KETONED



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Clinical Applications

- Provides Carbohydrate-Free Fuel for Muscles and Brain*
- Helps Promote Ketosis*
- Supports Energy, Performance, and Focus*

KETONED is a refreshing, cucumber-lime-flavored, easy-to-use powdered drink mix featuring mineral salts of beta-hydroxybutyrate (BHB) and medium-chain triglycerides. These ingredients provide direct carbohydrate-free fuel for the brain and muscles to support energy, performance, and focus.*

All Bonvera Formulas Meet or Exceed cGMP Quality Standards

Discussion

Glucose is the primary source of energy in the body that fuels every function from brain cognition to athletic performance. When dietary carbohydrates are consumed, they are immediately metabolized into glucose or stored in the body as glycogen, which is utilized when the body needs an energy source. When glycogen stores have been depleted, the body naturally goes into a ketogenic state. In this state, the liver uses fat stores to generate alternative fuel byproducts called ketones. The presence of ketones in the blood is known as ketosis.

Ketosis has been touted as desirable for multiple benefits, particularly for energy production, performance, and focus. Ketosis can be induced by fasting, by strictly limiting carbohydrate intake, by engaging in prolonged exercise without carbohydrate intake, or by supplementing with an exogenous source of ketones. The three primary types of ketone bodies formed in ketosis are acetate, acetoacetate, and beta-hydroxybutyrate (BHB). KETONED provides an exogenous source of ketones to promote a state of ketosis.*

GoBHB® (Beta-Hydroxybutyrate Salts)

Fuel/Energy Source

GoBHB is a patented and self-affirmed GRAS supplemental form of the BHB ketone body bound to mineral salts. It provides an exogenous source of ketones to help achieve ketosis without a ketogenic diet. When the body is in a natural state of ketosis, BHB is the ketone body present in the blood at the highest level;^[1] it appears to be better for energy production on a cellular level, and it is more stable than other naturally occurring ketones. Thus, most of the research on exogenous ketones utilizes either BHB salts or BHB esters.*

The first human study suggesting that exogenous ketones could rapidly increase the level of ketones in the blood was published in 2012. Healthy male and female subjects (n = 54) had elevated plasma levels of BHB and acetoacetate following the administration of a single dose of a ketone monoester delivered at 140, 357, or 714 mg/kg body weight in a meal replacement drink. The same three doses were administered three times daily over a five-day period to assess safety and tolerance. BHB levels remained elevated, but some gastrointestinal effects were reported and attributed to the large volumes of the milk-based drink, not the BHB.^{*[2]}

A variety of dietary strategies can be used to induce a ketogenic state; however, restriction of carbohydrates is a necessity, and higher amounts of dietary fats are typical. Some individuals may not tolerate a high fat intake and some may consider it personally undesirable. Additionally, due to a limited list of allowable foods, classic ketogenic diets may be difficult to adhere to over time. Exogenous ketones are a potentially useful adjunct to a ketogenic diet or a practical alternative to increasing circulating ketone body concentrations without having to undergo a ketogenic diet to induce ketosis.*

Performance

It has been hypothesized that during exercise, ketones essentially function as a "fourth" fuel source. They don't necessarily provide an advantage over carbohydrates, fats, and proteins, but they possibly preserve endogenous fuel. Limiting the breakdown of carbohydrates for energy during exercise might reduce fatigue and lactate accumulation,^[3] two factors that are likely to affect athletic performance. Ketosis as a performance enhancer was introduced in the early 1980s with the idea that chronic ketosis without caloric restriction could preserve submaximal exercise capability by sparing glycogen and conserving limited carbohydrate stores. A recent review of this stated that few human studies have yielded positive results and most yielded equivocal results.^{*(4)}

In five separate studies (n = 39) of high-performance athletes, the effects of exogenous ketone esters on induced ketosis for physical endurance were studied. Ketosis decreased muscle glycolysis and plasma lactate concentrations while providing an alternative fuel substrate. Ketosis also increased intramuscular triacylglycerol oxidation during exercise, even in the presence of normal muscle glycogen, co-ingested carbohydrate, and elevated insulin. These findings suggest a positive effect of exogenous ketones for improvement of performance.^[5] However, other studies with varying testing protocols suggest minimal or no effect on performance.^[6,7] Further studies are needed to confirm the positive effect of exogenous ketones on performance.*

Cognitive

The body of evidence supporting a ketogenic diet and/or exogenous ketones as an effective nutrition intervention for cognitive impairment and neurodegenerative issues continues to evolve with multiple animal studies, some single case reports, and a few small human trials.*⁽⁸⁻¹¹⁾

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*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Supplement Facts

rving Size: 1 Scoop (about 11.1 (rvings Per Container: About 30

	Amount Per Serving	%Daily Value
Calories	30	
Total Fat	1.5 g	2%†
Saturated Fat	1.5 g	8%†
Total Carbohydrate	2 g	1% †
Dietary Fiber	2 g	7%
Calcium (as goBHB® calcium beta-hydroxybutyrate)	385 mg	30%
Magnesium (as goBHB® magnesium beta-hydroxybutyrate)	50 mg	12%
Sodium (as goBHB® sodium beta-hydroxybutyrate)	385 mg	17%
goBHB® Calcium Beta-Hydroxybutyrate	2.5 g	**
goBHB® Sodium Beta-Hydroxybutyrate	2.25 g	**
Medium-Chain Triglycerides	1.5 g	**
goBHB® Magnesium Beta-Hydroxybutyrate	600 mg	* *
+ Percent Daily Values are based on a 2,000 calorie dist		

Percent Daily Values are based on a 2,000
** Daily Value not established.

Other ingredients: Gum acacia, citric acid, malic acid, silica, natural flavors (no MSG), stevia leaf extract, cellulose gum, xanthan gum and sea salt.



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Directions

Dissolve the contents of one scoop (about 11.1 g) daily in 12-14 oz of water according to taste preference, or use as directed by your healthcare practitioner. When in training: Take 30 minutes before a workout or in the morning on nontraining days.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

Although glucose is the predominant brain fuel, ketones are utilized when glucose is not available. When an individual is fasting, strenuously exercising, or on a ketogenic diet, the brain becomes receptive to ketone bodies as an alternative fuel. This was demonstrated in a study in adult subjects (n = 4) in whom ketones were shown to rapidly cross the blood-brain barrier and provide brain neurons with energy.^[12] This efficient utilization has been suggested to play a role in the improvement of memory, focus, and cognition when affected regions of the brain lose capacity to harness sufficient energy from glucose.*[11,13,14]

Medium-Chain Triglycerides

KETONED provides a patented medium-chain triglyceride (MCT) powder with a high caprylic and capric acid content (C8/C10) that also contains acacia fiber, a prebiotic that may promote gut health and help optimize the gut-brain axis. MCTs are easily absorbed, permeate the mitochondria without the aid of enzymes, and provide a quick energy source without impacting insulin levels. Unlike other dietary fats, MCTs are not stored as body fat to any significant degree. The liver metabolizes the MCTs into ketones, which can then be used as alternative energy sources for brain cells if they are deprived of glucose.*

Both animal and human studies have explored the potential role of MCTs in increasing ketones to support brain health. In a study of adults (n = 20) with cognitive impairment who were given MCTs or placebo, significant increases in BHB were observed 90 minutes post-treatment when recall tests were administered.[15] In a 90-day, randomized, double-blind, placebo-controlled, parallel group study, subjects (n = 152) with mild-to-moderate Alzheimer's disease were given an oral ketogenic MCT compound to determine if ketosis could affect cognitive performance. Significantly elevated levels of BHB were seen two hours after administration when compared to placebo. Correspondingly, elevated BHB levels resulted in significant differences in Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) scores when compared to placebo.*[16]

Research on MCTs as fuel for exercise also continues to emerge. A study using recreational athletes as subjects (n = 8) suggested that when consuming MCTs, blood lactate levels and rate of perceived exertion during moderateintensity exercise were significantly reduced.*[17]

Another small study suggested that endurance-trained cyclists (n = 6) who consumed MCTs during moderate-intensity exercise for two hours had significant improvements in time-trial performances during subsequent highintensity exercise.^[18] Additional research in larger trials is ongoing to further explore these effects.*

References

- 1. Cahill GF Jr, Fuel metabolism in starvation. Annu Rev Nutr. 2006;26:1-22, Review. [PMID: 16848698]
- 2. Clarke K, Tchabanenko K, Pawlosky R, et al. Kinetics, safety and tolerability of (R)-3-hydroxybutyl (R)-3-hydroxybutyrate in healthy adult subjects. Regul Toxicol Pharmacol. 2012 Aug;63(3):401-8. [PMID: 22561291] Eqan B, D'Agostino DP. Fueling performance: ketones enter the mix. Cell Metab. 2016 Sep 13;24(3):373-375. [PMID: 27626197]
- 4. Scott JM, Deuster PA. Ketones and human performance. J Spec Oper Med. Summer 2017;17(2):112-116. [PMID: 28599043]
- 5. Cox PJ, Kirk T, Ashmore T, et al. Nutritional ketosis alters fuel preference and thereby endurance performance in athletes. *Cell Metab.* 2016 Aug 9:24(2):256-68. [PMID: 27475046] 6. Leckey JJ, Ross ML, Quod M, et al. Ketone diester ingestion impairs time-trial performance in professional cyclists. *Front Physiol.* 2017 Oct 23;8:306. [PMID: 29109686]
- 7. O'Malley T, Myette-Cote E, Durrer C, et al. Nutritional ketone salts increase fat oxidation but impair high-intensity exercise performance in healthy adult males. Appl Physiol Nutr Metab. 2017 Oct;42(10):1031-1035. [PMID: 28750585] 8. Murray AJ, Knight NS, Cole MA, et al. Novel ketone diet enhances physical and cognitive performance. FASEB J. 2016 Dec;30(12):4021-4032. [PMID: 27528626]

9. Roberts MN, Wallace MA, Tomilov AA, et al. A ketogenic diet extends longevity and health span in adult mice. Cell Metab. 2018 May 1;27(5):1156. [PMID: 29719228] 10. Newport MT, VanItallie TB, Kashiwaya Y, et al. A new way to produce hyperketonemia: use of ketone ester in a case of Alzheimer's disease. Alzheimers Dement. 2015 Jan;11(1):99-103. [PMID: 25301680]

11. Cunnane SC, Courchesne-Loyer A, Vandenberghe C, et al. Can ketones help rescue brain fuel supply in later life? Implications for cognitive health during aging and the treatment of Alzheimer's disease. Front Mol Neurosci. 2016 Jul 8;9:53. [PMID: 27458340] 12. Pan JW, de Graaf RA, Petersen KF, et al. [2,4-13 C2]-beta-hydroxybutyrate metabolism in human brain. J Cereb Blood Flow Metab. 2002 Jul;22(7):890-8. [PMID: 12142574]

13. Veech RL, Bradshaw PC, Clarke K, et al. Ketone bodies mimic the life span extending properties of caloric restriction. IUBMB Life. 2017 May;69(5):305-314. [PMID: 28371201] 14. Croteau E, Castellano CA, Fortier M, et al. A cross-sectional comparison of brain glucose and ketone metabolism in cognitively healthy older adults, mild cognitive impairment and early Alzheimer's disease. Exp Gerontol. 2018 Jul 1;107:18-26. [PMID: 28709938]

15. Reger MA, Henderson ST, Hale C, et al. Effects of beta-hydroxybutyrate on cognition in memory-impaired adults. Neurobiol Aging. 2004 Mar;25(3):311-4. [PMID: 15123336]

16. Henderson ST, Vogel JL, Barr LJ, et al. Study of the ketogenic agent AC-1202 in mild to moderate Alzheimer's disease: a randomized, double-blind, placebo-controlled, multicenter trial. Nutr Metab (Lond). 2009 Aug 10;6:31. [PMID: 19664276]

17. Nosaka N, Suzuki Y, Nagatoishi A, et al. Effect of ingestion of medium-chain triacylglycerols on moderate- and high-intensity exercise in recreational athletes. J Nutr Sci Vitaminol (Tokyo). 2009 Apr:55(2):120-5. [PMID: 19436137]

18. Van Zyl CG, Lambert EV, Hawley JA, et al. Effects of medium-chain triglyceride ingestion on fuel metabolism and cycling performance. J Appl Physiol (1985). 1996 Jun;80(6):2217-25. [PMID: 88069331

Does Not Contain

Wheat, gluten, yeast, soy protein, animal or dairy products, fish, shellfish, peanuts, tree nut protein, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

> *These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

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