



Memo

To: Will Woodlee, Kleinfeld Kaplan Becker
From: Innovative Science Solutions, Inc.
Date: November 19, 2021
Re: Claim Substantiation Research for Delta Brain Luxury

Innovative Science Solutions, Inc. (ISS) was asked to perform a scientific assessment for Delta Brain Luxury dietary supplement product. Specifically, we were asked to summarize the competent and reliable scientific evidence that substantiates the broad marketing claim, “supports natural sleep”.

Literature searches were conducted to identify literature related to the desired structure/function claim for Delta Brain Luxury based on its constituent ingredients. Our searches were conducted using scientific literature databases (e.g., PubMed, Google Scholar), with a focus on randomized, placebo-controlled clinical studies (RCTs).

While not a comprehensive review of the literature, this review provides a representative sample of the available data in support of natural sleep claims. Additionally, although there are studies that have examined the effects of the ingredients in Delta Brain Luxury in children, it is our understand that Delta Brain Luxury will be marketed to adult consumers. Therefore, this memo focuses on research conducted in adult populations only.

EVIDENTIARY STANDARD TO SUBSTANTIATE MARKETING CLAIMS

Claims that describe how a nutrient or ingredient may affect the normal structure or function of the human body is a “structure/function claim” and is permitted for dietary supplements (FDA, 2021).

The evidentiary standard to substantiate structure/function marketing claims made for dietary supplements does not require studies on the formulated product. The Dietary Supplement Health and Education Act of 1994 (DSHEA) established regulatory requirements for dietary supplement structure/function claims:

“Structure/function claims may describe the role of a nutrient or dietary ingredient intended to affect the normal structure or function of the human body... In addition, they may characterize the means by which a nutrient or dietary ingredient act to maintain such structure or function” (FDA, 2021b).

Additionally, marketing claims for dietary supplements must adhere to the Federal Trade Commission's (FTC) truth-in-advertising rules. The scientific evidence summarized in this report meets the FTC standard of "competent and reliable scientific evidence," which has been defined as:

"tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that have been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results" (FTC, 2021).

GUIDANCE FOR BEVERAGES AND LIQUID PRODUCTS

Beverages are considered conventional foods under the Federal Food, Drug, and Cosmetic Act (FFDCA). Liquid products can be represented as conventional foods due to several factors including: labeling and advertising, packaging, serving size and recommended daily intake, directions of use, and product name. Specifically, product or brand names that use conventional food terms represent the liquid product as a conventional food (FDA, 2014).

The FDA recognizes that there may be overlap between the ingredients in some conventional foods and dietary supplements, however:

"It should be noted that a dietary ingredient that is lawful for addition to dietary supplements may or may not also be lawful for addition to conventional foods. To be lawful for use in a conventional food, the ingredient must be used in conformity with a food or color additive regulation prescribing the conditions of its use in food, be GRAS for its intended use in food, or qualify for one of the other exceptions to the food additive definition" (FDA, 2014).

Conventional foods, including beverages, may make certain type of claims about effects on the structure or function of the body ("structure/function claims"). Conventional foods may bear structure/function claims in their labeling if the claimed effect derives from the product's character as a food (i.e., taste, aroma, or nutritive value), however:

"if a structure/function claim promotes a product for a use other than providing taste, aroma, or nutritive value, such as blocking the absorption of carbohydrates in the gut, the claim may cause the product to be a drug under section 201(g)(1)(C) of the FD&C Act by changing its primary use. In other words, because of the use promoted in the claim, the product may no longer be consumed as a food—primarily for taste, aroma, or nutritive value—but rather as a drug for some other physiological effect" (FDA, 2014).

BACKGROUND INFORMATION ON DELTA BRAIN LUXURY

Delta Brain Luxury is a 60 ml once-a-day drink, taken before bedtime (Figure 1). It contains proteins, amino acids, a mixture of vitamins, and minerals which are intended to support natural sleep.

Figure 1. Delta Brain Luxury Label and Supplemental Facts

**DELTA
BRAIN
LUXURY™**

Best before: see bottle

5 - 2 FL OZ. (60 ML) BOTTLES
DIETARY SUPPLEMENT

**SUPPORTS
NATURAL
SLEEP¹**

More information on
brainluxury.com

HOW TO USE:
 ➤ COOL keep refrigerated below 45F
 ➤ SHAKE to activate
 ➤ DRINK 15-20 min before bedtime
 ➤ RECYCLE the box, the cap & the bottle

NIGHT

**CRISP
LEMON**

FOR OPTIMUM
RESULTS:
One bottle daily

CUT HERE →

Supplement Facts

Serving size 1 bottle (2 fl oz / 60 ml)
Servings Per Container 5

Amount Per Serving	% Daily Value
Calories 70	
Total Fat 6 g	8%*
Saturated Fat 1.5 g	8%*
Total Carbohydrate 3 g	1%*
Total Sugars 2 g	
Protein 1 g	2%*
Vitamin C 330 mg	367%
Vitamin D (as cholecalciferol) 25 mcg	125%
Vitamin E 8 mg	53%
Magnesium 20 mg	5%
Zinc 8 mg	73%
Sodium 5 mg	<1%
Glycine 3000 mg	**
Medium chain triglycerides (MCT) 1500 mg	**
Alpha-linoleic acid 1100 mg	**
Omega-9 fatty acids 730 mg	**
Docosahexaenoic acid 560 mg	**
L-Tryptophan 450 mg	**
Eicosapentaenoic acid 280 mg	**

* Percent Daily Values based on 2,000 calorie diet.
** Daily Value not established.

OTHER INGREDIENTS: Water, lemon juice, lime juice, flaxseed oil, medium chain triglyceride oil (from coconut oil), oil from microalgae Schizochytrium sp.

Developed and distributed by BrainLuxury, Inc., 6 St Johns Lane, New York, NY 10013. BrainLuxury™ is a registered trademark of BrainLuxury, Inc. Made in Germany. Patent pending formula.

Consult a physician before use if you are pregnant, planning a pregnancy, breastfeeding, taking medication, or have a medical condition. Keep out of reach of children. Do not use if seal is broken.

¹This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

VEGAN². GLUTEN-FREE. NO ADDED SUGAR. NO ARTIFICIAL FLAVOURS.

Processed in a facility that may also handle other allergens.
² ingredients not derived from animal sources.

It is our understanding that Delta Brain Luxury is lemon flavored (“lemon crisp”). However, there is no reason to believe that this flavoring would have any impact on the intended benefits of Delta Brain Luxury.

The following section briefly describes the ingredients in Delta Brain Luxury and their intended purpose in the product.

Protein

Proteins are molecules in living systems serving crucial functions in biological processes (Berg, 2002). Proteins consist of one or more amino acids, which are considered to be the building blocks of life (Shimomura & Kitaura, 2018). These include tryptophan, an essential amino acid which plays a vital role in the production of melatonin and serotonin, thereby helping to regulate the sleep-wake cycle (Jenkins et al., 2016; Medline, 2021). Research has also shown that consuming a lower calorie diet with a higher amount of protein improves sleep quality in overweight middle-aged adults (Zhou et al., 2016).

Vitamin C

Vitamin C, also known as L-ascorbic acid, is an essential dietary nutrient that is found at high levels in fresh fruits and vegetables (Jacob & Sotoudeh, 2002). Experimental studies suggests that vitamin C supplementation plays a protective role against sleep deprivation induced memory impairments by antagonizing oxidative stress (Mhaidat et al., 2015). Additionally, data suggests that vitamin C contributes to restorative sleep (Otocka-Kmiecik & Król, 2020).

Vitamin D

Vitamin D (D3) receptors, and the enzymes that control their activation and degradation, are expressed in several areas of the brain involved in sleep regulation (Romano et al., 2020; Yan et al., 2020). Vitamin D is also involved in the pathways of melatonin production, the hormone involved in the regulation of human circadian rhythm and sleep (Romano et al., 2020).

Magnesium

Magnesium is a chemical element that plays a critical role in over 300 cellular reactions, including protein synthesis, muscle and nerve function, blood glucose control, and blood pressure regulation (NIH, 2021a). Research indicates that magnesium deficiency can enhance inflammation or oxidative stress, which leads to a dampened immune response and disrupt healthy sleep (Chaudhary et al., 2007).

Vitamin E

Vitamin E is a strong antioxidant that has been shown to have neuroprotective effects on the brain (NIH, 2021b). Experimental studies in animals have demonstrated that chronic administration of vitamin E provides a protective effect on chronic sleep deprivation-induced

cognitive impairment, and it may play a beneficial role in normalizing hippocampus antioxidant mechanisms during sleep deprivation (Alzoubi et al., 2012).

Zinc

Zinc is a naturally occurring mineral found in food and is an essential component to both the adaptive and innate human immune systems (NIH, 2021c). Recent evidence indicates that zinc supplementation plays beneficial role for sleep and has been shown to increase the amount of sleep in both mice and humans (Cherasse & Yoshihiro, 2017). Additionally, data from the National Health and Nutrition Examination Survey has identified zinc as one of several vitamins and minerals whose dietary intake was associated with a modification of sleep amount, with very short sleepers (<5 hours) ingesting significantly less zinc than normal or long sleepers (Cherasse & Yoshihiro, 2017).

Glycine

Glycine is a non-essential amino acid that plays roles in both excitatory and inhibitory neurotransmission via N-methyl-D-aspartate type glutamate receptors and glycine receptors. A recent study reported that glycine ingested prior bedtime significantly improved subjective sleep quality in individuals with insomniac tendencies (Bannai & Kawai, 2012).

Medium Chain Triglycerides (MTC)

Medium-chain triglycerides (MCTs) comprise a glycerol molecule attached to three fatty acid chains ranging between six to 12 carbons in length (Shah et al., 2017). One study conducted in *Drosophila* flies found that consumption of MCTs promoted sleep by increasing the number of sleep episodes; however, the mechanism of action of this effect remains unknown (Pamboro et al., 2020).

Omega Fatty Acids

Omega-3 Fatty Acid: alpha-Linolenic acid, Eicosapentaenoic acid, and Docosahexaenoic acid

Omega-3 Fatty acid, also known as alpha-Linolenic Acid (ALA), is a polyunsaturated fatty acid (PUFA). ALA is an essential fatty acid derived from plants, that must be obtained through diet. ALA is the precursor of other long-chain omega-3 fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (NIH, 2021d). Data suggests that EPA and DHA may help improve comorbidities of obstructive sleep apnea such as hypertension, heart failure, or depression (Tittus et al., 2017). Moreover, experimental studies of dietary deficiency of omega-3 fatty acids have revealed a number of mechanisms through which DHA might specifically affect sleep regulation, such as impaired functioning of the superchiasmatic nuclei, altered melatonin release, and disruption to endocannabinoid signaling (Patan et al., 2021).

Omega-9 Fatty Acid (Oleic Acid)

Omega-9 fatty acid, or oleic acid, is a monounsaturated fatty acid (MUFA) produced in the body (Gonçalves-de-Albuquerque et al., 2016). Oleic Acid is a precursor of oleamide (a fatty acid amide). Oleamide is a lipid that has been shown to help induce sleep in animals, primarily by increasing non-REM sleep, with no significant effect on REM sleep (Mendelson & Basile, 2001). While the mechanism of action is still unclear, omega-9 fatty acid has also been shown to enhance *in vitro* responses to serotonin and GABA (Boger et al., 1998; Mendelson & Basile, 2001).

L-tryptophan

L-Tryptophan (an isomer of tryptophan) is an essential amino acid that is not made by the body, but consumed in the diet (Jenkins et al., 2016; Medline, 2021). Some examples of common sources of tryptophan are oats, bananas, milk, cheese, and turkey (Richard et al., 2009), which are often considered “sleep-inducing” foods”. One of the vital functions of L-tryptophan includes its role in the production of melatonin and serotonin, helping regulate sleep-wake (Jenkins et al., 2016; Medline, 2021)

ALIGNING THE SCIENTIFIC EVIDENCE FOR DELTA BRAIN LUXURY CLAIM: “SUPPORT NATURAL SLEEP”

In this section, we review the available scientific evidence as it applies to the proposed marketing claim for Delta Brain Luxury. In the table below, we provide a summary of the competent and reliable scientific evidence, based on the constituent ingredients in Delta Brain Luxury, that substantiates the broad marketing claim “supports natural sleep”, followed by a brief synthesis of the scientific evidence.



Table 1. RCTs Evaluating Ingredients Demonstrating Natural Sleep Support

Ingredient	Study	Lowest Efficacious Amount/Day	Form of Intake	Significant Outcomes	Population	Population Wellness
Vitamin D (as cholecalciferol)	Majid, 2017	3571 IU/day (equivalent to 89.3 mcg/day)	capsule	Increased sleep duration; Increased sleep efficiency; Decreased sleep latency; Decreased Pittsburg Sleep Quality Index (PSQI) score	Ages 20 to 50 years	Adults with sleep disorders
Magnesium	Abbasi, 2012	500 mg/day	capsule	Increased sleep duration; Increased sleep efficiency; Decreased sleep onset latency; Decreased insomnia severity index score	Average age 65 years	Adults with Insomnia
Zinc	Gholipour, 2018	73.3 mg/day (as zinc sulfate)	capsule	Decreased PSQI score; Decreased subjective sleep quality score; Decreased sleep latency score	Average age 31 years	Healthy ICU nurses
Glycine	Yamadera, 2007	3 g/day	granule (oral ingestion)	Decreased latency to sleep onset and to slow wave sleep; Improved subjective sleep quality and sleep efficacy	Ages 30 to 57 years	Healthy adults

Ingredient	Study	Lowest Efficacious Amount/Day	Form of Intake	Significant Outcomes	Population	Population Wellness
DHA; EPA	Patan, 2021	DHA: 900 mg/day EPA: 270 mg/day	capsule	DHA: Improved sleep efficiency and sleep latency EPA: Decreased total time in bed and total sleep time	Ages 29 to 49 years	Healthy adults
L-tryptophan	Bravo, 2012	Week 1: 22.5 mg tryptophan in 30 g of cereal (twice daily) Week 2: 60 mg tryptophan in 30 g of cereal (twice daily)	cereals enriched with tryptophan	Increased sleep efficiency; Increased actual sleep time; Increased immobile time; Decreased total nocturnal activity; Decreased sleep fragmentation index; Decreased sleep latency	Ages 55 to 75 years	Adults with sleep difficulties



In this report, we compared data from the scientific studies with the ingredients found in one serving of Delta Brain Luxury. We identified scientific evidence for a number of ingredients in Delta Brain Luxury that adequately support the broad marketing claim, “supports natural sleep”.

As described in the table above, vitamin D, magnesium, zinc, glycine, DHA/EPA, and L-tryptophan have each been shown to have statistically significant effects in healthy adults on a number of sleep-related endpoints, such as sleep onset, sleep efficiency, and sleep quality. However, it should be noted that some of the ingredients have only shown effectiveness in RCTs using different forms of intake (e.g., capsules, cereal) and/or in higher amounts than those found in one serving of 60 ml of Delta Brain Luxury.

Nevertheless, multiple ingredients in the Delta Brain Luxury formulation, albeit in different forms and amounts, have been shown to provide sleep benefits in high quality studies.

Conclusion:

As summarized in this memo, some of the ingredients found in Delta Brain Luxury have been investigated in various studies and shown to confer benefits in support of the broad structure/function claim area related to natural sleep support (although in different forms of intake and in higher levels than are found in the Delta Brain Luxury formulation). This broad claim area meets the dietary supplement structure/function claim requirements and is supported by the available scientific evidence.

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