

Keto-Nootropic™



Exogenous ketone formula for enhanced cognition, energy, focus, and neurological function

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Keto-Nootropic™ is a powerful blend of exogenous ketones (in the form of beta-hydroxybutyrate salts) and a patented American ginseng extract, delivered in a delicious and easy-to-dose powdered drink mix. This exciting nootropic formula is intended to support healthy cognitive function, sharp focus and mental acuity, and may be a helpful adjunct to conventional therapies for intractable neurological disorders. As a fast-acting and readily available fuel source, Keto-Nootropic™ may also offer a boost to athletic performance and give busy professionals an edge by way of sustained energy and mental clarity. This product is free of artificial sweeteners and is sweetened with the natural herb stevia. It also contains citric acid and malic acid, Krebs cycle intermediates which may help facilitate mitochondrial energy generation.

Highlights

- ▶ Carbohydrate-free fuel for muscle and brain
- ▶ Helps reduce hunger
- ▶ Supports improved cognition
- ▶ Stimulates “metabolic shift” away from glucose dependence
- ▶ Yields immediate and sustained energy fuel for exercise
- ▶ Offers the benefits of elevated ketones without the carbohydrate restriction

Research on the metabolic, physiologic and nootropic benefits of ketones and ketogenic diets is flourishing. The unique therapeutic effects of ketone bodies give these compounds enormous potential not only for enhanced cognition and mental focus in healthy individuals, but as helpful interventions for those with neurological and neurodegenerative conditions, for which conventional pharmaceuticals are either totally lacking or highly ineffectual.

Ketones are produced primarily in the liver, when acetyl-CoA derived from β -oxidation of fatty acids exceeds either the liver's energy needs or the availability of oxaloacetate, which would otherwise continue to send acetyl-CoA through the Krebs cycle to generate ATP. Ketones are exported from the liver to serve as fuel in other tissues, especially the brain, heart and skeletal muscle.

Ketones are produced at very low levels in most people during the overnight fast. In order to generate levels of beta-hydroxybutyrate (β OHB) considered to reach the range of nutritional ketosis (0.5-5.0 mmol/L),¹ a deliberate strategy is required, such as fasting or a ketogenic diet. However, many individuals find a ketogenic diet difficult to sustain, and even for people who enjoy this very low-carbohydrate, high-fat diet, it can be difficult to achieve and maintain therapeutic levels of ketones. In some cases, doing so may require modifications that are not always desirable in certain patient populations, such as protein restriction, extended fasting, or liberal use of medium-chain triglyceride (MCT) oil. The exogenous ketones in Keto-Nootropic™ are ideal for these situations. Even for healthy individuals without a serious need for sustained ketosis, the well-documented cognition-enhancing and energy-boosting effects of exogenous ketones may be desirable, and Keto-Nootropic™ provides these without a need to follow a ketogenic diet.

Once called “metabolism's ugly duckling,”² ketone bodies (KBs) have been celebrated as “not just a fuel, but a ‘superfuel’ more efficiently producing ATP energy than glucose or fatty acid.”³ Compared to glucose or fats, molecule for molecule, ketones generate more ATP, a potential boon for neurological disorders and neurotrauma related to cellular energy deficit, such as Alzheimer's disease. It should be noted that in these situations, there may be a window of opportunity for best effect: if ketogenic interventions are started early in the disease process, the beneficial impact may be greater than if they are begun after the disease is already advanced or has progressed to a severe state. Nevertheless, because there are few to no effective therapies for these disorders, exogenous ketones have the potential to offer at least some benefit even in late-stage illness.

Potential applications for exogenous β OHB

- **Athletic performance:** As an energy substrate, exogenous ketones provide fuel while at the same time being somewhat “carbohydrate sparing” and reducing reliance on glucose oxidation, thus preserving glycogen stores in endurance events and exercise performed up to 75% of maximal workload.^{28,29} By reducing glucose dependence, exogenous ketones may also reduce the need for gluconeogenesis, thus also sparing muscle protein breakdown. There may also be a role for exogenous ketones in facilitating recovery from exercise.³⁰ Owing to alterations in fuel substrate preference in the presence of ketones, exogenous ketones may not be as advantageous for activities that rely more heavily on glycolysis (e.g., sprinting or short-duration maximal effort activity).²⁹ More research is needed in this area among highly trained athletes as well as untrained subjects, but longer endurance-type events may be a more suitable application than short burst activities for exogenous ketones.
- **Alzheimer’s disease (AD):** The predominant abnormality of the Alzheimer’s brain is up to a 45% reduction in cerebral glucose metabolism.⁴ AD is often referred to as “type 3 diabetes” owing to the central role of diminished energy supply from glucose. Although brain uptake of KBs in healthy older individuals and those with dementia may be less efficient than in younger individuals, the transport system for KBs (unlike that for glucose) remains relatively intact with advancing age.⁵ Numerous studies have shown that KBs are a powerful alternative fuel for neurons with impaired capacity to harness energy from glucose and can compensate at least in part for the brain fuel deficit in this condition.^{6,7} It has been speculated that the brain’s downregulation of glucose utilization may be a defense mechanism against the ravages of long-term glycototoxicity and rampant oxidative stress and mitochondrial damage.^{8,9} In the absence of an alternative fuel source—such as ketones—this protective mechanism fails. An adequate supply of ketones would provide these struggling neurons with a usable fuel, but under the high-carb, highly insulinogenic metabolic milieu of the modern Western diet, ketone production is negligible, leaving affected neurons to atrophy and die due to energy shortage. Keto-Nootropic™ provides these critical KBs even for individuals consuming a high-carb diet. Most AD and mild cognitive impairment (MCI) subjects show improvement in cognition and behavior with ketones elevated via exogenous ketones or MCT oil.¹⁰⁻¹³ (ApoE4+ subjects typically do not respond as well as subjects with other genotypes.)
- **Parkinson’s disease (PD):** In a rat model of PD, β OHB protected against neuronal damage and death induced by MPP (intended to produce Parkinsonian defects in animals).¹⁴ Human research is limited, but many plausible mechanisms exist by which β OHB could be beneficial for this condition. In a small feasibility study looking at ketogenic diets in patients with Parkinson’s, five out of five patients who maintained a ketogenic diet for 28 days had improvements in Unified Parkinson’s Disease Rating Scale scores during hyperketonemia.¹⁵ Ketones may bypass the defect in mitochondrial complex I activity implicated in Parkinson’s disease.
- **Traumatic brain injury (TBI):** This is a new area of research focus that holds great promise for military service members and those with TBI or head trauma from accidents or sports. Research in humans is limited, but animal models of TBI indicate exogenous and endogenous ketones can serve a vital role in central and cerebral energy production and reduction of oxidative stress. The post-injury period is characterized by depressed glucose metabolism, decreased ATP generation and increased reactive oxygen species (ROS) production, along with increased expression of monocarboxylate transporters.¹⁶⁻¹⁸ These transporters facilitate the entry of ketones into cells and into mitochondria; thus, the injured brain seems primed to accept ketones while glycolysis is impaired. Indeed, cerebral uptake of ketones is increased following TBI in the presence of ketone infusion, resulting in alleviation of the expected ATP deficit.¹⁹ Pyruvate and lactate can be metabolized in the brain to provide limited amounts of energy, but ketones are the primary fuel that can provide substantial cerebral energy as an alternative to glucose while generating fewer ROS in an environment that is already highly damaged.²⁰ Hyperglycemia is associated with poorer outcomes in TBI patients, so a ketogenic diet may be beneficial in these cases, but exogenous ketones can clearly be instrumental in providing an efficient and “cleaner burning” fuel source.²¹
- **Amyotrophic lateral sclerosis (ALS):** Human studies regarding ketogenic interventions for ALS are limited but animal studies are promising, and mechanisms by which ketones are neuroprotective in AD, PD and TBI may also apply in this condition (e.g., improvement in cellular energetics, increased ATP production, fewer ROS).²²⁻²⁵ In rat models of ALS, animals treated with MCTs or a ketogenic diet showed increased ATP generation and increased spinal cord motor neuron survival compared to controls.^{26,27} Survival time was typically not increased, but motor performance improved, suggesting that ketogenic interventions may not prolong the life of afflicted individuals but could potentially improve the quality of life. As mentioned above, intervening with exogenous ketones as early as possible in the disease process could potentially result in a better outcome.

American Ginseng

The American ginseng (*Panax quinquefolius*) in Keto-Nootropic™ is a patented compound standardized to contain 10% ginsenosides. This unique ingredient is rich in ginsenoside Rb1 (Rb1), a compound known to improve spatial learning and memory in hippocampus-dependent tasks.³¹ Rb1 was shown in animal studies to reduce stress-related hippocampal dysfunction (indicated by increased levels of heat shock proteins and brain-derived neurotrophic factor [BDNF]).³² Compared to untreated control mice, mice injected with Rb1 showed higher density of synaptophysin, a synaptic marker protein, and had improved spatial learning ability likely accounted for by the observed increase in hippocampal synaptic density.³³ Rb1 has also been shown to facilitate the release of acetylcholine in the hippocampus,³⁴ and pretreatment with American ginseng extracts rich in ginsenosides was shown to protect against motor impairment and cell loss in a rodent model of Huntington's disease.³⁵ Rodents pretreated with the extract had significantly better motor function and smaller striatal lesions.

Who May Benefit

- ▶ Athletes
- ▶ Busy professionals
- ▶ Biohackers looking for an edge
- ▶ First responders who require quick & sustained energy
- ▶ Individuals with Alzheimer's disease, other dementias or cognitive impairment
- ▶ Individuals with other neurological disorders or injuries (Parkinson's disease, ALS, TBI)

Beyond the potential for isolated ginsenosides to support healthy cognition, studies of the patented American ginseng in this product show a potential for improved cognitive function through multiple mechanisms. In a mouse model of Alzheimer's disease, oral administration of this ingredient restored cognitive function impaired by A β 1-42-induced cytotoxicity.³⁶ American ginseng restored brain microtubule-associated protein 2 and synaptophysin, as well as acetylcholine concentration, with levels of this neurotransmitter typically being reduced in AD patients.

Studies evaluating the effects of American ginseng in humans support its effects on boosting cognitive function in healthy individuals. In a randomized, double-blind, placebo-controlled crossover trial (N=32 healthy adults age 18-40), compared to placebo, improvements in an array of memory and cognition tests as well as mood were demonstrated with American ginseng doses between 100-400mg/day.³⁷ At none of the doses was a significant impact on blood glucose levels observed, which is important for those who may use Keto-Nootropic™ in conjunction with a ketogenic diet or other blood glucose and insulin-lowering strategies. The cognition-boosting effects of this ingredient are independent of changes in blood glucose.

Similar results were realized in a study evaluating 200mg of American ginseng against placebo in slightly older healthy subjects (N=52, age 40-60 years): compared to placebo, ginseng improved cognitive performance in working memory at 3 hours, also with no significant effects on blood glucose.³⁸

Nutritional Ketosis vs Diabetic Ketoacidosis

Nutritionally induced ketosis is different from pathological diabetic ketoacidosis. Pathological ketoacidosis occurs in type 1 diabetes or late-stage type 2 diabetes involving beta-cell "burnout," when there is insufficient insulin to inhibit endogenous ketone production. In these cases, endogenous ketone production reaches dangerously high levels due to unchecked glucagon catabolizing body fat mass. This reduces blood pH, causing acidosis. Contrast this with nutritional ketosis, wherein blood ketone concentration stays within a safe range, providing the body with an efficient metabolic fuel. This level of ketosis does not induce adverse changes to blood pH. As shown in the table on the right, during nutritional ketosis and medically therapeutic ketosis, ketone levels do not approach those of diabetic ketoacidosis.

Ketone Levels Produced Endogenously in Different Metabolic States	
Metabolic State	Blood Ketones (β OHB, mmol/L)
Mixed (high-carb) diet ³⁹	0.1-0.2
Overnight fast on mixed diet ²	<0.5
Nutritional ketosis ¹	0.5-5.0
Medically therapeutic ketosis ²	2.0-7.0
Total starvation ³	5.0-8.0
Diabetic ketoacidosis ¹	15-25

Note: As an energy substrate—particularly for neurons and muscle cells—the exogenous ketones in Keto-Nootropic™ may offer a therapeutic benefit for athletes and individuals with neuromuscular and neurodegenerative conditions who may be unable to follow a ketogenic diet. However, the nootropic effects of βOHB are separate from the insulin- and glucose-lowering effects of a low-carb or ketogenic diet. Exogenous ketones may be used to ease an individual's transition to a low-carb or ketogenic diet by potentially reducing carb cravings, controlling appetite and boosting energy, but Keto-Nootropic™ is not a substitute for a reduced-carbohydrate diet and insulin-lowering lifestyle interventions in those with type 2 diabetes, obesity, metabolic syndrome or other conditions stemming from insulin resistance. In such conditions, the clinical efficacy is realized mainly from reductions in insulin and glucose, not solely from the presence of ketones.

Supplement Facts		
Serving Size 18 grams (approx. one scoop)		
Servings Per Container 30		
Amount Per Serving	% Daily Value	
Calcium (from goBHB®)	555 mg	43%
Magnesium (from goBHB®)	220 mg	52%
Sodium (from goBHB®)	960 mg	42%
Potassium (as Potassium Glycinate Complex)	540 mg	11%
Beta-Hydroxybutyrate (goBHB®) (Sodium Beta-Hydroxybutyrate, Calcium Beta-Hydroxybutyrate, Magnesium Beta-Hydroxybutyrate)	10 g	*
American Ginseng Extract (<i>Panax quinquefolius L.</i>)(root) [standardized to contain 10% ginsenosides]	200 mg	*

*Daily Value not established.

Other Ingredients: Citric acid, malic acid, stevia leaf extract, natural flavors, silicon dioxide.

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Recommended Use

- As a dietary supplement, mix 18 grams (approx. one scoop) in 10-12 ounces of water per day, or as directed by your health care practitioner.

Keto-Nootropic™ may be used along with other DFH products in the following applications:

- **Athletic Performance:** PreTrain NRG™, MCT Colada™, BCAA Powder with L-Glutamine
- **Brain Health & Cognition:** Brain Vitale™, CogniAid™, MCT Colada™, GPC
- **Mitochondrial Health & Neurological Function:** Mitochondrial NRG™, Mito-PQQ™, MCT Colada™, GPC, Acetyl L-Carnitine

For a list of references cited in this document, please visit:

http://catalog.designsforhealth.com/assets/itemresources/Keto-Nootropic_References.pdf

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