Neuro Health Plus

PRODUCT TECHNICAL EDUCATION SHEET

Neuro Health PLUS, is a sophisticated brain and nervous system supplement formulated to support optimal neuronal health and overall brain function. Neuro Health PLUS is a therapeutic strength, research-based formulation that nourishes the brain and neurons, unlocking the brain's true potential day and night. When taken during the day, Neuro Health PLUS offers support for nervous system health, overall stamina, focus, concentration, decision making, memory, and learning. At night, it further supports all aspects of brain health by leveraging the power of deep, restorative sleep, proven to facilitate many of these important neurological and cognitive processes.

INDICATIONS

- Brain health
- Memory
- Cognitive function
- Mental stamina
- Concentration
- Recall
- Learning
- Decision making
- Nervous system health

INGREDIENTS

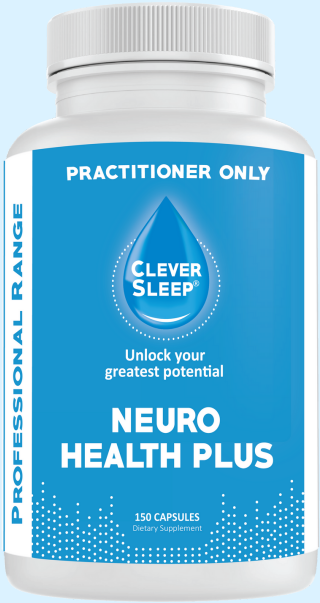
Ingredient	Elemental Per Capsule	Elemental Per 5 Cap Daily Dose
Ginkgo biloba (*Ginkgo*)	28mg	140mg
Humulus lupulus (*Hops*)	10mg	50mg
L-Theanine	40mg	200mg
Magnesium Citrate	52mg	260mg
Magnesium Phosphate	28mg	140mg
Phosphatidylserine	40mg	200mg
Prunus cerasus (Tart Cherry)	90mg	450mg
Pyridoxine (Vitamin B6)	4mg	20mg

COMPANION PRODUCTS

CleverSleep® Practitioner Only Products: Ultimate MAG, MAX Sleep and Liquid MAG.

FEATURES & BENEFITS

Feature	Benefit
Two scientifically researched, bioavailable forms of Magnesium	Magnesium is needed by every cell in the body, is crucial for brain health and healthy deep sleep, the important body process which facilitates memory consolidation. Magnesium supports the entire nervous system.
Magnesium oxide free formula	Gentle on the digestive system. Superior absorption.
Therapeutic doses of magnesium	Facilitates overall health and wellbeing by providing the required amount of elemental magnesium providing additional requirements to correct nutritional deficiencies.
Phosphatidylserine	It is an essential component of healthy cell membranes, critical to brain metabolism and function, contributing to nervous system health by clearing out neuronal metabolites, and supports brain-cell connections.
L-Theanine	A natural supplement which is shown in clinical studies to support the ability to focus and aids in quality sleep.
Vitamin B6	Supports management of the stress hormone cortisol and nervous system health. It is used in the synthesis of neurotransmitter production.
Hops	Hops is a herbal medicine shown to decrease stress hormones and positively impact on mental health as well as support sleep.
Ginkgo	Research shows that Ginkgo improves cognitive function because it improves blood circulation in the brain and protects neuronal health.
All natural	Neuro Health Plus uses scientifically validated natural ingredients that support brain and nervous system health, cognitive function and memory consolidation day and night. The ingredients are non-habit forming.



DOSAGE INSTRUCTIONS

For best results, use for a minimum of three months or as directed by your healthcare professional.

Adults:
Take two capsules with water each morning and three capsules at night before bed.

Note: Due to the stimulating nature of this high strength product, some people may require additional natural relaxation to achieve sleep at night. Should this be the case consider prescribing MAX Sleep, Ultimate MAG or Liquid MAG from the CleverSleep® range.

If sleep disturbances are an issue for your patient the full dose can be taken in the morning.

Available in 150 capsule, one month supply bottle.

CleverSleep®. For educational purposes only.

NEURO HEALTH PLUS

PRODUCT TECHNICAL EDUCATION SHEET

GINKGO BILOBA (GINKGO)

The Ginkgo biloba (Ginkgo) extract is an ancient Chinese herb that has been used to treat cerebral vascular insufficiency, cognitive disorders, dementia, memory loss, and mental health conditions worldwide. Clinical studies have shown Ginkgo can slow the progression of age-related conditions due to its powerful antioxidant (flavonoids) and circulatory qualities (terpenoids). (See Figure 1.0)[1]

INGREDIENT RESEARCH

Studies suggest that Ginkgo acts by:

- Supporting healthy circulation;[2 3]
- Helping maintain the normal function and tone of blood vessels;[4 5]
- Supporting healthy oxygen and glucose metabolism in the brain;[6 7 8 9]
- Stabilising capillaries and making them less fragile; [10 11 12]
- Supporting ideal clotting and coagulation of blood; [13 14]and
- Supporting healthy aging in the brain.[15 16 17 18 19]

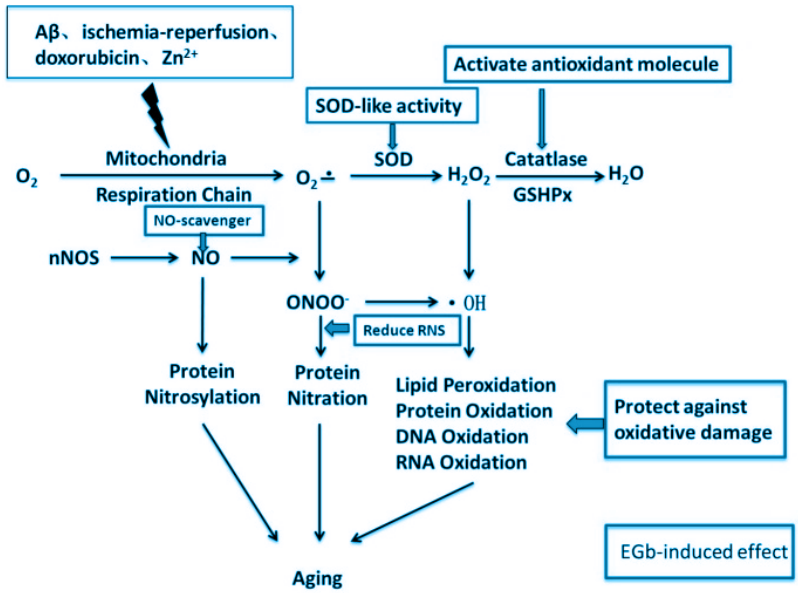


Figure 1.0 The role and effect of Gingko biloba extract (EGb) in protecting pathways for oxidant generation in aging. (EGb-induced effect in blue boxes)

Adapted From Zuo, W., Yan, F., Zhang, B., Li, J., & Mei, D. (2017). Advances in the Studies of Ginkgo Biloba Leaves Extract on Aging-Related Diseases. Aging and disease, 8(6), 812–826. https://doi.org/10.14336/AD.2017.0615[20]

- A randomised, controlled, and multicentre clinical trial treated 348 acute stroke patients with three daily doses of 150mg Gingko biloba extract (GBE) combined with aspirin for six months after stroke onset and compared it to a control group taking only aspirin. Both groups were concomitantly in a regular treatment strategy, which included lipid-lowering, antihypertension, glucose-lowering, and neuroprotection. The Montreal Cognitive Assessment (MoCA) was used to evaluate the cognitive executive function at admission, and at 12, 30, 90, and 180 days. Lower scores predicting the worst outcomes. MoCA scores were overall higher in the GBE group. A statistically significant difference ($p<0.05$) was detected in the deMoCA (decline of the MoCA) for the GBE group, indicating that GBE combined with aspirin treatment may promote an improvement of the cognitive and neurological deficits after acute ischaemic stroke. (See Figure 2.0)[21]

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GINKGO BILOBA (GINKGO) CONTINUED

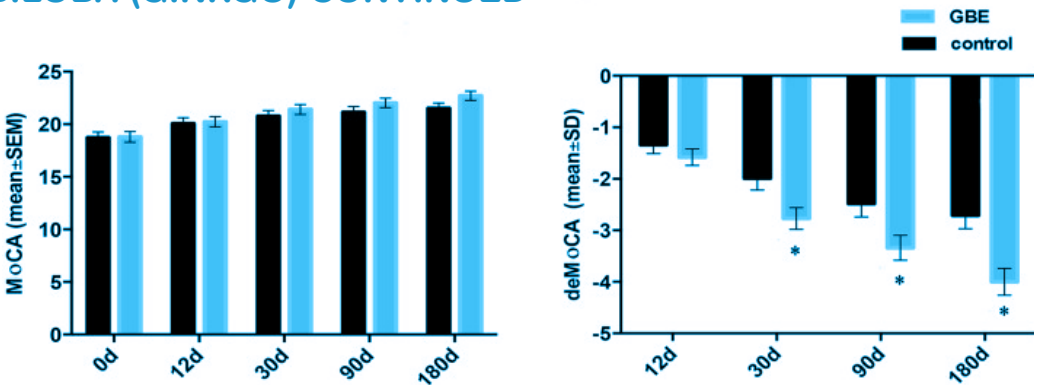

Figure 2.0 Montreal Cognitive Assessment (MoCA and deMoCA) scores as a measure of post-stroke cognitive function in control vs GBE treatment group at admission, 12, 30, 90 and 180 days.

Adapted From Li S, Zhang X, Fang Q, Zhou J, Zhang M, Wang H, Chen Y, Xu B, Wu Y, Qian L, Xu Y. Ginkgo biloba extract improved cognitive and neurological functions of acute ischaemic stroke: a randomised controlled trial. Stroke Vasc Neurol. 2017 Dec 18;2(4):189-197. doi: 10.1136/svn-2017-000104. Erratum in: Stroke Vasc Neurol. 2018 Sep 21;3(3):189. PMID: 29507779; PMCID: PMC5829919[21]

HUMULUS LUPULUS (HOPS)

Hops are the common name of the Humulus lupulus L. plant and have been traditionally used in herbal medicine for the relief of insomnia, excitability, and restlessness associated with tension headaches and nervous tension.[22]

INGREDIENT RESEARCH

- Kyrou et al (2017) have shown that hops significantly decreased DASS-21 anxiety (see Figure 3.0) depression scores and stress scores (figure 4.0), which were significantly greater compared to the placebo (all p values <0.05).[22]

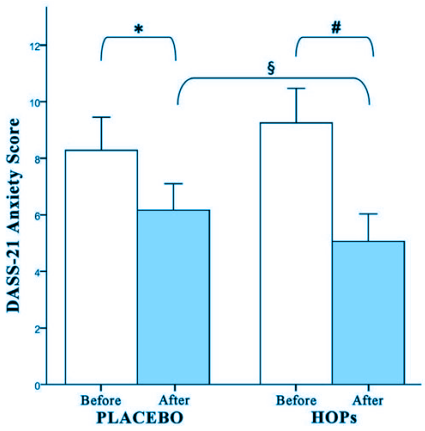

Figure 3.0 Depression Anxiety stress scale-21 anxiety scores at baseline and after hops and placebo 4-week treatment.

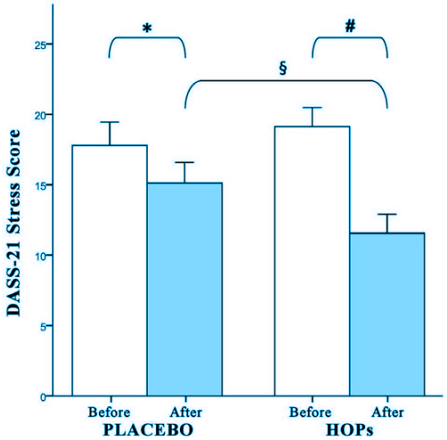

Figure 4.0 Depression anxiety stress scale-21 (DASS-21) stress scores at baseline and after hops and placebo 4-week treatment

Adapted From Kyrou I, Christou A, Panagiotakos D, Stefanaki C, Skenderi K, Katsana K, Tsigos C. Effects of a hops (Humulus lupulus L.) dry extract supplement on self-reported depression, anxiety and stress levels in apparently healthy young adults: a randomized, placebo-controlled, double-blind, crossover pilot study. Hormones (Athens). 2017 Apr;16(2):171-180. doi: 10.14310/horm.2002.1738. PMID: 28742505.[22]

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PRODUCT TECHNICAL EDUCATION SHEET

HUMULUS LUPULUS (HOPS) CONTINUED

- The effects of the Hops extract have been shown to be comparable with melatonin, although the onset of action is earlier for the melatonin (60 min after i.p. administration).[23]
- A randomised, double-blind, controlled clinical trial demonstrated equivalent efficacy and tolerability (hops-valerian preparation versus benzodiazepine) according to DSM-IV criteria evaluating sleep quality, fitness, and quality of life. The patients' state of health improved during therapy and then deteriorated after cessation with both preparations. The conclusion was that the investigated hop-valerian preparation in the appropriate dose could be a sensible alternative to benzodiazepine for the treatment of non-chronic and non-psychiatric sleep disorders.[24]

L-THEANINE (THEANINE)

L-Theanine is an amino acid, naturally found in green and black tea. Research suggests that it may support GABA, serotonin, and dopamine which positively influences mood, sleep, emotion, and cortisol levels.

INGREDIENT RESEARCH

- The increase in anxiety, stress, and heart rate that occurred in subjects given mental tasks was attenuated with theanine (200mg/daily) compared to placebo.[25]
- A multi-centre study showed the administration of L-Theanine decreased the stress-related symptoms of the subjects and improved cognitive function in areas such as verbal fluency and letter fluency, which were significantly better than a placebo in a healthy population.[26]
- L-Theanine appears to have a role in the formation of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). GABA stimulates the release of the neurotransmitters dopamine and serotonin and may have a key role in the relaxation effect. [27](See Figure 5.0)[28]

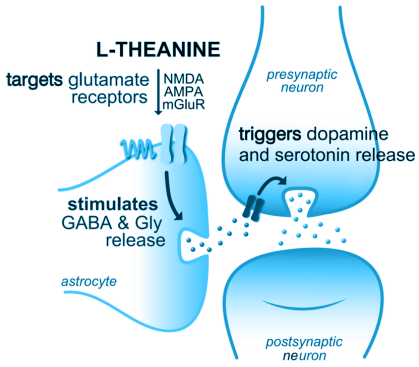

Figure 5.0 The effect of L-Theanine on GABA and Neurotransmitters demonstrating a key role in the relaxation effect.

Adapted From https://www.zrtlab.com/blog/archive/l-theanine-green-tea-neurotransmitter-anxiety[28]

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PRODUCT TECHNICAL EDUCATION SHEET

MAGNESIUM

Magnesium is required as a cofactor for over 600 enzymatic processes, having a crucial role in energy production (ATP) required universally for every bodily function. For example, ATP is required to support muscles and nerve function (see Figure 6.0). glucose utilisation, synthesis of fat, protein, nucleic acids, and coenzymes. Therefore, it is important to highlight that ATP metabolism, muscle contraction, relaxation, normal neurological function, and release of neurotransmitters are all magnesium-dependent.[29]

Magnesium acts on several physiological steps involved in mediating the stress response of the central nervous system. One mechanism is that it indirectly reduces the release of two key stress hormones, adrenocorticotropic hormone and cortisol. Magnesium also exerts long-term neuroprotective and anti-oxidant effects against future stress.[30]

INGREDIENT RESEARCH

Clinical uses of Magnesium:

- Support sleep, stress, and insomnia
- Increase slow-wave sleep (The most restorative sleep phases, theta and delta)[30]
- Mediate the stress response of the sympathetic nervous system.[30]
- Reduce cortisol (stress hormone) overproduction
- Help reduce restless leg syndrome.[31]

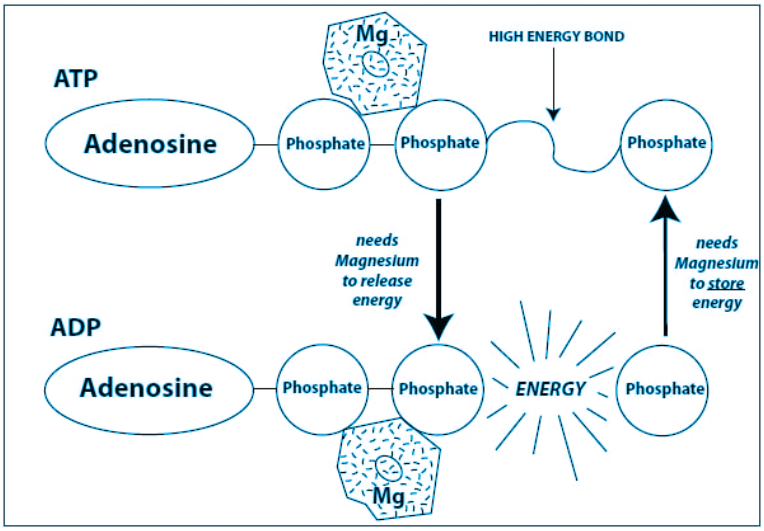

Figure 6.0 The role of Magnesium (Mg) in ATP production and ATP storage.
Adapted From Seelig, M. S., Rosanoff, A. (2003). The Magnesium Factor. United States: Avery[32]

MAGNESIUM CITRATE

INGREDIENT RESEARCH

- Evidence shows superior absorption and significantly increased plasma and salivary Mg concentrations after 60 days of supplementation compared to Mg Oxide and Mg amino acid chelate. (See Figure 7.0) Well absorbed by the digestive system.[33]
- A highly effective form of magnesium supplementation.[34]

NEURO HEALTH PLUS

PRODUCT TECHNICAL EDUCATION SHEET

MAGNESIUM CITRATE CONTINUED

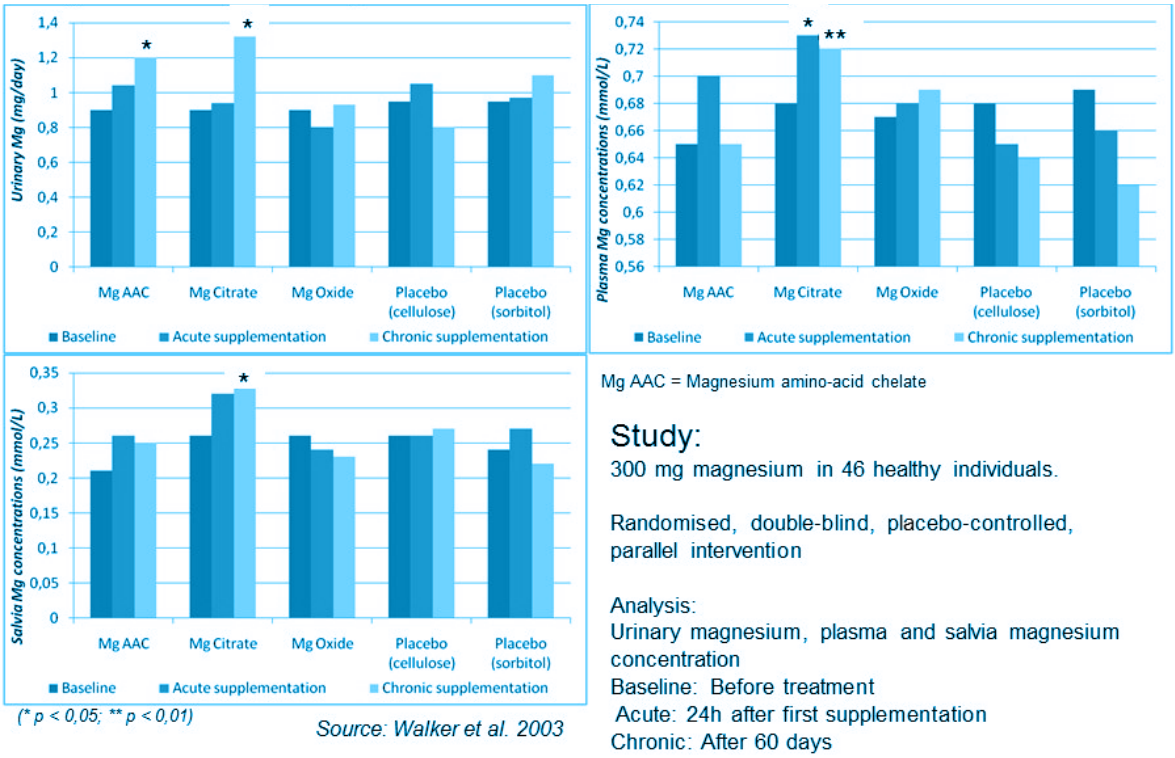

Figure 7.0 Urinary magnesium, plasma and saliva magnesium concentration measured at baseline and following acute and chronic Magnesium supplementation

Adapted From Walker AF, Marakis G, Christie S, Byng M. 2003. Mg citrate found more bioavailable than other Mg preparations in a randomised double-blind study. Magnes Res. 16(3):183-91[32]

MAGNESIUM PHOSPHATE

INGREDIENT RESEARCH

- It is a form of magnesium that has an excellent affinity with nerves and muscles.
- Indicated to support energy production, normal nerve function and muscle function.
- Indicated to reduce muscle cramp, spasm, twitch, and headaches.[35]
- Research has shown magnesium phosphate supplementation significantly improved muscle spasticity, a symptom of severe spastic paraplegia causing muscle weakness and stiffness. (See Figure 8.0)[36]

MAGNESIUM PHOSPHATE CONTINUED

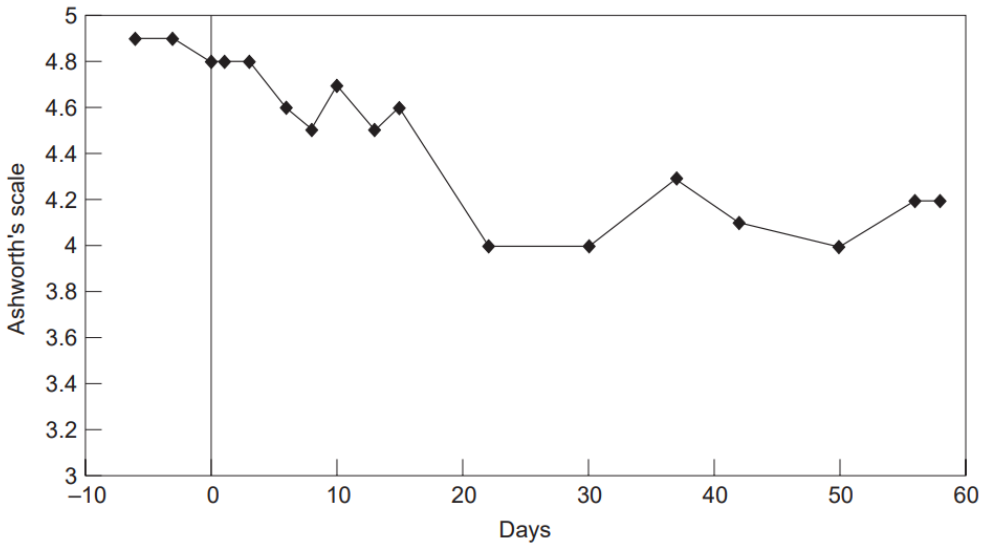

Figure 8.0 Evolution of the spasticity in the legs measured using the modified Ashworth scale and using an average of 10 measures, during the treatment of magnesium. The treatment started at day 0 with 100 mg elemental magnesium (no significant change is seen when increasing the dose to 150 mg on the 42nd day)

From Rossier P, van Erven S, Wade DT. The effect of magnesium oral therapy on spasticity in a patient with multiple sclerosis. Eur J Neurol. 2000 Nov;7(6):741-4. doi: 10.1046/j.1468-1331.2000.00142.x. PMID: 11136367.[36]

PHOSPHATIDYLSERINE (PS)

Phosphatidylserine (PS) is one of the most prevalent phospholipids in the brain and is an essential component of myelin, critical to brain metabolism and function, and supporting brain-cell connections.[37] PS is localised exclusively in the cytoplasmic leaflet (plasma membranes) where it is responsible for the activation of several key signalling pathways. These include the Akt (protein kinase B), protein kinase C (PKC), and Raf-1 signalling which is known to stimulate the genesis, growth, and survival of the entire neuronal and synapsis chain. The modulation of the PS level in the membrane of neurons is extremely relevant for these processes. (See figure 9.0)[38]

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PHOSPHATIDYLSERINE (PS) CONTINUED

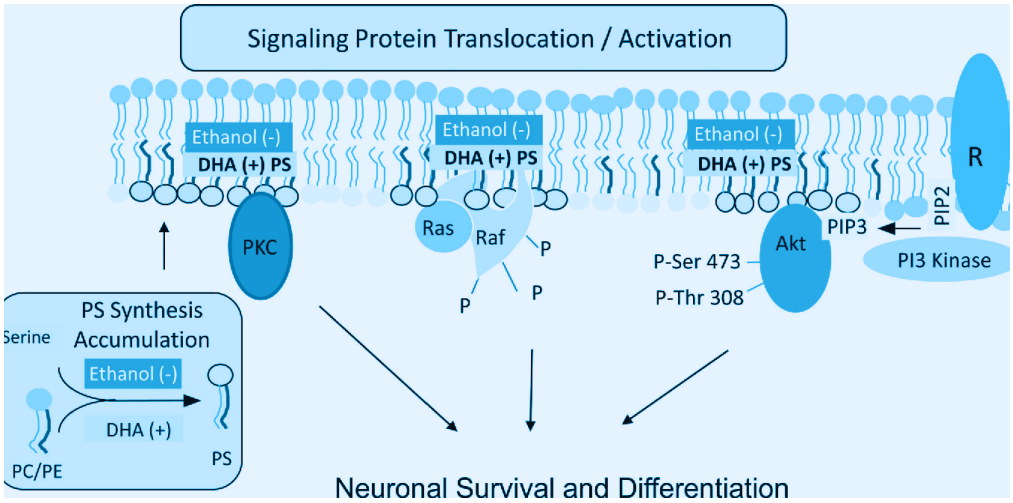

Figure 9.0 Activation of neuronal signalling pathways facilitated by Phosphatidlyserine (PS) leading to neuronal differentiation and survival.

Adpated From Kim, H. Y., Huang, B. X., & Spector, A. A. (2014). Phosphatidylserine in the brain: metabolism and function. Progress in lipid research, 56, 1–18. https://doi.org/10.1016/j.plipres.2014.06.002.[36]

INGREDIENT RESEARCH

- Research has shown Phosphatidylserine (PS) promotes healthy cognitive function, healthy memory, concentration and attention. Additionally, PS improves brain glucose metabolism and stimulates the production of acetylcholine, a key neurotransmitter of the parasympathetic nervous system.[39]
- A randomised controlled trial found that 300 mg of PS per day for 8 weeks normalised the EEG patterns of Alzheimer's Disease patients, whilst 400 mg of PS per day improved brain glucose metabolism, normalised EEG patterns, and improved cognition.[40]
- Improved cognitive performance in elderly adults with memory deficits.[41]
- Enhanced cognitive performance in school children and adults.[42]
- PS significantly improved ADHD symptoms and short-term auditory memory in children. PS supplementation might be a safe and natural nutritional strategy for improving mental performance in young children suffering from ADHD.[42]
- Restored impaired neuronal calcium and glucose uptake and metabolism in an aging brain.[43]
- A precursor of neuronal membrane phospholipid that is responsible for neuroplasticity, learning, and memory.[43]
- The benefits from PS supplementation can also be seen in patients with early stages of dementia. The most important benefits noted are improved ability to learn and recall names of familiar persons, the location of misplaced objects, details from the prior week and telephone numbers. Their ability to concentrate while reading, conversing and task performance also improved.[43]

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PRUNUS CERASUS (TART CHERRY)

Tart Montmorency cherries (Prunus cerasus) are rich in numerous phytochemicals and acts as a powerful antioxidant that could protect against the development of neurological disorders and sleeping disorders.

INGREDIENT RESEARCH

- Clinical studies have reported a reduction in inflammatory and oxidative markers in healthy people.[44]
- The use of Tart Cherry in conjunction with pharmacological therapies has been shown to decrease adipose inflammation, drug doses, and ultimately, drug-induced adverse effects.[44]
- Potent antioxidant – reduces inflammatory chemicals possibly attributed to sleeping problems.[44]
- Reduces C-reactive protein.[44]
- Natural source of melatonin. A randomised, double-blind, placebo-controlled study found that total urinary melatonin content was significantly elevated after 7 days of Tart cherry supplementation. (See Figure 10.0)[45]. The treatment group also showed significant improvement in sleep duration and reduced sleep latency[45]

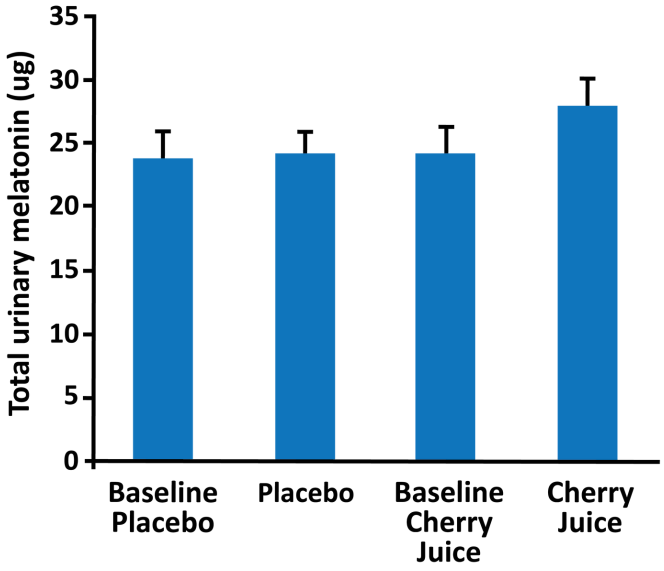

Figure 10.0 Mean (±SEE) urinary melatonin (aMT6) secretion for the group following baseline placebo (control), placebo, baseline cherry juice (control) and cherry juice trials. Cherry juice supplementation resulted in significantly greater total urinary melatonin than baseline and placebo trials (P B 0.05)

Adapted from Howatson G, Bell PG, Tallent J, Middleton B, McHugh MP, Ellis J. Effect of tart cherry juice (Prunus cerasus) on melatonin levels and enhanced sleep quality. Eur J Nutr. 2012 Dec;51(8):909-16. doi: 10.1007/s00394-011-0263-7. Epub 2011 Oct 30. PMID: 22038497. [45]

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PYRIDOXINE (VITAMIN B6)

Pyridoxine is one of three related isoforms that are known as vitamin B6. Its absorption takes place in the small intestine, being converted into pyridoxal 5'-phosphate (PLP), the active metabolite of B6, a key factor for the modulation of more than 150 enzymatic reactions. Therefore, it is significantly involved in various pathways related to mood, sleep cycle, mental function, stress, and inflammation, possibly playing a relevant role in depressive disorders. (See Figure 11.0)[46]

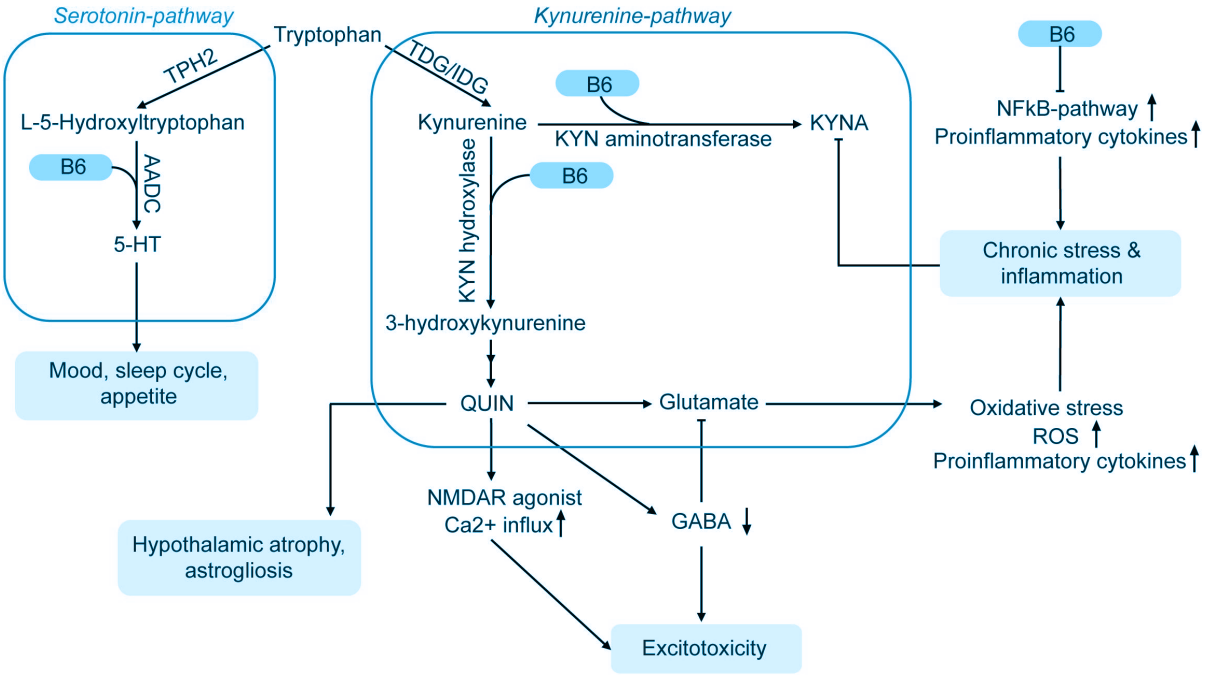

Figure 11.0 The role of Vitamin B6 (Pyridoxine) in the Serotonin and Kynurenine-pathways related to mood, sleep cycle, mental function, stress and inflammation.

Adapted From Aly J, Engmann O. The Way to a Human's Brain Goes Through Their Stomach: Dietary Factors in Major Depressive Disorder. Front Neurosci. 2020 Dec 7;14:582853. doi: 10.3389/fnins.2020.582853. PMID: 33364919; PMCID: PMC7750481[46]

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PRODUCT TECHNICAL EDUCATION SHEET

PYRIDOXINE (VITAMIN B6) CONTINUNED

INGREDIENT RESEARCH

- Pyridoxine deficiency is a significant predictor of increased overall psychological distress and pyridoxine deficiency status is associated with increases in depression, fatigue, and low mood levels.[47]
- High tissue levels of pyridoxal 5'-phosphate (PLP) are believed to mitigate the physiological consequences of stress, both peripherally and centrally. As compared to DOPA decarboxylase, the enzymes 5-hydroxytryptophan decarboxylase and glutamate decarboxylase have a relatively low affinity for PLP. Thus, pyridoxine deficiency tends to selectively reduce the brain's production of serotonin and GABA, while having relatively little impact on levels or turnover of dopamine and norepinephrine. Therefore, pyridoxine administration can often boost the central production of serotonin and GABA.[48]
- Pyridoxal 5'-phosphate (PLP)-dependent enzymes are involved in the following reactions:
  - Decarboxylation of amino acids to amines, with several important neurotransmitters and hormones related to this process including dopamine, norepinephrine and serotonin, tyramine, tryptamine, taurine, histamine, gamma-aminobutyric acid, and even acetylcholine indirectly;
  - Transamination of amino acids to keto-acids, which are then oxidised and used as metabolic fuel;
  - Participation in the production of a precursor to heme;
  - Participation in phospholipid synthesis.[49]

CAUTIONS

Neuro Health Plus should be administered two hours away from medications, especially from tetracycline and quinolone antibiotics.

People taking blood thinners need to alert their physician prior to taking this product to monitor their blood parameters. The effect of platelet-aggregation inhibitors may be enhanced.

Magnesium supplementation may decrease the absorption and efficacy of some medications.

Magnesium supplementation can cause loose bowel movements. The threshold at which this may occur varies between people. The effect is normally temporary but if your patient feels uncomfortable, or this is not manageable please split the dosage until bowel movements stabilise.

CONTRAINDICATIONS

Anyone with an allergy or sensitivity to one or more of the ingredients.

This technical education sheet was created by CleverSleep® Research team for healthcare professionals. This information is not intended to replace medical advice. It is designed to provide the most updated information about our products. All the scientific research used to validate this document is available upon request or through the research section of our website www.cleversleep.co.nz.