesis, β -ALA is more efficiently utilized in physiological processes compared to direct carnosine supplementation, which must be broken down by carnosinase before reaching cells. Additionally, carnosine supplementation is significantly more expensive due to the complex manufacturing processes required to produce both histidine and β -ALA molecules.

Healthy Aging Support

β -ALA and carnosine have been shown to slow the process of age-related cardiovascular, metabolic, and neurological decline, with substantial implications for older adults who experience deficits in muscle and brain health (Szcześniak, 2014; Hipkiss, 2009).

β -ALA supplementation provides significant benefits for older adults by delaying age-related declines in muscle capacity. A 2007 study revealed that carnosine levels decline significantly in older subjects (65-80 vs. 20-35 years) (Tallon, 2007). The older subjects demonstrated a 47% decrease in muscle carnosine content, contributing to a 7% decrease in total muscle buffering capacity compared to the younger subjects. Another study observed a 16% decrease in muscle mass from young adults (19-30 years) to middle-aged adults (31-50 years) (Everaert, 2011). The decline in muscle carnosine reduces muscle capacity and is influenced by changes in diet and physical activity levels in older adults.

Brain Health

Clinical studies demonstrate that β -ALA supplementation enhances brain health, including focus and cognition. The most recent study involving 100 older adults (mean age 70.6) found that 10 weeks of β -ALA supplementation significantly improved cognitive function in participants with baseline MoCA scores at or below normal (≤ 26), with improvements at the midpoint (13.6%, $p = 0.009$) and at week 10 (11.8%, $p = 0.016$) compared to the placebo group. Additionally, β -ALA supplementation reduced depression scores in these participants (Ostfeld, 2023). A follow-up study revealed that β -ALA supplementation also improved brain tissue integrity, with significant increases in fractional anisotropy scores in the right hippocampus ($p = 0.033$) and left amygdala ($p = 0.05$) (Ostfeld, 2024). These findings suggest that β -ALA supplementation may enhance cognitive function and brain health in older adults.

Researchers have also found improvements in cognitive function and resistance to mental fatigue using chicken essence containing carnosine and anserine (Yamano, 2013; Szczeniak, 2014). A subsequent mechanism study, investigated through a series of double-blind, randomized controlled trials, concluded that subjects who took carnosine or carnosine and anserine supplements improved their cognitive function in verbal episodic memory tests (Ding, 2018; Rokicki, 2015). The researchers

observed increased brain blood flow and white matter microstructure in the prefrontal area of these subjects, which is critical for brain function.

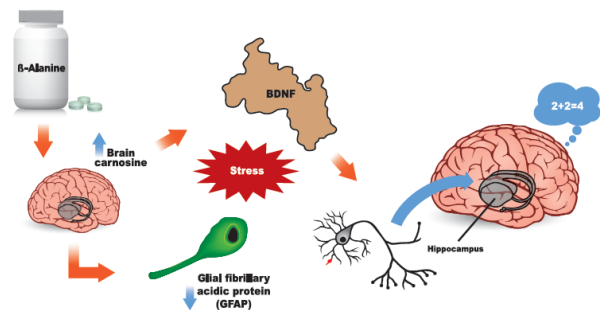
Function theory for brain health

Numerous studies have demonstrated the effectiveness of β -ALA at reducing episodic anxiety and depression in various stress models (Murakami, 2010; Hoffman, 2015, 2017, 2019). In several animal studies, β -ALA ingestion consistently increased neurotrophins in the hippocampus, an area responsible for behavior and memory. Neurotrophins support neurons, helping to maintain normal brain function, as stressful conditions coincide with decreased expression of neurotrophins.

Studies on β -ALA supplementation and brain function in mice observed significant increases in carnosine content in the cerebral cortex and hypothalamus (Murakami, 2010). This was associated with an increase in brain-derived neurotrophic factor (BDNF) and a decrease in 5-hydroxyindoleacetic acid, a serotonin metabolite. These biochemical changes corresponded to improved maze-solving times, suggesting that β -ALA may reduce anxiety during stressful activities.

A subsequent study examined the effects of β -ALA on PTSD-like behavioral changes in rodents exposed to predator-scent stress (PSS) (Hoffman, 2015). Animals given β -ALA before PSS exposure spent more time in the open arms of an elevated plus maze, had more entries into the open arms, and exhibited a lower anxiety index compared to animals fed a normal diet. BDNF expression in the hippocampus remained stable in mice supplemented with β -ALA, suggesting carnosine reduces anxiety by maintaining BDNF expression in the hippocampus.

Figure 4: Function theory of action of TriBsyn™ on brain function



Muscle Health

β-ALA supplementation effectively increases muscle carnosine content in healthy older subjects by buffering intracellular pH, resulting in improved muscle endurance. This is important in geriatric care for preventing falls and maintaining health and independent living (Furst, 2018; Stout, 2008; McCormack, 2013). This improvement is positively correlated with an increase in muscle carnosine.

Function theory for muscle health

Decreased carnosine content in skeletal muscle reduces its capacity to buffer hydrogen ions formed during moderate to high-intensity exercise resulting in a decrease in muscle pH and subsequent fatigue (Harris, 2012). Over one hundred peer reviewed clinical studies covering different ages and activity levels have shown that muscle capacity increases with β-ALA supplementation. An evidence based meta-analysis confirmed its efficacy to improve capacity and performance in a wide range of exercise modalities (Saunders, 2016).

Several well respected athletic committees and research institutes have reviewed and confirmed the benefits of beta-alanine supplementation, including the International Society of Sports Nutrition (ISSN), the National Institutes of Health (NIH), and the International Olympic Committee (IOC). The IOC published a consensus statement, "Dietary Supplements and the High-Performance Athlete," which lists β-ALA as one of the supplements with good to strong evidence of directly improving sports performance (Maughan, 2018).

Table 1. Overview of beta-alanine IOC consensus statement: Dietary supplements and the high-performance athlete

Supplements with good to strong evidence of achieving benefits to performance when used in specific scenarios	
Overview	Beta-alanine augments intracellular buffering capacity, having potential beneficial effects on sustained high-intensity exercise performance.

Synergistic Interaction and Multifunction

The interaction between muscle and cognitive function is a complex and fascinating aspect of health, with carnosine playing a pivotal role in this relationship. While the multiple benefits of carnosine may seem too good to be true, they are well-supported by clinical evidence and scientific research. Carnosine not only enhances mitochondrial energy production but also plays a critical role in detoxification processes within the body. By improving muscle performance and reducing fatigue, carnosine supports not only physical capacity but also cognitive resilience, demonstrating its multifaceted impact on overall health and well-being.

Multiple clinical studies have shown that β-ALA supplementation improves everyday health for middle-aged and older adults, including muscle and brain health (Stout, 2008; McCormack, 2013; Furst, 2018). Additionally, life function, measured by sit-to-stand tests, muscle strength, and evaluated by grip force, improved in subjects aged 50 and older (McCormack, 2013).

Other Health Benefits of Carnosine

Mood improvement

A recent double-blind, placebo-controlled study demonstrated that 10 weeks of β-ALA supplementation significantly reduced the Geriatric Depression Scale (GDS) scores in older adults (Ostfeld, 2023). In another study that provided more than 100 adults with a soft drink containing carnosine, it was reported that the consumption of one bottle a day for four-weeks resulted in significant reductions in feelings of intermittent depression compared to those adults consuming a placebo drink (Shirotsuki, 2017).

Anti-aging and longevity

A clinical study used carnosine as an active ingredient in facial cream. After 56 days of application, they observed improvement in facial contour, skin deformation, elasticity, hydration, and complexion (Garre, 2017). A redefining effect was observed after day 56, with a significant average decrease in sagging jawline (7%), and significant increases in hydration (12%), firmness (29%), and elasticity (20%).

A Russian study on mice demonstrated the anti-aging effects of carnosine in improving life span and appearance. Parameters of morphological and physiological aging, including loss of glossiness, skin ulcers, periophthalmic lesions, and spinal lordokypshosis, were improved significantly by carnosine supplementation compared to the control group (Yuneva, 1999). Physiological behavior assessments also concluded the anti-aging effect. These are consistent with the finding that carnosine diminishes lipid peroxides. The investigator also observed a 20% increase in survival rate, as well as increased life span in the carnosine group. The neuroprotective potential of carnosine against cerebral ischemia indirectly reduces mortality (Szczeniak, 2014).

Eye health and wound healing

Diabetic rats treated with carnosine showed delayed progression in lens opacification during the earlier stages of opacification formation (Yan 2008). N-acetyl-carnosine eye drops are used to treat age-related cataracts (Babizhayev, 2004). Another study shows that oral carnosine treatment protects retinal capillary cells in experimental diabetic retinopathy (Pfister, 2011).

Carnosine is a precursor for histamine synthesis, and immune response. *In vivo* and *in vitro* studies have shown that carnosine increases expression of growth factors and cytokines involved in wound healing (Ansurudeen, 2012). They also show that carnosine increases the viability of human dermal fibroblasts and microvascular-endothelial cells in the presence of high glucose.

Heart health, neuro and systemic protection

Numerous animal studies, as well as a study of chronic heart failure patients, show that carnosine prevents early oxidation of fats in the bloodstream, reducing tissue damage and inflammation (Lombardi, 2015). Patients who received carnosine supplements showed significant improvements in physical condition and life function after six months, measured by their quality-of-life scores, six-minute walking distance, peak exercise workload, and cardiopulmonary stress test (Lombardi, 2015). Some studies suggest that this is because carnosine acts as a modulator of calcium-regulated proteins in cardiac muscle cells and is consequently an important determinant of contractility and cardiac function (Roberts, 2000).

Animal studies show that carnosine effectively prevents cardiometabolic syndrome and related neurological disorders by reducing oxidative stress (Hipkiss, 2014; Baye, 2016). *In vitro* studies also show carnosine suppresses the neurotoxicity of amyloid peptides and fragments in cultured cells (Aloisi, 2013; Preston, 1998; Attanasio, 2013).

Bone health support

Bone protein glycation influences the activity of osteoclasts and osteoblasts (Hein, 2006). Carnosine benefits bone health by its anti-glycation action and its role in muscle health. Carnosine with zinc was shown to prevent bone loss in ovariectomized rats (Kishi, 1994). An *in vitro* study also showed carnosine promotes the production of vimentin, a protein required for maintaining bone integrity (Ikeda, 1999).

Importance of carnosine for vegetarians and vegans

Maintaining adequate carnosine levels can be challenging due to dietary restrictions (e.g., vegetarianism), aging, and stress (Johnson, 1992; Tallon, 2007; Everaert, 2011). A comparison of carnosine levels in the skeletal muscle of vegetarians and non-vegetarians found vegetarians had as much as 50% less carnosine due to their lack of dietary β -ALA, found most abundantly in beef, pork, fish, and chicken (Harris, 2012). As a result, vegetarians have significantly higher AGE plasma content (Krajcovicová-Kudláčková, 2002). More than 20 clinical studies have shown β -ALA supplementation increases carnosine level in various subjects with different diet routines and different levels of muscle carnosine.

Conclusion

TriBsyn™ is a patent-pending formula that represents an innovative advancement in β -ALA supplementation, providing an effective and safe means to enhance natural carnosine levels in the body. Supported by clinical evidence, TriBsyn™ offers substantial health benefits for muscle, brain, heart, bone, overall systemic health, and anti-aging support—providing a comprehensive solution for aging adults.

TriBsyn™ is also ideal for specific consumers, such as individuals using GLP-1 receptor agonists, for whom one of the most significant health concerns and side effects is muscle mass loss and decreased physical performance. TriBsyn™ helps counterbalance these challenges while supporting overall performance and quality of life.

Using proprietary Hydro Oleo technology, TriBsyn™ addresses the common side effects associated with conventional β -ALA formulations by enabling lower efficacious dosing that effectively eliminates paresthesia. This paves the way for an improved user experience, consistent compliance, and clinically proven health outcomes.

Formulation Suggestions

For adults, take 386 mg of TriBsyn™ powder (270 mg active β -ALA), two times per day.

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