

Brain Calm



Clinical Applications

- Supports Healthy Brain Magnesium Levels*
- Promotes Concentration, Mental Clarity, and Focus*
- Supports Cognitive Health*
- Promotes Mental and Physical Energy and Motivation to Exercise*

*Brain Calm provides a unique blend of patented, stimulant-free, non-habit forming ingredients. Methylcobalamin supports cognition and contributes to healthy energy metabolism; magnesium L-threonate supplies highly bioavailable magnesium to the brain, which is vital to cognitive function; and theacrine promotes mental and physical energy, focus, and motivation.**

All Get Healthy / Angel Pure MD Formulas Meet or Exceed cGMP Quality Standards

Discussion

Cognition, including learning and memory, is dependent upon neurons in the human brain communicating with each other through synaptic connections. Age, genetics, diet, exercise, and environment may affect how efficiently neurons communicate and, thus, overall cognitive health. Individuals who desire improvement in focus and motivation often look for formulas that target cognitive health, and these often contain ingredients that promote brain stimulation. Brain Calm contains a targeted blend of key ingredients designed to promote mental and physical energy and fuel motivation and clarity without overstimulation.*

Magtein™ (Patented Magnesium L-Threonate)

Magnesium is involved in more than 300 essential metabolic reactions, justifying the necessity of adequate magnesium levels to support overall health, including that of the brain. In the United States, dietary intakes of this mineral are consistently below age-specific minimum recommended levels.*^[1]

More than ten years of research at MIT went into the development of Magtein, a highly bioavailable compound comprised of magnesium and L-threonate. When brain magnesium levels are not optimal, synapse function deteriorates, suggesting that magnesium plays a significant role in promoting synaptic plasticity in the brain. Ingesting conventional magnesium compounds does not appear to elevate brain magnesium, but animal studies have shown that Magtein crosses the blood-brain barrier, resulting in increased deposits in neural synapses, increased neural synaptic density, and improved brain function.^[2-4] One particular study demonstrated that Magtein enhanced magnesium bioavailability and produced a significant increase (7%-15%) in rat cerebrospinal fluid when compared to other magnesium compounds.^[2] These small but significant increases in brain magnesium levels produced profound effects on neurological function.*

Maintaining extracellular magnesium in the brain has been observed to help preserve synaptic density and synapse function.^[2,5] Early research on Magtein suggested that increasing magnesium concentration in the extracellular fluid permanently enhanced synaptic plasticity in networks of cultured hippocampal neurons.^[6] More recent studies have shown that magnesium increased signaling of the receptors in the hippocampus that play a pivotal role in memory processes. A 2016 study that explored magnesium L-threonate's mechanism of action demonstrated that L-threonate is the only ligand to efficiently transport magnesium into the cerebrospinal fluid and then into neurons.^[6] Data from these studies showed that Magtein enhances both short-term synaptic facilitation and long-term potentiation and thereby supports synaptic plasticity and learning and memory functions.^[2,3,6,7] By delivering magnesium into synapses, Magtein supports cognitive function by helping brain cells respond to signals with clarity and vigor without being overactivated.*

The effects of Magtein were studied in a randomized, double-blind, placebo-controlled trial on human cognition (n = 51). Patients 50–70 years of age who were administered a dose of 1.5 g/d to 2 g/d (25 mg/kg/d) of Magtein for 12 weeks demonstrated reduced cognitive declines compared to age-matched controls. Furthermore, the researchers calculated a particularly compelling impact of Magtein using normative TMT-B data from age-matched subjects. After six weeks of treatment, the average brain age of the Magtein group decreased from 69.6 ± 4.2 years to 60.6 ± 5.6 years, an improvement of 9.0 ± 3.5 years, and persisted after 12 weeks of treatment with 9.4 ± 3.5 years of improvement.^[8] Although future larger trials studying the effects of Magtein on the human brain would be ideal, it is clear from the research to date that Magtein has a significant effect on cognitive well-being.*

TeaCrine® (Theacrine)

Theacrine is a purine alkaloid found in certain coffee and tea species that has a similar chemical structure to caffeine yet with very different physiological effects. Both caffeine and theacrine inhibit adenosine activity via the A1 and A2A receptors, but caffeine is known to act as an orthosteric inhibitor whereas theacrine is likely to act as an indirect, allosteric modulator of these receptors and contribute to differences in habituation. Inhibitory action of the adenosine receptors plays a role in the biochemical processes that prevent fatigue. Additionally, theacrine is a dopamine D1 and D2 receptor agonist, and its actions help increase dopamine signaling associated with attention, movement, task initiation and completion, mood, learning, and the brain's "reward center."*

Whereas habituation typically occurs with caffeine in as little as five days of consumption, a significant attribute of theacrine is the lack of habituation or tachyphylaxis (decrease in response). Following an eight-week study with subjects (N = 60) receiving either 200 mg or 300 mg of Teacrine or placebo, participants demonstrated no signs of the rapid tachyphylaxis typically associated with caffeine and other stimulants. Baseline values for energy, focus, concentration, anxiety, motivation to exercise, and a Profile of Mood States (POMS) questionnaire remained stable across the entire eight-week study period. Additionally, all values for clinical safety markers were within normal limits.*^[9]

***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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Brain Calm

Supplement Facts

Serving Size: 2 Capsules
Servings Per Container: 30

	Amount Per Serving	%Daily Value
Vitamin B12 (as methylcobalamin)	2000 mcg	83,333%
Magnesium (as magnesium L-threonate) ^{S1}	70 mg	17%
Magnesium L-Threonate ^{S1}	1 g	**
Theacrine ^{S2}	200 mg	**

** Daily Value not established.

Other Ingredients: Capsule (hypromellose and water), microcrystalline cellulose, ascorbyl palmitate, silica, medium-chain triglyceride oil, and calcium silicate.

S1. Magtein[®] is protected under a family of U.S. patents and pending patents and is protected worldwide. Magtein[®] is a registered trademark of Magceutics[®], Inc. and is distributed exclusively by ADP, Inc.

TEACRINE

S2. TeaCrine[®] is a registered trademark and is protected by Patents Pending, Serial No. 61/903,362; under exclusive global distribution by Compound Solutions, Inc.

In a randomized, double-blind, placebo-controlled, crossover pilot study, subjects (n = 15) ingested 200 mg of Teacrine over a three-hour post-dosing period using a 100 mm visual analogue scale (VAS) to detect change in various aspects of physical and mental energy and performance. Side-effect profiles, hemodynamics, and biochemical markers of safety were also collected. The 200 mg dose was found to significantly improve concentration and energy and reduce fatigue. No changes were noted in systemic hemodynamics and no side effects were observed. A subset of subjects underwent a separate seven-day, open-label, repeated-dose study comparing 100 mg, 200 mg, and 400 mg of Teacrine. The seven-day assessment demonstrated improved subjective measurements for energy, fatigue, concentration, anxiety, motivation to exercise, and libido in the 200 mg dose group.^{*[10]}

In a small double-blind, placebo-controlled, crossover study, subjects (n = 8) received 25 or 125 mg of theacrine, 150 mg of caffeine, or a combination of theacrine (125 mg) and caffeine (150 mg). Results suggested that while theacrine had no impact on caffeine pharmacokinetics, the combination of caffeine and theacrine led to enhanced bioavailability. Additionally, a broad spectrum of clinical safety markers, including heart rate and blood pressure, were unaffected by concomitant use indicating a strong safety profile at the doses administered.^{*[11]}

Methylcobalamin (B12)

Cogniquil contains high-potency MecobalActive[™], a patented pure form of methylcobalamin that is the physiologically active form of vitamin B12. Vitamin B12 plays a role in the maintenance of a healthy nervous system; chronic insufficiency affects peripheral nerves, the optic nerve, and the brain. Methylcobalamin is a cofactor in myelin synthesis; in the methylation of homocysteine, a substance thought to damage neurons; and in the synthesis of monoamine neurotransmitters.^[12-14] Studies have suggested supplemental B12 alone or in combination with folate supports healthy homocysteine levels already within the normal range.^[15] Increased homocysteine levels have been associated with declining cognitive function.*

B12 is also integral to the complex biochemical processes involved in energy metabolism. It is involved in the conversion of lipids, proteins, and carbohydrates into glucose to fuel energy production and ATP for cellular energy.^{*[16]}

Directions

Begin with two capsules daily to determine response. Increase to a maximum of two capsules twice daily, or take as directed by your healthcare professional.

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

Formulated To Exclude

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

References

1. What We Eat in America: Mean Energy and Mean Nutrient Amounts per 1000 kcal Consumed per Individual, by Gender and Age. U.S. Department of Agriculture, Agricultural Research Service. https://www.ars.usda.gov/ARSUserFiles/80400530/pdf/1314/Table_41_DEN_GEN_13.pdf. 2013-2014. Accessed November 18, 2017.
2. Slutsky I, Abumaria N, Wu LJ, et al. Enhancement of learning and memory by elevating brain magnesium. *Neuron*. 2010 Jan 28;65(2):165-77. [PMID: 20152124]
3. Li W, Yu J, Liu Y, et al. Elevation of brain magnesium prevents synaptic loss and reverses cognitive deficits in Alzheimer's disease mouse model. *Mol Brain*. 2014 Sep 13;7(1):65. [PMID: 25213836]
4. Abumaria N, Yin B, Zhang L, et al. Effects of elevation of brain magnesium on fear conditioning, fear extinction, and synaptic plasticity in the infralimbic prefrontal cortex and lateral amygdala. *J Neurosci*. 2011 Oct 19;31(42):14871-81. [PMID: 22016520]
5. Slutsky I, Sadeghpour S, Li B, et al. Enhancement of synaptic plasticity through chronically reduced Ca²⁺ flux during uncorrelated activity. *Neuron*. 2004 Dec 2;44(5):835-49. [PMID: 15572114]
6. Sun Q, Weinger JG, Mao F, et al. Regulation of structural and functional synapse density by L-threonate through modulation of intraneuronal magnesium concentration. *Neuropharmacology*. 2016 Sep;108:426-39. [PMID: 27178134]
7. Wang D, Jacobs SA, Tsien JZ. Targeting the NMDA receptor subunit NR2B for treating or preventing age-related memory decline. *Expert Opin Ther Targets*. 2014 Oct;18(10):1121-30. [PMID: 25152202]
8. Liu G, Weinger JG, Lu ZL, et al. Efficacy and safety of mmsf-01, a synapse density enhancer, for treating cognitive impairment in older adults: a randomized, double blind, placebo-controlled trial. *J Alzheimers Dis*. 2015 Oct 27;49(4):971-90. [PMID: 26519439]
9. aylor L, Mumford P, Roberts M, et al. Safety of TeaCrine[®], a non-habituating, naturally occurring purine alkaloid over eight weeks of continuous use. *J Int Soc Sports Nutr*. 2016 Jan 13;13:2. [PMID: 26766930]
10. Habowski S, Sandrock J, Kedia A, et al. The effects of Teacrine[™], a nature-identical purine alkaloid, on subjective measures of cognitive function, psychometric and hemodynamic indices in healthy humans: a randomized, double-blinded crossover pilot trial. *J Int Soc Sports Nutr*. 2014;11(Suppl 1):P49. doi:10.1186/1550-2783-11-S1-P49.
11. He H, Ma D, Crone LB, et al. Assessment of the drug-drug interaction potential between theacrine and caffeine in humans. *J Caffeine Res*. 2017 Sep 1;7(3):95-102. [PMID: 28875060]
12. Ansari Z. Homocysteine and mild cognitive impairment: are these the tools for early intervention in the dementia spectrum? *J Nutr Health Aging*. 2016 Feb;20(2):155-60. [PMID: 26812511]
13. Garcia A, Zanibbi K. Homocysteine and cognitive function in elderly people. *CMAJ*. 2004 Oct 12;171(8):897-904. [PMID: 15477631]
14. Puri V, Chaudhry N, Goel S, et al. Vitamin B12 deficiency: a clinical and electrophysiological profile. *Electromyogr Clin Neurophysiol*. 2005 JulAug;45(5):273-84. [PMID: 16218195]
15. Clarke R. Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomised trials. *Indian Heart J*. 2000 Nov-Dec;52(7 Suppl):S59-64. [PMID: 11339443]
16. Shane B. Folic acid, vitamin B-12, and vitamin B-6. In: Stipanuk M, ed. *Biochemical and Physiological Aspects of Human Nutrition*. Philadelphia: W.B. Saunders Co.; 2000:483-518.

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