



MITO-NR™

SUPPORTS CELLULAR ENERGY (ATP) PRODUCTION AND CARDIOVASCULAR HEALTH

60 VEGETARIAN CAPSULES | NPN80124223 | MCNR60-CN

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Mito-NR™ is uniquely formulated to support cellular energy production, cellular repair, and healthy aging. This formula contains clinically relevant amounts of Niagen®, a form of nicotinamide riboside chloride (NR) and coenzyme Q10 (CoQ10). NR is a pyridine nucleoside form of vitamin B3 (niacin) and a building block of nicotinamide adenine dinucleotide (NAD+).¹

Mito-NR™ provides 300 mg of nicotinamide riboside chloride as Niagen® and 200 mg of CoQ10 per daily dose that support energy production using multiple biochemical mechanisms; therefore, they may have synergistic effects on energy production.¹ They may also support mitochondrial health and healthy aging. Mito-NR™ may be ideal for individuals concerned with age-related illnesses, those in need of cellular energy support, and those who may require support for healthy mitochondrial function.

Ingredient Highlights

- Features 300 mg of Niagen®, a form of nicotinamide riboside chloride for optimal cellular health
- Includes synergistic compounds to support mitochondrial function and cellular health
- Contains 200 mg of coenzyme Q10 to support energy production and mitochondrial health
- Gluten-free, dairy-free, and soy-free
- Non-GMO

Nicotinamide Riboside and NAD+

NAD+ is found in every living cell and is essential to many important cellular processes including energy production in the mitochondria. NAD+ is involved in more than 500 chemical reactions in the human body, including reduction-oxidation reactions, most anabolic and catabolic reactions, such as fatty acid beta-oxidation, glycolysis, tricarboxylic acid cycle, and the synthesis of cholesterol, steroids, and fatty acids.² Biosynthesis of NAD+ is derived from tryptophan or salvage pathways from one of its four precursors: nicotinamide riboside (NR), nicotinic acid, nicotinamide, and nicotinamide mononucleotide (NMN). Synthesis of NAD+ from tryptophan requires eight steps, whereas synthesis from NR to NAD+ requires two or three steps depending on the salvage pathway, with NMN as an intermediary.²

Silent information regulators (Sir), such as Sir2, are histone deacetylases that require NAD+ to perform their enzymatic activity.³ There are seven sirtuins in mammalian cells that play a variety of roles in cellular function, including energy homeostasis, cell cycle, and apoptosis. Sirtuins (SIRT) are NAD+-consuming enzymes, and NAD+ acts as a SIRT activator. NAD+ substrates, such as NADH and nicotinamide, act as inhibitors of SIRT.^{4,5} Increasing NAD+ levels have been shown to activate SIRT1 to mitigate some of the age-related effects and other downstream effects of reduced SIRT1 activity, such as mitochondrial function.⁶ These may also mediate inflammatory and stress responses, and support cardiovascular and neurological function.⁷

Supporting NAD+ status in the body may aid healthy aging. Animal and human studies have found an association between advanced age and significantly lower levels of NAD+.^{8,9} Studies have found an association between NAD+ deficiency and type 2 diabetes, Alzheimer's disease (AD), other neurodegenerative disorders, cardiovascular disease, and various other age-related diseases.⁹⁻¹⁴

Supplementation with NR has been shown to improve mitochondrial function, SIRT activity, and increase NAD+ levels in multiple tissues.² NR does not induce flushing and has been regarded as a favorable NAD+ precursor.² In both animal and

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human populations, twice-daily doses of 1,000 mg of NR were shown to significantly increase whole-blood levels of NAD+ and promote NAD+ metabolism.²

NR and Mitochondrial Health

Mitochondrial disorders are a common cause of metabolic disease in both adults and children.¹⁵ Clinical manifestations of mitochondrial disorders can impact every body system and can include fatigue, shortness of breath, muscle weakness, and other muscular myopathies, gastrointestinal upset, neuropathy, cardiovascular illnesses, and endocrine problems.¹⁶

A controlled animal study administered NR to mouse models simulating mitochondrial myopathy. NR was shown to increase mitochondrial mass, help attenuate mitochondrial DNA mutations, help promote mitochondrial biogenesis, and improve mitochondrial structure.^{15,16}

In a clinical study, supplementation with 1,000 mg of NR for 9 days was shown to increase blood levels of NAD+ in healthy volunteers.¹ An 8-week randomized, double-blind controlled clinical trial explored the impact of NR supplementation on blood NAD+ levels at varying doses. NR as Niagen® was administered at 100 mg, 300 mg, and 1,000 mg serving levels. Within 2 weeks, significant increases in whole blood NAD+ levels were 22%, 51%, and 142%, respectively. No dose-dependent adverse events or incidences of flushing were reported.¹⁷

NR and Aging

The presence of senescent cells and neuroinflammation have been associated with many age-related illnesses such as AD.¹⁸ Neuroinflammation has been linked to reductions in NAD+ levels during the natural aging process.¹⁹ An animal study explored the impact of NR administration on mouse models of AD. Increases in NAD+ levels were observed.^{18,19} Decreases in the number of senescent cells and pro-inflammatory cytokines interleukin (IL)-6, IL-1β, and tumor necrosis factor-alpha (TNF-α) were also reported.^{18,19}

An animal study involving NR administration showed improvements in motor deficits and attenuation of neuronal loss in the presence of Parkinson's disease (PD). NR has also been shown to play a supportive role in the presence of neurodegenerative diseases including AD and other age-related illnesses.²⁰

A randomized, controlled, crossover clinical trial explored the efficacy of NR supplementation on skeletal muscle NAD+ metabolomics in aged men. Twelve men with a median age of 75 years were randomized to a placebo or a treatment arm consisting of daily supplementation of 1,000 mg of NR for 21 days. NR was shown to increase skeletal muscle NAD+ and decrease certain pro-inflammatory cytokines, including IL-6, IL-5, IL-2, and TNF-α.²¹

Additional Ingredients

CoQ10 is also known as ubiquinone because it is present everywhere in the human body. It is a powerful antioxidant and helps protect mitochondrial membranes from oxidative damage.²² It acts as an electron carrier in the mitochondrial electron transport chain during oxidative phosphorylation.²² It helps protect cell membranes, and regulate mitochondrial permeability, and it is involved in the metabolism of pyrimidines, fatty acids, and mitochondrial uncoupling proteins.²² CoQ10 helps support oxidative status, the inflammatory response, healthy metabolism, healthy aging, and mitochondrial function.²²

NAD+ is needed for the continuous recycling of ubiquinol to ubiquinone.²³ Suboptimal CoQ10 status has been shown to compromise Sirt1 activity within the cell by multiple mechanisms.²⁴ CoQ10 is an essential cofactor for mitochondrial electron transfer to generate energy as adenosine triphosphate (ATP). Insufficient CoQ10 leads to a backup of electrons at sites 1 and 2 in the mitochondrial ETC causing increased reactive oxygen species (ROS) and reduced ATP generation. CoQ10-deficiency also decreases Sirt1 and Sirt3 deacetylase activity due to a reduced cytoplasmic and mitochondrial NAD+/NADH ratio, slowing NAD+ availability to the mitochondria. Increased ROS production decreases Sirt1 stability and has been shown to lower messenger RNA expression of Sirt1 protein.²⁴ Research suggests that correcting CoQ10 deficiency may encourage increased Sirt1 and Sirt3 activities, and ultimately, mitochondrial health and function.²⁴

BENEFITS

- Promotes cellular energy production
- Supports normal cellular repair
- Supports optimal mitochondrial function
- Promotes overall cellular health
- Helps promote NAD+ status in the body

Medicinal Ingredients (per capsule):

Coenzyme Q10.....100 mg
Nicotinamide riboside chloride (NIAGEN®) 150 mg

Non-Medicinal Ingredients: Microcrystalline cellulose, Hypromellose, Silicon dioxide, Annatto extract, Quillaja extract, Magnesium stearate. **Recommended Dose:** Adults 18 years and older: Consult a healthcare practitioner prior to use. Take 1 capsule 2 times per day with food, or as directed by a healthcare practitioner. For use beyond 12 weeks, consult a healthcare practitioner.

Refer to the product label for dosing instructions, age-appropriateness, and relative risk statements. Healthcare practitioners are encouraged to use clinical judgement with case-specific dosing based on intended goals, subject body weight, medical history, and concomitant medication and supplement usage.

REFERENCES

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