

Synapsin[®]

Patent Pending Technology



A Unique Powder Blend for Use in Dietary Supplement Formulations

PCCA # 30-4969

Support neuro-health, one patient at a time.

Synapsin is an innovative, patent-pending powder blend of ginsenoside Rg3 and nicotinamide riboside along with components to aid in solubilization and dispersion. It is an ingredient designed to be used in dietary supplement formulations for the support of neurological health and cognitive health.† Synapsin was invented by renowned author, pharmacist and functional medicine speaker Jim LaValle, RPh, CCN, ND, and is commonly used in combination with methylcobalamin or hydroxocobalamin in formulations to support neuronal function and cognition.†

BRAIN HEALTH INFORMATION

The support of healthy neurological function is a significant need in the marketplace. Traumatic brain injury (TBI) is a leading cause of injury, death and disability in the U.S.^{1,2} A 1999 CDC report to Congress estimated that 5.3 million residents in the U.S. were living with TBI-related disabilities, including long-term cognitive and psychological impairments.³ Globally, TBI is estimated to occur at a rate of 106 per 100,000.⁴ According to the CDC, approximately 2.4 million traumatic brain injuries were treated in U.S. emergency rooms in 2009, with an estimated 75% occurring as concussions. Of these, approximately 16.5% are associated with sports-related injury.^{2,3} A study of nearly 3,000 serious head trauma cases reported that 52% of survivors were moderately to severely disabled at one-year post accident.⁵ The annual economic cost of TBI in the U.S., including direct medical and rehabilitation costs and indirect societal economic costs, is estimated to be approximately \$76.5 billion.^{6,7}

Additionally, as we age, memory impairment is thought to be a consequence of decline in neuronal function and increase in neurodegeneration, with oxidative stress as a

major factor in brain aging and memory impairment. More than one million adults in the U.S. are diagnosed annually with a chronic brain disease or disorder, with Alzheimer's disease being the most prevalent cause of adult-onset brain disorders.⁸ Research estimates that in the U.S., 35.8% of those 85 or older have moderate or severe memory impairment, and individuals 85 years and older are the fastest growing segment of the population.⁸

In 2016, it was estimated that 5.4 million Americans had Alzheimer's disease, with Alzheimer's and other dementias accounting for \$236 billion in health care costs.⁹ By mid-century, it is projected that 14 million will have Alzheimer's,¹⁰ with treatment and care amounting to over \$1 trillion.⁹

NUTRIENT SUPPORT SUMMARY OF SYNAPSIN

- Supports neuronal health†
- Supports NAD⁺ production in the central and peripheral nervous system, and supports healthy sirtuin expression†
- Supports healthy mitochondrial function†
- Supports the attenuation of microglial activation^{11†}

FORMULATION EXAMPLES

For formulation examples, please contact your local compounding pharmacy.

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FREQUENTLY ASKED QUESTIONS

Is Synapsin sterile?

No. Synapsin is a non-sterile powder, and it should not be used in sterile preparations.

Does Synapsin need to be refrigerated?

Yes. To maintain the stability of the nicotinamide riboside, Synapsin needs to be refrigerated, and so does the final Synapsin preparation.

Do Synapsin preparations require a prescription?

Yes. Synapsin formulations should only be compounded and dispensed as prescribed by a health care professional.

ABOUT GINSENOSE Rg3

Rg3 is one of several triterpene saponins (ginsenosides) found in the plant genus *Panax*, including *Panax ginseng* (Asian ginseng) and *Panax quinquefolius* (American ginseng). Laboratory studies report that Rg3 extracted from *Panax ginseng* supports neuroprotection,[†] helping to support healthy microglial activity[†] and healthy neuronal function.^{12,13,14†}

ABOUT NICOTINAMIDE RIBOSIDE

Nicotinamide riboside (NR) is a form of vitamin B3 found in cow's milk.¹⁵ Laboratory studies report administration of nicotinamide riboside supports healthy levels of NAD⁺ in yeast and cultured human and mammalian cells.[†] NR is reported to be incorporated into the cellular NAD⁺ pool via the action of nicotinamide riboside kinase (Nrk) pathway or via nicotinamide (Nam) salvage after conversion to Nam by phosphorolysis.^{15,16,17†} Laboratory studies have also reported the supportive and neuroprotective role for NAD⁺.^{16†} In laboratory studies, nicotinamide riboside supports neuronal NAD⁺ synthesis without inhibiting sirtuins, which are important regulators of metabolism and longevity.^{18,19†}

REFERENCES

1. Faul, M., Xu, L., Wald, M. M., & Coronado, V. G. (2010). Traumatic brain injury in the United States: Emergency department visits, hospitalizations and deaths 2002–2006. Retrieved from https://www.cdc.gov/traumaticbraininjury/pdf/blue_book.pdf
2. Centers for Disease Control and Prevention (2010). QuickStats: Injury and Traumatic Brain Injury (TBI)-Related Death Rates, by Age Group --- United States, 2006. *Morbidity and Mortality Weekly Report*, 59(10), 303. Retrieved from <https://www.cdc.gov/mmwr/PDF/wk/mm5910.pdf>
3. Centers for Disease Control and Prevention. (1999). Report to Congress: Traumatic brain injury in the United States. Retrieved from https://www.cdc.gov/traumaticbraininjury/pubs/tbi_report_to_congress.html#
4. Hyder, A. A., Wunderlich, C. A., Puvanachandra, P., Gururaj, G., & Kobusingye, O. C. (2007). The impact of traumatic brain injuries: A global perspective. *NeuroRehabilitation*, 22(5), 341–353.
5. Thornhill, S., Teasdale, G. M., Murray, G. D., McEwen, J., Roy, C. W., & Penny, K. I. Disability in young people and adults one year after head injury: Prospective cohort study. *The BMJ*, 320, 1631–1635. <https://doi.org/10.1136/bmj.320.7250.1631>
6. Humphreys, I., Wood, R. L., Phillips, C. J., & Macey, S. (2013). The costs of traumatic brain injury: A literature review. *Journal of ClinicoEconomics and Outcomes Research*, 5, 281–287. <https://doi.org/10.2147/CEOR.S44625>
7. Wright, D. W., Kellermann, A., McGuire, L. C., Chen, B., & Popovic, T. (2013). CDC grand rounds: Reducing severe traumatic brain injury in the United States. *Morbidity and Mortality Weekly Report*, 62(27), 549–552. Retrieved from <https://www.cdc.gov/mmwr/pdf/wk/mm6227.pdf>
8. Federal Interagency Forum on Aging-Related Statistics. (2000). *Older Americans 2000: Key Indicators of Well-Being*. Retrieved from <https://agingstats.gov/docs/PastReports/2000/OA2000.pdf>

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† Statements made are for educational purposes and have not been evaluated by the U.S. Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

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REFERENCES (continued)

- Alzheimer's Association. (2016). *2016 Alzheimer's disease facts and figures*. Retrieved from <http://www.alz.org/facts/>
- Centers for Disease Control and Prevention. (2015). *Alzheimer's disease*. Retrieved from <https://www.cdc.gov/aging/aginginfo/alzheimers.htm>
- Hernandez-Ontiveros, D. G., Tajiri, N., Acosta, S., Giunta, B., Tan, J., & Borlongan, C. V. (2013). Microglia activation as a biomarker for traumatic brain injury. *Frontiers in Neurology*, 4. <https://doi.org/10.3389/fneur.2013.00030>
- Joo, S. S., Yoo, Y. M., Ahn, B. W., Nam, S. Y., Kim, Y. B., Hwang, K. W., & Lee, D. I. (2008). Prevention of inflammation-mediated neurotoxicity by Rg3 and its role in microglial activation. *Biological and Pharmaceutical Bulletin*, 31(7), 1392-1396. <http://doi.org/10.1248/bpb.31.1392>
- Bao, H. Y., Zhang, J., Yeo, S. J., Myung, C. S., Kim, H. M., Kim, J. M., . . . Kang, J. S. (2005). Memory enhancing and neuroprotective effects of selected ginsenosides. *Archives of Pharmacol Research*, 28(3), 335-342.
- Mannaa, F., Abdel-Wahhab, M. A., Ahmed, H. H., & Park, M. H. (2006). Protective role of *Panax ginseng* extract standardized with ginsenoside Rg3 against acrylamide-induced neurotoxicity in rats. *Journal of Applied Toxicology*, 26(3), 198-206. <https://doi.org/10.1002/jat.1128>
- Bieganski, P., & Brenner, C. (2004). Discoveries of nicotinamide riboside as a nutrient and conserved NRK genes establish a Preiss-Handler independent route to NAD⁺ in fungi and humans. *Cell*, 117(4), 495-502. Retrieved from [http://www.cell.com/cell/pdf/S0092-8674\(04\)00416-7.pdf](http://www.cell.com/cell/pdf/S0092-8674(04)00416-7.pdf)
- Belenky, P., Bogan, K. L., & Brenner, C. (2007). NAD⁺ metabolism in health and disease. *Trends in Biochemical Sciences*, 32(1), 12-19. <http://dx.doi.org/10.1016/j.tibs.2006.11.006>
- Yang, S. J., Choi, J. M., Kim, L., Park, S. E., Rhee, E. J., Lee, W. Y. . . . Park, C. Y. (2014). Nicotinamide improves glucose metabolism and affects the hepatic NAD-sirtuin pathway in a rodent model of obesity and type 2 diabetes. *The Journal of Nutritional Biochemistry*, 25(1), 66-72. <http://dx.doi.org/10.1016/j.jnutbio.2013.09.004>
- Suave, A. A. (2008). NAD⁺ and vitamin B3: From metabolism to therapies. *The Journal of Pharmacology and Experimental Therapeutics*, 324(3), 883-893. <https://doi.org/10.1124/jpet.107.120758>
- Chi, Y., & Suave, A. A. (2013). Nicotinamide riboside, a trace nutrient in foods, is a vitamin B3 with effects on energy metabolism and neuroprotection. *Current Opinion in Clinical Nutrition and Metabolic Care*, 16(6), 657-661. <https://doi.org/10.1097/MCO.0b013e32836510c0>