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# Clinical Applications

- Supports Healthy Brain Magnesium Levels\*
- Supports Healthy Synapse Number and Function\*
- Supports Cognitive Health\*
- Supports Stress Management, Sleep Quality, and a Healthy Mood\*
- Helps Ensure an Optimal Magnesium Intake for Overall Health\*

Calm Fx features Albion chelated magnesium plus Magtein™ (magnesium L-threonate), the only form of magnesium proven in animal studies to cross the blood-brain barrier. Boosting the brain's magnesium level is vital to healthy cognition, which includes long- and short-term memory, learning, stress management, and sleep.\*

All Apex Medicinals, LLC Formulas Meet or Exceed cGMP Quality Standards

## **Discussion**

### Calm Fx - Optimizes Magnesium Delivery to Body and Brain

Dietary intakes of magnesium are consistently below minimum recommended levels, and an insufficiency of magnesium is implicated in a wide range of health concerns, including those that affect the brain.[1] Because many forms of magnesium have low bioavailability, Apex Medicinals, LLC carefully selected magnesium compounds backed by research and studies to formulate Calm Fx. Built upon the long-term clinical success of Magnesium Chelate, Calm Fx features a unique combination of Magnesium Chelate's highly absorbable, organic Albion minerals—di-magnesium malate and TRAACS® magnesium lysinate glycinate chelate—and Magtein™. Magtein is a groundbreaking organic magnesium compound that was developed by MIT (Massachusetts Institute of Technology) researchers to support "brain power."

#### Magtein - Patented Magnesium L-Threonate

Magtein is the result of 10 years of research at MIT. This novel form of magnesium is changing the way we support brain health. Unlike other brain products on the market that work via brain stimulation (often overstimulation), Magtein works via a completely different mechanism. When brain magnesium levels are not optimal, synapse function deteriorates. By delivering magnesium into synapses, Magtein helps brain cells stay healthy, without being overactivated; consequently, brain cells respond to signals with clarity and robustness.\*

#### Magtein Raises Brain Magnesium Levels

Studies show that Magtein crosses the blood-brain barrier and raises the brain's magnesium levels, which result in increased magnesium deposits in neural synapses, increased neural synaptic density, and improved brain function. [2-4] One animal study showed that when the bioavailability of several magnesium compounds was compared to controls, only Magtein significantly enhanced magnesium bioavailability and produced a significant increase (7% to 15%) in rat cerebrospinal fluid.[2] These small but significant increases in brain magnesium levels produced profound effects on neurological function.\*

#### Magtein Supports Healthy Synaptic Number and Function

Maintaining extracellular magnesium in the brain helps preserve synaptic density and keeps the synapses working properly.\*[2.5]

By increasing magnesium concentration in the extracellular fluid, researchers observed permanent enhancement of synaptic plasticity in networks of cultured hippocampal neurons. [5] Delving deeper into the mechanisms involved, later animal research showed that magnesium increased receptor signaling; specifically, the signaling of the NR2B-containing N-methyl-D-aspartate (NMDA) receptor. NMDA receptors are rich in the hippocampus and play a pivotal role in memory processes.\*

Data from these studies suggest that increasing brain magnesium with Magtein "enhances both short-term synaptic facilitation and long-term potentiation and thereby supports synaptic plasticity and learning and memory functions in rats."\*[2,3,6]

#### **Magtein Supports Cognitive Health**

The cognitive effects of Magtein were studied by Liu et al in a randomized, double-blind, placebo-controlled trial (n = 51). At a dose of 1.5 g/d to 2 g/d (25 mg/kg/d) for 12 weeks, patients 50-70 years of age taking Magtein demonstrated reduced cognitive declines compared to age-matched controls.[7] 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. These clinical benefits have been supported by the data of several animal studies.\*

Several pre-clinical animal studies that used assessments such as the NORT (novel object recognition test), T-maze, Morris water maze, conditioned fear memory, and conditioned taste aversion have also validated Magtein's effectiveness."

‡The Trail Making Test - Part B (TMT-B) assesses executive function as well as impulsivity, visual search, visual attention, and motor speed.

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#### **Supplement Facts** Servings Per Container: About 30 Amount Per Serving %Daily Value Calories Total Carbohydrate 2 a 1%<sup>†</sup> Magnesium (as Albion® di-magnesium malate, 48% 200 ma Magtein™ magnesium L-threonate, and TRAACS® magnesium lysinate glycinate chelate) Magtein™ (magnesium L-threonate) 1 g † Percent Daily Values are based on a 2,000 calorie diet. \* Daily Value not established

Other Ingredients: Citric acid, malic acid, natural flavors (no MSG), stevia leaf extract, and anthocyanin extract (color).

Albion and TRAACS are registered trademarks of Albion Laboratories, Inc. Malate covered by US patent 6,706,904 and patents pending.

Magtein is protected under US patents 8,178,118; 8,142,803; 8,163,301; and other pending patents.



#### ...continued

In these studies, researchers demonstrated that when brain magnesium levels were increased, significant benefits were detected in multiple aspects of learning and memory in young and aged rodents. [2-4,8] For instance, NORT tests performed by Slutsky et al revealed that short-term memory improved approximately 135% and long-term memory improved approximately 85% in aged rats treated with Magtein compared to control (untreated) rats.\*

One study examined the effects of Magtein in test mice (genetically altered mice that model age-related cognitive changes). Li et al found that the test mice not given Magtein exhibited "unequivocal learning deficits," while the test mice given Magtein performed similarly to normal mice.[3] In short, Magtein helped preserve normal brain function. When magnesium levels in the brain tissue were quantified, the relationship became even clearer: According to researchers, brain magnesium levels positively correlated with cognitive function; that is, the lower a mouse's brain magnesium level, the poorer its memory function in the NORT task. Furthermore, histological analysis of brain tissue showed that Magtein administration preserved synapse density and NMDA receptor signaling and also had positive effects on the expression of certain proteins associated with changes in memory.\*[3]

### Magnesium in Stress Management, Sleep Quality, and Mood

Magnesium is known to benefit the body in ways that counter stress, promote restful sleep, and support a healthy mood. In rats, magnesium administration attenuated neurologic changes brought on by chronic mild stress.[9] Additionally, by increasing fear memory extinction, Magtein showed promise as a modulator of worry.<sup>[4,10]</sup> In human studies, magnesium supplementation partially reversed sleep changes associated with aging and improved objective and subjective measures of sleep [11-13] Improving sleep quality and countering the effects of chronic stress positively impact mood—another area that is beneficially influenced by optimal magnesium

## **Directions**

Dissolve one level scoop in 4 oz water or adjust amount of water to desired sweetness. First week: one serving per day immediately before dinner or one hour before bedtime. Thereafter: one serving during the day, preferably mid-afternoon, and a second serving before bedtime; or use as directed by your healthcare practitioner.

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.

#### References

- 1. Moshfegh AJ, Goldman JD, Ahuja JK, et al. U.S. Department of Agriculture, Agricultural Research Service. What we eat in America, Nhanes 2005-2006. Usual nutrient intakes from food and water compared to 1997 dietary reference intakes for vitamin D, calcium, phosphorus, and magnesium. http://www.ars.usda.gov/SP2UserFiles/ Place/80400530/pdf/0506/usual\_nutrient\_intake\_vitD\_ca\_phos\_mg\_2005-06.pdf. Published July 2009. Accessed November 21, 2014.
- 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. 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]
- Oct, 16(10). 1121-30. [PMID. 26132202]
  7. Liu G, Weinger JG, Lu ZL, et al. Efficacy and safety of mmfs-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]
  8. Mickley GA, Hoxha N, Luchsinger JL, et al. Chronic dietary magnesium-L-threonate speeds extinction and reduces spontaneous recovery of a conditioned taste aversion. *Pharmacol Biochem Behav.* 2013 May;106:16-26. [PMID: 23474371] 9. Pochwat B, Szewczyk B, Sowa-Kucma M, et al. Antidepressant-like activity of magnesium in the chronic mild stress model in rats: alterations in the NMDA receptor
- subunits. Int J Neuropsychopharmacol. 2014 Mar;17(3):393-405. [PMID: 24067405] 10. Abumaria N, Luo L, Ahn M, et al. Magnesium supplement enhances spatial-context pattern separation and prevents fear overgeneralization. Behav Pharmacol. 2013 Aug;24(4):255-63. [PMID: 23764903]
- 11. Held K, Antonijevic IA, Künzel H, et al. Oral Mg(2+) supplementation reverses age-related neuroendocrine and sleep EEG changes in humans. Pharmacopsychiatry. 2002 Jul;35(4):135-43. [PMID: 12163983]
- 12. Abbasi B, Kimiagar M, Sadeghniiat K, et al. The effect of magnesium supplementation on primary insomnia in elderly: A double-blind placebo-controlled clinical trial. J Res Med Sci. 201 Dec;17(12):1161-69. [PMID: 23853635].
- 13. Hornyak M, Voderholzer U, Hohagen F, et al. Magnesium therapy for periodic leg movements-related insomnia and restless legs syndrome: an open pilot study. Sleep. 1998 Aug 1;21(5):501-05. [PMID: 9703590]
  14. Fromm L, Heath DL, Vink R, et al. Magnesium attenuates post-traumatic depression/anxiety following diffuse traumatic brain injury in rats. *J Am Coll Nutr.* 2004
- 0ct;23(5):529S-533S. [PMID: 15466958]
  15. Eby GA, Eby KL. Rapid recovery from major depression using magnesium treatment. *Med Hypotheses*. 2006;67(2):362-70. [PMID: 16542786]

# Does Not Contain

Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, 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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