

Vagus Nirvana™



THIS INFORMATION IS FOR PHYSICIANS AND OTHER LICENSED HEALTH CARE PRACTITIONERS ONLY. THE INFORMATION IS INTENDED TO ASSIST PRACTITIONER DECISION MAKING AS TO WHETHER OR NOT THESE PRODUCTS FIT THE NEEDS OF THEIR PATIENT. THE SCIENTIFIC INFORMATION AND DIETARY SUPPLEMENT PRODUCTS PROVIDED BY ALIGHT HEALTH FORMULAS ARE NOT INTENDED FOR USE BY CONSUMERS AS A MEANS TO CURE, TREAT, PREVENT, DIAGNOSE, OR MITIGATE ANY DISEASE OR OTHER MEDICAL CONDITION.

Vagus Nirvana™ is a first-of-its-kind herbal glycerite blend to address the vagal system and is safe for children, and adults. Vagus Nirvana™ supports a calming effect on the nervous system by addressing the vagal tone and balancing autonomic nervous system function. This product is entirely free of alcohol and naturally tastes sweet with no added sugars or sweeteners.

Vagal dysfunction is a common and expected result of autoimmune assaults on the central nervous system. Certain herbs have been used for millennia in Chinese and Ayurvedic traditions to transition the nervous system back to a state of calm.

The autonomic nervous system is wired to prioritize safety over all things. The two branches, sympathetic and parasympathetic, are in constant flux, depending on the perceived level of threat at any given moment. They seek a state of balance, which allows bodily functions to run optimally.

Since safety is necessary for survival, the autonomic system allows the sympathetic branch to dominate the parasympathetic branch whenever threats are perceived.

When the brain is chronically inflamed from chronic infections, toxicants, or trauma, the sympathetic system may get stuck in overdrive, continuously overriding the parasympathetic branch. In sympathetic dominance, the background functions governed by the parasympathetic branch are blunted, such as rest, digest, restore, and creating a feeling of safety.

The herbs in Vagus Nirvana™ were meticulously selected for their balancing effects on the central nervous system and vagal tone. Time-trusted botanicals that have a record of safe use in children promote normal parasympathetic functions, while reducing sympathetic tone.

Brain chemistry isn't the whole story. The inflammation which caused the alarm in the first place needs to be addressed, otherwise the imbalance in neurotransmitters will simply rebound. Herbs targeting neuroinflammation which also have a calming effect have been cleverly added to reduce the bioactive components involved in neuroinflammation, such as mast cell migration and microglial activation. Even though Vagus Nirvana™ is non-sedating, it may promote restorative sleep phases.

Supplement Facts	
Serving Size 1/4 tsp. (1.25mL)	
Servings Per Container 48	
Amount Per Serving	% Daily Value
Proprietary blend:	369mg h/w equivalence*
Perilla leaf (Perilla frutescens)	
Mombin leaf (Spondias mombin)	
Sacred Lotus leaf (Nelumbo nucifera)	
Feverfew aerial (Fresh Tanacetum parthenium)	
White Mulberry leaf (Morus alba)	

*Daily Value not established.
Other Ingredients: Organic glycerin and distilled water
Free from alcohol, gluten, dairy, soy, GMOs.

Recommended Use

Child-safe dose (50lb): Take ¼ tsp as needed up to 4 times daily, or as directed by your health care practitioner. Adjust for others using a weight-adjusted dose.

Perilla

Perilla's role in the blend is primarily to manage the neuroinflammation triggering components. It also has a protective effect on dopaminergic neurons, the target of autoimmune attack in PANDAS and PANS, with an effect of suppressing dopaminergic neuronal loss and subsequent behavioral dysfunction. Mouse studies suggest that perilla aldehydes had favorable alterations in serum cytokines and depressive-like behavior, and inhaled perilla aldehydes showed antidepressant-like activity through olfactory nervous function.

Perilla is rich in anti-inflammatory flavones, such as apigenin and luteolin, as well as rosmarinic acid. It has an inhibitory effect on mast cell-mediated immediate-type allergic reactions and IgE-mediated immediate hypersensitivity reactions. Studies show that perilla extract reduced the plasma histamine levels in a dose-dependent manner. In addition, it down-modulates the Th17 response.

Mombin

The leaves of mombin have been traditionally used as a non-sedating anxiolytic and antidepressant, as well as to treat many digestive complaints, such as abdominal discomfort, diarrhea, and ulcers, further reinforcing the gut-brain connection. Mombin has active constituents with known antioxidant and anti-inflammatory activities, being high in quercetin and catechins. These activities along with its neuroprotective effects, mediated through anxiolytic and antioxidant activities, are why it was selected for Vagus Nirvana™. Mombin possesses antidopaminergic activity while also having action as a GABA agonist. Animal studies suggest that it attenuates oxidative stress and regulates ionic homeostasis under states of neurotoxic stress.

Mombin has added antibacterial, antifungal, and antiviral activity, with studies showing that the extract potentiates antibiotic and antifungal drug activity. With this added mechanism, mombin also helps to manage the infective neuroinflammatory triggers.

Sacred Lotus

Sacred lotus has been used traditionally in South East Asia as an ethnobotanical medicine for various CNS disorders including stress, anxiety, depression, insomnia, and cognitive conditions. Its uplifting effects may be due to increasing the level of 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA), and reducing the level of dopamine (DA), norepinephrine (NE), acetylcholine (ACh) in the hypothalamus.

The alkaloids of sacred lotus display varying degrees of opioid receptor affinity along with a cannabinoid-type effects, while having no effect on cannabinoid receptors, garnering its label as being safe to use in children. For those with sleep issues due to neuroinflammation, the neuropharmacological findings of sacred lotus show that it promotes non-REM sleep by regulating GABAergic receptors.

Sacred lotus' bioactive alkaloid neferine mitigates microglial neuroinflammation through Nrf2 activation, a commonly disrupted antioxidant pathway with mold exposure. Through this action and by altering the expression of the NLRP3 inflammasome, sacred lotus also helps to mitigate the neuroinflammatory effects leading to vagal dysfunction.

Made without the use of alcohol. Free from added sweeteners.

Taste-tested by both kids and adults. Glycerin provides a pleasantly sweet taste.

Feverfew

Though many are familiar with feverfew as a “head” remedy, used for headaches and migraines, feverfew approaches vagal dysfunction primarily from the bottom up, from the gut to the brain. The bidirectional cross-talk between the brain and gut is an often overlooked contributor to vagal dysfunction. Feverfew ameliorates colon inflammation through regulating the T-Regulator-Th17 balance in a gut microbiota-dependent manner, meaning the higher the dose and the more supported the gut microbiome, the stronger the effect. The plant’s major component, parthenolide, displayed reduction of LPS-stimulated microglial activation by inhibition of proinflammatory agents.

However, make no mistake, feverfew does exert CNS effects as well, being shown to be effective in reducing prostaglandin release and IL-1 β gene expression, while increasing gene expression of brain-derived neurotrophic factor (BDNF). Additionally, parthenolide decreases extracellular dopamine levels, having an overall calming effect.

White Mulberry

White mulberry has a long history of safe use treating nerve disorders as well as improving cognitive function, learning processes, and reducing memory impairment — effects confirmed by many animal models. It has also been studied in clinical trials to reduce blood glucose and cholesterol levels and enhance cognitive ability. White mulberry meets Alight Health’s sustainability standards by being a fast-growing shrub that produces ample leaves for harvesting.

White mulberry’s anxiolytic effects involve direct action on the neurochemistry, as well as terrain effects involving suppression of histaminergic systems in the CNS with action on the histamine-3 (H3) receptor. The H3 receptor is highly expressed in the CNS and presynaptically inhibits the release of a number of other neurotransmitters.

White mulberry’s calming effect may be due to its antidopaminergic activity. White mulberry is specific to the dopamine receptor damage and subsequent excitatory state observed in PANDAS and PANS, displaying activity as a dopamine 1 and 2 (D1R/D2LR) antagonist, while being a dopamine 3 and 4 (D3R/D4R) agonist.

Therapeutic Differences by Composition



Glycerin was chosen as the extraction menstruum for the herbs in this formula for more than its alcohol-free benefits. Whereas ethanol has 2-carbon atoms and only one hydroxyl group to share, glycerin has 3-carbon atoms and three hydroxyl groups to share, making it superior for extracting more therapeutic properties from the herbs, including higher concentrations of polyphenols and flavonoids.

In addition, glycerol aquaporins within the fatty acid backbone of the cell membrane preferentially allow glycerins through the cell membrane resulting in maximum absorption and bioavailability.

For more information about Alight Health Formulas®, email contact@alighthealthformulas.com

References

- Masaki Y, Izumi Y, Matsumura A, Akaike A, Kume T. Protective effect of Nrf2-ARE activator isolated from green perilla leaves on dopaminergic neuronal loss in a Parkinson's disease model. *Eur J Pharmacol.* 2017 Mar 5;798:26-34. doi: 10.1016/j.ejphar.2017.02.005. Epub 2017 Feb 4. PMID: 28167258.
- Ito N, Nagai T, Oikawa T, Yamada H, Hanawa T. Antidepressant-like Effect of l-perillaldehyde in Stress-induced Depression-like Model Mice through Regulation of the Olfactory Nervous System. *Evid Based Complement Alternat Med.* 2011;2011:512697. doi: 10.1093/ecam/nen045. Epub 2011 Jun 22. PMID: 18955354; PMCID: PMC3136537.
- Gaihre YR, Iwamoto A, Oogai S, Hamajima H, Tsuge K, Nagata Y, Yanagita T. Perilla pomace obtained from four different varieties have different levels and types of polyphenols and anti-allergic activity. *Cytotechnology.* 2022 Apr;74(2):341-349. doi: 10.1007/s10616-022-00522-6. Epub 2022 Feb 11. PMID: 35464159; PMCID: PMC8975982.
- Kamei R, Fujimura T, Matsuda M, Kakihara K, Hirakawa N, Baba K, Ono K, Arakawa K, Kawamoto S. A flavanone derivative from the Asian medicinal herb (*Perilla frutescens*) potently suppresses IgE-mediated immediate hypersensitivity reactions. *Biochem Biophys Res Commun.* 2017 Jan 29;483(1):674-679. doi: 10.1016/j.bbrc.2016.12.083. Epub 2016 Dec 13. PMID: 27986566.
- Shin TY, Kim SH, Kim SH, Kim YK, Park HJ, Chae BS, Jung HJ, Kim HM. Inhibitory effect of mast cell-mediated immediate-type allergic reactions in rats by *Perilla frutescens*. *Immunopharmacol Immunotoxicol.* 2000 Aug;22(3):489-500. doi: 10.3109/08923970009026007. PMID: 10946827.
- Maeda A, Hirano K, Maeda S, Okuizumi A, Hirakawa N, Baba K, Fujimura T, Kawamoto S. A methoxyflavanone from the medicinal herb *Perilla frutescens* down-modulates Th17 response and ameliorates collagen-induced arthritis. *Biochem Biophys Res Commun.* 2022 Dec 31;637:294-299. doi: 10.1016/j.bbrc.2022.11.033. Epub 2022 Nov 14. PMID: 36413851.
- Dos Santos Sampaio TI, de Melo NC, de Freitas Paiva BT, da Silva Aleluia GA, da Silva Neto FLP, da Silva HR, Keita H, Cruz RAS, Sánchez-Ortiz BL, Pineda-Peña EA, Balderas JL, Navarrete A, Carvalho JCT. Leaves of *Spondias mombin* L. a traditional anxiolytic and antidepressant: Pharmacological evaluation on zebrafish (*Danio rerio*). *J Ethnopharmacol.* 2018 Oct 5;224:563-578. doi: 10.1016/j.jep.2018.05.037. Epub 2018 May 28. PMID: 29852265.
- Santo GD, de Veras BO, Rico E, Magro JD, Agostini JF, Vieira LD, Calisto JFF, Mocelin R, de Sá Fonseca V, Wanderley AG. Hexane extract from *Spondias mombin* L. (Anacardiaceae) prevents behavioral and oxidative status changes on model of Parkinson's disease in zebrafish. *Comp Biochem Physiol C Toxicol Pharmacol.* 2021 Mar;241:108953. doi: 10.1016/j.cbpc.2020.108953. Epub 2020 Dec 10. PMID: 33310063.
- Ayoka AO, Akomolafe RO, Iwalewa EO, Akanmu MA, Ukponmwan OE. Sedative, antiepileptic and antipsychotic effects of *Spondias mombin* L. (Anacardiaceae) in mice and rats. *J Ethnopharmacol.* 2006 Jan 16;103(2):166-75. doi: 10.1016/j.jep.2005.07.019. Epub 2005 Sep 26. PMID: 16188408.
- Akinmoladun AC, Adelabu AA, Saliu IO, Adetuyi AR, Olaleye MT. Protective properties of *Spondias mombin* Linn leaves on redox status, cholinergic dysfunction and electrolyte disturbance in cyanide-intoxicated rats. *Sci Prog.* 2021 Apr-Jun;104(2):368504211011866. doi: 10.1177/00368504211011866. PMID: 33913392; PMCID: PMC10454855.
- Santo GD, de Veras BO, Rico E, Magro JD, Agostini JF, Vieira LD, Calisto JFF, Mocelin R, de Sá Fonseca V, Wanderley AG. Hexane extract from *Spondias mombin* L. (Anacardiaceae) prevents behavioral and oxidative status changes on model of Parkinson's disease in zebrafish. *Comp Biochem Physiol C Toxicol Pharmacol.* 2021 Mar;241:108953. doi: 10.1016/j.cbpc.2020.108953. Epub 2020 Dec 10. PMID: 33310063.
- de Freitas MA, da Cruz RP, Dos Santos ATL, Almeida-Bezerra JW, Machado AJT, Dos Santos JFS, Rocha JE, Boligon AA, Bezerra CF, de Freitas TS, do Nascimento Silva MK, Mendonça ACAM, da Costa JGM, Coutinho HDM, da Cunha FAB, Filho JR, Moraes-Braga MFB. HPLC-DAD analysis and antimicrobial activities of *Spondias mombin* L. (Anacardiaceae). *3 Biotech.* 2022 Mar;12(3):61. doi: 10.1007/s13205-022-03126-1. Epub 2022 Feb 7. PMID: 35186658; PMCID: PMC8818589.

References

- Santos ÉMD, Ataíde JA, Coco JC, Fava ALM, Silvério LAL, Sueiro AC, Silva JRA, Lopes AM, Paiva-Santos AC, Mazzola PG. Spondias sp: Shedding Light on Its Vast Pharmaceutical Potential. *Molecules*. 2023 Feb 16;28(4):1862. doi: 10.3390/molecules28041862. PMID: 36838849; PMCID: PMC9963416.
- Ogunro OB, Oyeyinka BO, Gyebi GA, Batiha GE. Nutritional benefits, ethnomedicinal uses, phytochemistry, pharmacological properties and toxicity of *Spondias mombin* Linn: a comprehensive review. *J Pharm Pharmacol*. 2023 Feb 8;75(2):162-226. doi: 10.1093/jpp/rgac086. PMID: 36632807.
- Yang Y, Wu Y, Xu P, Guo F, Guo F, Yang B. Nyctinastic herbs decoction improves para-chlorophenylalanine-induced insomnia by regulating the expression level of neurotransmitters. *Ann Transl Med*. 2021 Oct;9(20):1524. doi: 10.21037/atm-21-4462. PMID: 34790730; PMCID: PMC8576665.
- Kumarihamy M, León F, Pettaway S, Wilson L, Lambert JA, Wang M, Hill C, McCurdy CR, ElSohly MA, Cutler SJ, Muhammad I. In vitro opioid receptor affinity and in vivo behavioral studies of *Nelumbo nucifera* flower. *J Ethnopharmacol*. 2015 Nov 4;174:57-65. doi: 10.1016/j.jep.2015.08.006. Epub 2015 Aug 7. PMID: 26260436; PMCID: PMC4636954.
- Jo K, Kim S, Hong KB, Suh HJ. *Nelumbo nucifera* promotes non-rapid eye movement sleep by regulating GABAergic receptors in rat model. *J Ethnopharmacol*. 2021 Mar 1;267:113511. doi: 10.1016/j.jep.2020.113511. Epub 2020 Oct 23. PMID: 33148434.
- Zhang X, Li J, Cao C, Liu Z, Chen Q, Gu Z, Wang W, Fang D, Ge Q, Ding L, Pang C, Wang X. Nrf2 activation by neferine mitigates microglial neuroinflammation after subarachnoid hemorrhage through inhibiting TAK1-NF- κ B signaling. *Int Immunopharmacol*. 2024 Mar 30;130:111693. doi: 10.1016/j.intimp.2024.111693. Epub 2024 Mar 1. PMID: 38428144.
- Zhu JJ, Yu BY, Huang XK, He MZ, Chen BW, Chen TT, Fang HY, Chen SQ, Fu XQ, Li PJ, Lin ZL, Zhu JH. Neferine Protects against Hypoxic-Ischemic Brain Damage in Neonatal Rats by Suppressing NLRP3-Mediated Inflammasome Activation. *Oxid Med Cell Longev*. 2021 May 8;2021:6654954. doi: 10.1155/2021/6654954. PMID: 34046147; PMCID: PMC8128543.
- Liu YJ, Tang B, Wang FC, Tang L, Lei YY, Luo Y, Huang SJ, Yang M, Wu LY, Wang W, Liu S, Yang SM, Zhao XY. Parthenolide ameliorates colon inflammation through regulating Treg/Th17 balance in a gut microbiota-dependent manner. *Theranostics*. 2020 Apr 6;10(12):5225-5241. doi: 10.7150/thno.43716. PMID: 32373209; PMCID: PMC7196297.
- Magni P, Ruscica M, Dozio E, Rizzi E, Beretta G, Maffei Facino R. Parthenolide inhibits the LPS-induced secretion of IL-6 and TNF- α and NF- κ B nuclear translocation in BV-2 microglia. *Phytother Res*. 2012 Sep;26(9):1405-9. doi: 10.1002/ptr.3732. Epub 2012 Feb 23. PMID: 22359368.
- Recinella L, Chiavaroli A, di Giacomo V, Antolini MD, Acquaviva A, Leone S, Brunetti L, Menghini L, Ak G, Zengin G, Di Simone SC, Ferrante C, Orlando G. Anti-Inflammatory and Neuromodulatory Effects Induced by *Tanacetum parthenium* Water Extract: Results from In Silico, In Vitro and Ex Vivo Studies. *Molecules*. 2020 Dec 23;26(1):22. doi: 10.3390/molecules26010022. PMID: 33374525; PMCID: PMC7793142.
- Tam DNH, Nam NH, Elhady MT, Tran L, Hassan OG, Sadik M, Tien PTM, Elshafei GA, Huy NT. Effects of Mulberry on The Central Nervous System: A Literature Review. *Curr Neuropharmacol*. 2021;19(2):193-219. doi: 10.2174/1570159X18666200507081531. PMID: 32379591; PMCID: PMC8033976.
- Batiha GE, Al-Snafi AE, Thuwaini MM, Teibo JO, Shaheen HM, Akomolafe AP, Teibo TKA, Al Kuraishy HM, Al-Garbeeb AI, Alexiou A, Papadakis M. *Morus alba*: a comprehensive phytochemical and pharmacological review. *Naunyn Schmiedeberg's Arch Pharmacol*. 2023 Jul;396(7):1399-1413. doi: 10.1007/s00210-023-02434-4. Epub 2023 Mar 6. PMID: 36877269; PMCID: PMC10244279.
- Chan EW, Lye PY, Wong SK. Phytochemistry, pharmacology, and clinical trials of *Morus alba*. *Chin J Nat Med*. 2016 Jan;14(1):17-30. doi: 10.3724/SP.J.1009.2016.00017. PMID: 26850343.

References

Batiha GE, Al-Snafi AE, Thuwaini MM, Teibo JO, Shaheen HM, Akomolafe AP, Teibo TKA, Al Kuraishy HM, Al-Garbeeb AI, Alexiou A, Papadakis M. Morus alba: a comprehensive phytochemical and pharmacological review. *Naunyn Schmiedebergs Arch Pharmacol*. 2023 Jul;396(7):1399-1413. doi: 10.1007/s00210-023-02434-4. Epub 2023 Mar 6. PMID: 36877269; PMCID: PMC10244279.

Lee S, Kim DH, Lee JH, Ko ES, Oh WB, Seo YT, Jang YP, Ryu JH, Jung JW. Involvement of histaminergic system in the anxiolytic-like activities of Morus alba leaves in mice. *Biol Pharm Bull*. 2013;36(11):1692-9. doi: 10.1248/bpb.b13-00126. Epub 2013 Aug 22. PMID: 23965748.

Yadav AV, Nade VS. Anti-dopaminergic effect of the methanolic extract of Morus alba L. leaves. *Indian J Pharmacol*. 2008 Oct;40(5):221-6. doi: 10.4103/0253-7613.44154. PMID: 20040961; PMCID: PMC2792621.

Paudel P, Park SE, Seong SH, Jung HA, Choi JS. Novel Diels-Alder Type Adducts from Morus alba Root Bark Targeting Human Monoamine Oxidase and Dopaminergic Receptors for the Management of Neurodegenerative Diseases. *Int J Mol Sci*. 2019 Dec 10;20(24):6232. doi: 10.3390/ijms20246232. PMID: 31835621; PMCID: PMC6940761.

Kowalska G, Baj T, Kowalski R, Szymańska J. Optimization of Glycerol-Water Extraction of Selected Bioactive Compounds from Peppermint and Common Nettle. *Antioxidants (Basel)*. 2021 May 20;10(5):817. doi: 10.3390/antiox10050817. PMID: 34065576; PMCID: PMC8160696.