PROTOCOL FOR LIFE BALANCE®

Dietary Supplement Information
for Physicians with Naturokinetics®
PRODUCT CODE: P3414
CATEGORY: BRAIN HEALTH*

RememBRAIN™

TECHNICAL SUMMARY

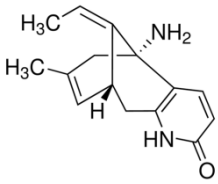
Acetylcholine (ACh) is the primary neurotransmitter involved in memory formation, alertness, and muscle movement. ACh production, however, tends to decrease with age. RememBRAIN™ is a combination of ingredients formulated to support healthy ACh production and function.* With huperzine A (Hup A), which helps to maintain ACh in the brain, Alpha-GPC, a bioavailable form of choline, and phosphatidyl serine (PS), which is critical for efficient signaling in nerve cells, RememBRAIN™ is a comprehensive formula utilizing clinically relevant doses of Hup A and PS, which help to support normal healthy ACh levels and neurological function.*

Allergen and Additive Disclosure: Not manufactured with wheat, gluten, milk, egg, fish, shellfish or tree nut ingredients. Produced in a GMP facility that processes other ingredients containing these allergens.

Delivery Form: Vegetable capsules

HUPERZINE A

Structure Formula:



Chemical Name: Lycopodium alkaloid (Hup, [(5R, 9R, 11E)-5-amino-11-ethylidene-5, 6, 9, 10-tetrahydro-7- methyl-5, 9-methano-cycloocteno[b] pyridine-2(1H)-one]).

ROLE AS NUTRIENT/FUNCTION

Huperzine A is an alkaloid isolated from club moss (*Huperzia serrata*), a plant native to India and Southeast Asia. It has been traditionally consumed in the form of herbal infusions and tinctures.

Huperzine A is a competitive, reversible inhibitor of the enzyme acetylcholinesterase (AChE), shown to support healthy cognitive function in various animal models.* Additional neuroprotective effect may include regulation of Aβ-amyloid precursor protein metabolism, and maintenance of normal Aβ-amyloid and glutamate metabolism.*

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Liberation: Disintegration of RememBRAIN™ capsules is within 60 minutes (in water).

Absorption: In a pharmacokinetic study with 12 healthy human volunteers, a single oral dose of 400 mcg of huperzine A resulted in rapid absorption. Huperzine A started to appear in the plasma after 5–10 minutes and reached the peak concentrations in the plasma (T_{max}) 1 hour after ingestion.

Distribution: Huperzine A distributes widely in the body and is able to cross the blood-brain barrier.

Supplement Facts

Serving Size 2 Veg Capsules — Servings Per Container 30

	Amount Per Serving	% Daily Value
Vitamin B-12 (as Methylcobalamin)	5 mg (5,000 mcg)	208,333%
Huperzine A (*Huperzia serrata* Extract) (Moss)	200 mcg	†
Alpha-GPC (L-alpha-glycerylphosphorylcholine)	300 mg	†
Phosphatidyl Serine	300 mg	†

† Daily Value not established.

Other ingredients: Cellulose (capsule), Cellulose Powder, Silica, Magnesium Stearate (vegetable source) and Stearic Acid (vegetable source). Phosphatidyl Serine from soy.

- **Supports Healthy Neurological Function***
- **With Huperzine A, Alpha-GPC & Phosphatidyl Serine**

SUGGESTED USAGE: Take 2 capsules 1 to 2 times daily, or as directed by your healthcare practitioner.

Metabolism: Metabolism of huperzine A has not been sufficiently studied.

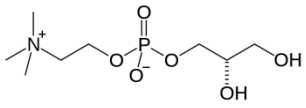
Elimination: Huperzine A follows a two-compartmental pharmacokinetic open model with α and β half-lives of 21 and 716 minutes, respectively.

CLINICAL VALIDATION

- In a double-blind, placebo-controlled, randomized clinical trial with 78 subjects (average age 72 years), supplementation with huperzine A (100 mcg twice daily for 12 weeks) resulted in a significant difference vs. control group and baseline for the mini-mental state examination score and activities of daily living score.*
- In a pilot double-blind, placebo-controlled, randomized clinical trial with 34 healthy adolescents (average age 15 years) huperzine A (100 mcg twice daily for up to 4 weeks) resulted in a statistically significant difference vs. placebo when measuring memory function.*

ALPHA-GPC

Structure Formula:



Chemical Name: L-α-glycerylphosphorylcholine, choline alphoscerate

ROLE AS NUTRIENT/FUNCTION

Milk is the main source of dietary glycerylphosphorylcholine; it can also be produced from soy lecithin. Alpha-GPC is known to be an acetylcholine precursor.*

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

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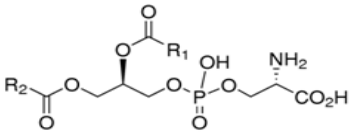
Alpha-GPC is a rapidly absorbed source of choline that does not carry the electrical charge of regular choline, making it easier for the compound to cross the blood-brain barrier.

CLINICAL VALIDATION

- Alpha-GPC has been clinically evaluated in age-related cognitive disorders, typically at a daily dose of 1,200 mg. These investigations have consistently shown significant differences vs. placebo on most of the evaluated parameters such as MMSE, basic activities of daily living, ADAS-cog.*

PHOSPHATIDYL SERINE

Structure Formula:



Chemical name. (R1, R2 – fatty acids)

ROLE AS NUTRIENT/FUNCTION

Phosphatidyl serine (PS) is present in common foods in small amounts. Soy-derived PS is a product of enzymatic reaction of soybean lecithin with the amino acid L-serine. Until PS from plant lecithin became commercially available, bovine brain was the most significant dietary source of PS. PS is most often considered a semi-essential nutrient. Although it can be synthesized *in vivo,* its multistep biosynthesis is energetically costly. PS and other phospholipids form the basic structure of all cellular membranes, and the PS concentration is higher in brain cell membranes than elsewhere in the body. Membrane phospholipids play an important role in cell-to-cell communication, particularly in the central nervous system, where PS concentration correlates with neuroplasticity, normal function of neurotransmitter systems, and cognitive performance.*

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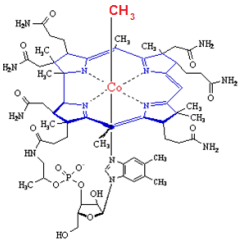
PS absorption follows the pathway typical for fatty acids. Following oral administration, serum PS concentration peak occurs in 1-4 hours. The majority of PS is distributed in lipoprotein particles, preferentially in high-density lipoprotein particles. PS crosses the blood-brain barrier, where it appears to have affinity to the hypothalamus.

CLINICAL VALIDATION

- In a double-blind, randomized, placebo-controlled study conducted with 78 volunteers (50-69 years old), supplementation with soy-derived PS (100 or 300 mg/day for 5 months) significantly increased memory scores in the subjects with relatively low scores at baseline ($P < 0.001$), while those of the placebo group remained unchanged.* The memory improvements in the PS-supplemented groups were mostly attributed to the increase in delayed verbal recall, which is typically associated with age-related cognitive decline.*

METHYLCOBALAMIN

Structure Formula:



Chemical Name: Co-methyl (dimethyl-5,6-benzimidazolyl) cobamide, methyl vitamin B_{12}

ROLE AS NUTRIENT/FUNCTION

Vitamin B_{12} is most often found in food of animal origin. Vitamin B_{12} is an essential nutrient that cannot be synthesized in the human body.

Vitamin B_{12} is a cofactor for two enzymes: methionine synthase and L-methylmalonyl-CoA mutase.* Vitamin B_{12} deficiency has high prevalence among people 65 years and older and results in accumulation of homocysteine, which is linked to cognitive decline and depression. Cobalamin-dependent metabolites are also responsible for production of energy from fats and proteins, synthesis of hemoglobin and functional integrity of myelin sheath.*

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Absorption. Cobalamin is absorbed via active and passive mechanisms:

- Active absorption of cobalamin requires the presence of intrinsic factor (IF), which is secreted in the stomach. IF-cobalamin complexes attach to specialized epithelial receptors in the distal ileum where it is then absorbed. The time from oral ingestion to entry into the bloodstreams can typically take up to 4 hours. The total amount of vitamin B_{12} absorbed via IF-mediated mechanism doesn't exceed 3 mcg of cobalamin at a time.
- Absorption through passive diffusion occurs independently of IF at all mucosal sites including sublingual epithelium. Although only 1 to 2% of the cobalamin is absorbed, passive transport results in significant increase in serum cobalamin concentrations when higher doses are administered. Absorption of Methyl B_{12} 10,000 mcg lozenge (Protocol for Life Balance®; Product #P0497) has been studied in healthy volunteers, with T_{max} of approximately 7 hours (Fig. 1).

Distribution. Absorbed cobalamin is transported via specific proteins (transcobalamins, haptocorrins). The majority of vitamin B_{12} is stored in the liver (2,000-5,000 mcg). Transport of cobalamin across cellular membranes depends on several binding proteins. Methylcobalamin passes through the blood-brain barrier using an active transport mode.

Metabolism. Following transport into the cell, cobalamin is converted to either methylcobalamin or 5-deoxyadenosylcobalamin, the two coenzyme forms of vitamin B_{12}.

Elimination. Unabsorbed vitamin B_{12} is mostly eliminated through feces. When plasma amounts exceed its plasma binding capacity, vitamin B_{12} is also lost through urine. An estimated 1.4 mcg/day of cobalamin is cleared

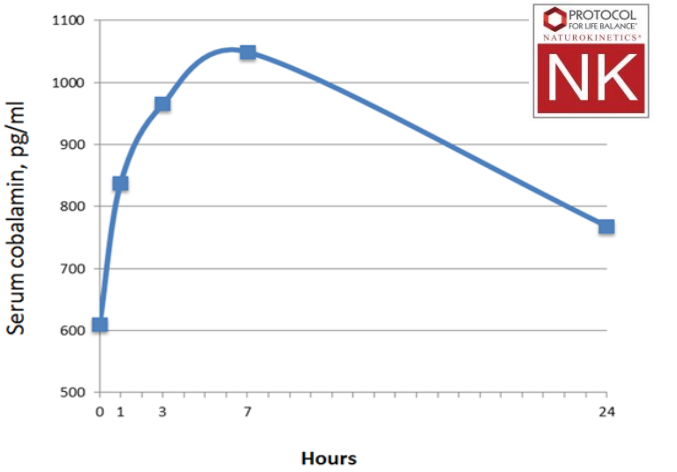

Fig.1. Average serum cobalamin concentration following a single administration of a methylcobalamin lozenge (Protocol for Life Balance®, Product # P0497; 10,000 µg) in healthy adult volunteers.

and excreted into the bile, 70 % to 90 % of which is normally reabsorbed. The daily amount of vitamin B_{12} excreted from the body is 0.1%-0.2% of total body stores.

CLINICAL VALIDATION

- In a randomized, open-label, controlled study with 135 post-stroke patients, methylcobalamin supplementation (1,500 µg/d for 2 years) significantly improved objective measurements of distal nerve conduction and sensory function as compared with control group not receiving supplementation.*

SAFETY INFORMATION

Tolerability: Due to its cholinergic effect, supplementation with huperzine A may be associated with nausea, sweating, diarrhea, dizziness, muscle cramping, high blood pressure, blurred vision, hyperactivity, anorexia, decreased heart rate, and fasciculation. When huperzine A is used at the highest recommended dose (800 mcg/day for 24 weeks), it was generally well-tolerated with most common complaint being nausea.

Contraindications: Do not use if pregnant or nursing.

INTERACTIONS

Drug Interactions: Huperzine A may have an additive effect when combined with other acetylcholinesterase inhibitors and cholinergic drugs including bethanechol (Urecholine®), donepezil (Aricept®), echothiophate (Phospholine Iodide), edrophonium (Enlon®, Reversol, Tensilon), neostigmine (Prostigmin), physostigmine (Antilirium), pyridostigmine (Mestinon®, Regonol®), succinylcholine (Anectine®, Quelicin®), and tacrine (Cognex®); and may counteract the effect of anticholinergic drugs including atropine, benztropine (Cogentin®), biperiden (Akineton), procyclidine (Kemadrin), and trihexyphenidyl (Artane®).

Supplement Interactions: No known interactions.

Interaction with Lab Tests: No known interactions.

STORAGE

Store in cool, dry & dark environment.