



Pterostilbene + Caffeine Co-Crystal / Nicotinamide riboside

Compounded Sublingual Spray

Product Summary	
Nutrient	Formula Use(s)
Pterostilbene/Caffeine Co-Crystal (57% trans-pterostilbene/43% Caffeine)	<ul style="list-style-type: none"> • Antioxidant/stimulant • Neuroprotective • May help improve energy levels and cognitive function
Nicotinamide riboside	<ul style="list-style-type: none"> • Neuroprotective • Mitochondrial health • Increased neuronal NAD⁺ pools • Decreased axonal neurodegeneration • Regulation of sirtulin expression
* Daily value not established.	

Pharmacology Summary:

- Improves cognitive function and energy levels.
- Neuroprotection.
- Helps decrease inflammatory processes and oxidative stress in neurological tissue.
- Helps improve NAD⁺ production in the central and peripheral nervous system and regulate sirtulin expression.
- Improves mitochondrial function and energy levels.

Supporting Research:

Pterostilbene/Caffeine Co-Crystal

- Pterostilbene is a polyphenol phytochemical primarily found in blueberries (*Vaccinium* sp.), grapes (*Vitis vinifera*) and the Indian Kino tree (*Pterocarpus marsupium*).
 - Pterostilbene**
 - Neuroprotective
 - Decreases oxidative stress and inflammation in neurological tissue
- Chemically, pterostilbene is classified as a phytoalexin and is a methoxylated analog of the popular dietary supplement resveratrol.
- Laboratory studies report pterostilbene has significant antioxidant and anti-inflammatory activity including decreasing the upregulation of TNF-alpha, IL-, and the COX-2 isoenzyme.^{1,2,3}
- Laboratory studies have reported that pterostilbene is neuroprotective, including helping to decrease oxidative stress and neuroinflammation while improving cognitive function.^{4,5}
- Pterostilbene is also reported to increase levels of PPAR- α , an upstream inducer of MnSOD, and decrease levels of phosphorylated JnK and tau, both of which can lead to increased oxidative stress and subsequent signaling dysfunction in Alzheimer's disease.⁶
- Caffeine is a central nervous system (CNS) stimulant that has been studied for increasing performance (physical and mental).^{7,8}
 - Caffeine**
 - Stimulant
 - Improves energy and focus
 - Helps improve cognition
 - Thermogenic aid
- Caffeine also is reported to help promote weight loss, increase energy and performance and decrease fat storage.
- Pterostilbene/Caffeine Co-Crystal is a patented blend of trans-resveratrol and caffeine.
- Pterostilbene/Caffeine Co-Crystal is reported to deliver approximately 30% more caffeine into the bloodstream than caffeine alone.

- The half-life of caffeine in pterostilbene/caffeine Co-crystal formulation is about 25% more than that of ordinary caffeine.

Nicotinamide riboside

- Nicotinamide riboside (NR) is a form of vitamin B3 found in cow’s milk.⁹
- Laboratory studies report administration of nicotinamide riboside increases NAD⁺ levels in yeast and cultured human and mammalian cells.^{10,11,12}
- NR is reported to be incorporated into the cellular NAD⁺ pool via the action of Nrk pathway or via Nam salvage after conversion to Nam by phosphorylation.¹³
- Laboratory studies have reported a neuroprotective role for NAD⁺.¹⁴
- NR is a unique precursor to nervous system health when de novo synthesis of NAD⁺ from tryptophan is not sufficient.¹⁵
- In laboratory studies, nicotinamide riboside supports neuronal NAD⁺ synthesis without inhibiting sirtuins, which are important regulators of metabolism and longevity.^{16,17}
- Stimulation of NAD⁺ production is reported to decrease axonal degeneration in laboratory studies.¹⁸ Axonal degeneration is observed after physical damage to axons after traumatic injury and in a variety of neuropathological conditions, including diabetic neuropathies, demyelinating diseases, and neurodegenerative diseases including Alzheimer’s disease, amyotrophic lateral sclerosis (ALS), and Parkinson’s disease.^{19,20,21}
- **Age-related mitochondrial dysfunction:** NAD⁺ is a rate-limiting co-substrate for the sirtuin enzymes and helps to regulate sirtuin function and subsequent regulation of oxidative metabolism.²²

- Neuroprotective
- Helps increase neuronal NAD⁺ production and decrease neuronal degeneration
- Helps manufacture NAD⁺ without inhibiting sirtuins.

Compounded Formula Concentration:

Sublingual Spray (1 spray = approximately 0.1ml):

- Pterostilbene/Caffeine Co-Crystal..... 52.6 mg/ml
- Nicotinamide Riboside..... 20.0 mg/ml

Toxicity, Contraindications, or Side Effects: Ingredients contained in compounded *Pterostilbene/Caffeine/Nicotinamide riboside* are reported safe when used appropriately. However, caffeine is reported to cause insomnia, may increase heart rate and increase nervousness and may lead to headaches. Caution should be used when administering caffeine to those on medications and/or if a pre-existing medical condition that would be contraindicated with using caffeine is present, including hypertension. Caffeine is reported to interact with several OTC and prescription medications.

This produce is available by prescription only.

DISCLAIMER: Statements made are for educational purposes and have not been evaluated by the US Food and Drug Administration. They are not intended to diagnose, treat, cure, or prevent any disease.

¹ Hougee S, Faber J, Sanders A, et al. Selective COX-2 inhibition by a Pterocarpus marsupium extract characterized by Pterostilbene and its activity in healthy human volunteers. *Planta Medica*. 2005;71(5):387-92.

² Acharya JD, Ghaskadbi SS. Protective effect of Pterostilbene against free radical mediated oxidative damage. *BMC Complement Altern Med*. 2013;13:238.

³ Csuk R, Albert S, Sierwert B. Synthesis and radical scavenging activities of resveratrol analogs. *Arch Pharm (Weinheim)*. 2013;346(7):504-10.

⁴ Chang J, Rimando A, Pallas M, et al. Low-dose pterostilbene, but not resveratrol, is a potent neuromodulator in aging and Alzheimer's disease. *Neurobiology of Aging*. 2012;33(9):2062–2071.

⁵ Joseph JA, Fisher DR, Cheng V, Rimando AM, Shukitt-Hale B. Cellular and behavioral effects of stilbene resveratrol analogues: implications for reducing the deleterious effects of aging. *Journal of Agricultural and Food Chemistry*. 2008;56(22):10544–10551.

⁶ Chang J, Rimando A, Pallas M, et al. Low-dose pterostilbene, but not resveratrol, is a potent neuromodulator in aging and Alzheimer's disease. *Neurobiology of Aging*. 2012;33(9):2062–2071.

⁷ Cox GR, Desbrow B, Montgomery PG, et al. Effect of different protocols of caffeine intake on metabolism and endurance performance. *J Appl Physiol*. 2002; 93(3):990-9.

⁸ Belza A, Frandsen E, Kondrup J. Body fat loss achieved by stimulation of thermogenesis by a combination of bioactive food ingredients: a placebo-controlled, double-blind 8-week intervention in obese subjects. *Int J Obes (Lond)*. 2007 Jan;31(1):121-30. Epub 2006 Apr 25.

⁹ Bieganowski P, Brenner C. Discoveries of nicotinamide riboside as a nutrient and conserved NRK genes establish a Preiss-Handler independent route to NAD⁺ in fungi and humans. *Cells*. 117;495-502.

¹⁰ Belenky P, Bogan KL, Brenner C. NAD⁺ metabolism in health and disease. *Trends Biochem Sci*. 2007;32(1):12-9.

¹¹ Bieganowski P, Brenner C. Discoveries of nicotinamide riboside as a nutrient and conserved NRK genes establish a Preiss-Handler independent route to NAD⁺ in fungi and humans. *Cells*. 117;495-502.

¹² Yang SJ, Choi JM, Kim L, et al. Nicotinamide improves glucose metabolism and affects the hepatic NAD-sirtuin pathway in a rodent model of obesity and type 2 diabetes. *J Nutr Biochem*. 2014;25(1):66-72.

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- ¹³ Bieganowski P, Brenner C. Discoveries of nicotinamide riboside as a nutrient and conserved NRK genes establish a Preiss-Handler independent route to NAD⁺ in fungi and humans. *Cells*. 117;495-502.
- ¹⁴ Belenky P, Bogan KL, Brenner C. NAD⁺ metabolism in health and disease. *Trends Biochem Sci*. 2007;32(1):12-9.
- ¹⁵ Sasaki Y, Araki T, Milbrandt J. Stimulation of nicotinamide adenine dinucleotide biosynthetic pathways delay axonal degeneration after axotomy. *J Neurosci*. 2006;26(33):8484-91.
- ¹⁶ Suave AA. Nicotinamide and vitamin B3: from metabolism to therapies. *J Pharmacol Exp Ther*. 2008;324(3):883-93.
- ¹⁷ Chi Y, Suave AA. Nicotinamide riboside, a trace nutrient in foods, is a vitamin B3 with effects on energy metabolism and neuroprotection. *Curr Opin Clin Nutr Metab Care*. 2013;16(6):657-61.
- ¹⁸ Sasaki Y, Araki T, Milbrandt J. Stimulation of nicotinamide adenine dinucleotide biosynthetic pathways delay axonal degeneration after axotomy. *J Neurosci*. 2006;26(33):8484-91.
- ¹⁹ Won SJ, Choi BY, Yoo BH, et al. Prevention of traumatic brain injury-induced neuron death by intranasal delivery of nicotinamide adenine dinucleotide. *J Neurotrauma*. 2012;29(7):1401-9.
- ²⁰ Sasaki Y, Araki T, Milbrandt J. Stimulation of nicotinamide adenine dinucleotide biosynthetic pathways delay axonal degeneration after axotomy. *J Neurosci*. 2006;26(33):8484-91.
- ²¹ Belenky P, Racette FG, Bogan KL, et al. Nicotinamide riboside promotes Sir2 silencing and extends lifespan via Nrk and Urh1/Pnp1/Meu1 pathways to NAD⁺. *Cell*. 2007;129(3):473-84.
- ²² Canto C, Houtkooper RH, Pirinen E, et al. The NAD(+) precursor nicotinamide riboside enhances oxidative metabolism and protects against high fat diet-induced obesity. *Cell Metab*. 2012;15(6):838-47.