



Rg3 / Nicotinamide Riboside/ Methylcobalamin

Compounded Intranasal Spray

Product Summary	
Nutrient	Formula Use(s)
Nicotinamide Riboside	<ul style="list-style-type: none"> • Neuroprotective • Mitochondrial health • Increased neuronal NAD⁺ pools • Decreased axonal neurodegeneration • Regulation of sirtulin expression
Methylcobalamin (Vitamin B12)	<ul style="list-style-type: none"> • Neuroprotective • Helps improve methylation and decrease homocysteine formation • Helps decrease cognitive decline
Rg3 - 90% Isolated from <i>Panax ginseng</i> , C.A. Meyer	<ul style="list-style-type: none"> • Neuroprotective • Neuroinflammation • Helps attenuate microglial activation in neurons
* Daily value not established.	

Pharmacology Summary:

- Neuroprotection
- Cognitive decline and related conditions, including dementia, Alzheimer's Disease
- Helps improve NAD⁺ production in the central and peripheral nervous system and regulate sirtulin expression.
- Improves mitochondrial function.
- Decreases microglial activation and subsequent oxidative stress and neuronal inflammation. Microglial activation is reported to occur in cognitive decline.¹
- Improves methylation and decreases homocysteine formation. Elevated homocysteine levels are reported to increase cognitive decline including those with Alzheimer's Disease and vascular dementia.^{2,3}

Background Facts:

- 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 US are diagnosed annually with a chronic brain disease or disorder. With Alzheimer's disease being the most prevalent cause of adult-onset brain disorders.⁴
- Research estimates that in the United States alone, 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.⁵
- By 2020, it is estimated that almost one million persons will be age 85+ in California alone – twice as many as there are today.
- Alzheimer's disease is the 6th leading cause of death in the US, with more than 5.2 million Americans diagnosed with the disease, with an estimated 5 million of these aged 65 and older.
- In 2013, Alzheimer's disease will cost the US \$203 billion, and is expected to rise to \$1.2 trillion by 2050.⁶
- Three major pathologies characterize Alzheimer's disease: senile plaques, neurofibrillary tangles, and neuroinflammation.
- Increased microglial activation and resulting increases in neuroinflammatory processes that lead to neuronal cell death are reported to be a causative factor in cognitive decline and neurodegenerative disorders including dementia, Alzheimer's disease, Parkinson's disease and stroke.⁷
- Hyperhomocysteinemia has been reported to be associated with declining cognitive function and increased vascular dementia, especially in elderly individuals.⁸
- Homocysteine may decrease cognition by:^{9,10}
 - Direct toxicity on glutamate neurotransmission and cerebrovascular endothelium
 - Indirect inhibition of transmethylation reactions in neurological tissue
 - Increased microglial activation and neuroinflammation

- Potentiation of amyloid neurotoxicity and promotion of tau phosphorylation

Supporting Research:

Rg3 (from *Panax ginseng*)

- Rg3 is one of several triterpene saponins (ginsenosides), which are found in the plant genus *Panax* (including Asian or *Panax ginseng* and American ginseng or *Panax quinquefolius*).
- Rg3 is produced by steaming the ginseng root, then extracting and isolating the Rg3 constituent.
- Laboratory studies report that Rg3 extracted from *Panax ginseng* is neuroprotective, helping to decrease microglia activation and neuroinflammatory processes.^{11,12,13}
- Rg3 is reported to have anti-inflammatory activity via COX-2 inhibition and reduction of inducible nitric oxide synthase (iNOS) and pro-inflammatory cytokine expression, including TNF-alpha and IL-1B.¹⁴

- Neuroprotective
- Decreases microglial inflammatory processes
- Attenuates microglia activation
- Decreases oxidative stress of neurological tissue

Methylcobalamin

- Methylcobalamin is one of the 2 coenzyme forms of vitamin B12 found in the body, the other being adenosylcobalamin.
- Methylcobalamin helps improve methylation processes in the body, leading to decreased formation of homocysteine.
- Lowering homocysteine levels are reported to significantly reduce cognitive decline in patients with Alzheimer's Disease or vascular dementia.¹⁵
- In laboratory and human studies, methylcobalamin is reported to help decrease somatic and autonomic symptoms of diabetic neuropathy.^{16,17}
- As a dietary supplement, methylcobalamin is more readily absorbed and bioavailable than other forms of vitamin B12.

- Neuroprotective
- Helps improve methylation and decrease homocysteine formation
- Helps decrease symptoms of peripheral neuropathy

Nicotinamide riboside

- Nicotinamide riboside (NR) is a form of vitamin B3 found in cow's milk.¹⁸
- Laboratory studies report administration of nicotinamide riboside increases NAD⁺ levels in yeast and cultured human and mammalian cells.^{19,20,21}
- 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 phosphorolysis.²²
- Laboratory studies have reported a neuroprotective role for NAD⁺.²³
- NR is a unique precursor to nervous system health when de novo synthesis of NAD⁺ from tryptophan is not sufficient.²⁴
- In laboratory studies, nicotinamide riboside supports neuronal NAD⁺ synthesis without inhibiting sirtuins, which are important regulators of metabolism and longevity.^{25,26}
- Stimulation of NAD⁺ production is reported to decrease axonal degeneration in laboratory studies.²⁷ 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.^{28,29,30}
- **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.³¹

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

Compounded Formula Concentration:

Intranasal Spray (1 spray = 0.1 ml)

- Rg3 - 2 mg/ml
- Nicotinamide riboside - 2 mg/ml
- Methylcobalamin - 50mg/ml

Toxicity, Contraindications, or Side Effects: There is no known toxicity or side effects from taking ingredients found in sublingual **Rg3/Nicotinamide riboside/Methylcobalamin**. This compounded product 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.

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