PRODUCT SPECIFICATIONS





Code: 9428 NPN: 80121612 Size: 60 Vegetarian Capsules Actual Size: 21.45 mm x 7.54 mm

NMN

Supports Cellular Metabolism and Energy 150 mg

- Provides 150 mg of nicotinamide mononucleotide (NMN) per serving, shown to increase blood levels of NAD⁺ in clinical trials
- NMN is the immediate precursor to NAD⁺ and replenishes age-related decline in NAD⁺ levels
- NAD⁺ is a critical coenzyme for numerous pathways related to energy production, mitochondrial health, and DNA repair, and its decline is strongly associated with aging
- Vegetarian capsules with a clinically established dosage

PRODUCT SUMMARY

NMN is a bioavailable precursor to nicotinamide adenine dinucleotide (NAD⁺), a key coenzyme needed for over 500 enzymatic reactions. As many of these enzymatic reactions are related to cellular metabolism, aging, inflammation, circadian rhythm, mitochondrial respiration, glycolysis, and DNA repair, NAD⁺ is considered critical to human health and longevity. NAD⁺ is also needed for the expression of sirtuins, enzymes with numerous cellular regulatory effects particularly important for inflammation, DNA repair, and energy metabolism. Considerable research shows a decline in NAD⁺ and sirtuin expression with aging, leading to an impairment of mitochondrial function and biogenesis and increased oxidative damage, driving the aging process itself as well as many diseases associated with aging, including cardiovascular and metabolic diseases.

NMN has been shown to significantly increase blood levels of NAD⁺ in human clinical trials, in part because it is only one enzymatic step from NAD⁺. Controlled clinical trials have demonstrated multiple benefits of NMN supplementation, including improvements in insulin sensitivity and signalling among women with impaired glucose metabolism, as well as aerobic capacity in healthy runners, and reduced drowsiness and improved sit-to-stand in older adults. Indicative of its potential to address aging pathways by restoring NAD⁺ levels, NMN supplementation for 12 weeks found a trend toward reduced arterial stiffness, an aging-related independent risk factor for cardiovascular and metabolic diseases.



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Serving Size: 1 Vegetarian Capsule Servings Per Container: 60

Each Vegetarian Capsule Contains:

Non-medicinal Ingredients: Vegetarian capsule (carbohydrate gum [cellulose], purified water), microcrystalline cellulose, vegetable grade magnesium stearate (lubricant), stearic acid, silica.

Recommended Adult Dose: 1 capsule 2 times per day or as directed by a health care practitioner. Consult a health care practitioner for use beyond 6 weeks.

Recommended Use: Source of vitamin B3, a factor in the maintenance of good health.

Caution: Consult a health care practitioner prior to use if you are pregnant or breastfeeding, or if you have diabetes. Keep out of reach of children.

Contraindications: No known contraindications.

Drug Interactions: No known drug interactions.

Contains no artificial colours, preservatives, or sweeteners; no dairy, starch, sugar, wheat, gluten, yeast, soy, corn, egg, fish, shellfish, animal products, salt, tree nuts, or GMOs. Suitable for vegetarians/vegans. Sealed for your protection. Do not use if seal is broken. For freshness, store in a cool, dry place.

References available at bioclinicnaturals.com



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Head office Assured Natural Distribution Inc., 104 – 3886 Bonneville Place, Burnaby, BC, Canada VSN 416 | U.S. Distribution office 14224 16/¹⁰ Avenue SE, Monroe, WA, USA 982/2 **Customer Service** 1-888-826-9625 · **Fax** 1-877-433-9862 · **Email** customerservice@bioclinicnaturals.com

NMN – Nicotinamide Mononucleotide



About NMN

- Nicotinamide mononucleotide, or NMN, is a bioavailable building block for nicotinamide adenine dinucleotide (NAD⁺). NAD⁺ is a critical component for over 500 enzymes and is important for a wide range of biological processes.¹
- Many of the enzymatic reactions that use NAD⁺ are among a cell's most important functions, including energy production, DNA repair, oxidative stress and inflammation reduction, and mitochondrial function.^{1,2}
- NAD⁺ is known to decline with age. This decline has been linked to many aspects of the aging process as well as age-related diseases, including cardiovascular and metabolic diseases.^{2,3}
- Supplementation with NMN has been shown to increase NAD⁺ levels in human clinical trials. Other precursors require several steps to be converted to NAD⁺, while NMN is only one step away.^{4,5}
- A number of benefits have been observed in clinical trials with NMN supplementation. Among women with impaired glucose metabolism, for example, supplementation was shown to improve insulin sensitivity.⁶ Supplementation has also been associated with improved exercise (aerobic) capacity in healthy runners, and reduced drowsiness and improved sit-to-stand ability (a marker for muscle function/strength) in older adults.^{7,8}
- Supplementation for 12 weeks was also associated with a trend toward reduced arterial stiffness in adults. Arterial stiffness has been associated with the aging process and is an independent risk factor for metabolic and cardiovascular disease.⁹

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• Take 1 capsule 2 times per day or as directed by a health care practitioner. Consult a health care practitioner for use beyond 6 weeks.

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• No known drug interactions.

Quick Tips for Optimal Health

- Maintaining healthy diet and lifestyle patterns has been clearly shown to promote healthy aging and reduce the risk of most age-related diseases.
- Perhaps the most well-studied dietary approach is the Mediterranean diet, which is rich in vegetables, fruits, legumes, unrefined cereals, nuts, and olive oil while limiting dairy products, meat, poultry, and saturated fat. Greater adherence to this diet has been associated with a lower risk for many age-related diseases, including neurodegenerative and cardiovascular diseases, as well as all-cause mortality.^{10,11}
- ☐ The Mediterranean diet and its components have also been shown to improve mitochondrial function and reduce oxidative stress and inflammation, which may underlie its multiple benefits.¹² Many phytonutrients present in plant foods have also been suggested to reduce oxidative stress and improve mitochondrial function, thereby promoting healthy aging.¹³
- Maintaining a healthy body weight is also important to healthy aging, at least in part by limiting inflammation.¹⁴
- While a low-calorie diet has been shown to be effective in promoting longevity in animal-based trials, it needs to be better established in humans. There is also a concern that a low-protein intake (as part of a low-calorie diet) may have negative consequences for older adults, such as loss of muscle strength/mass.¹⁵
- Physical activity, including both aerobic and resistance exercise, should be an important foundation for healthy aging. Exercise increases the "health span" (the period of life without disease and with good function) through many mechanisms, while sedentary time is associated with detrimental effects.^{16,17}
- Healthy sleep is also connected to a longer health span.
 In a large cohort with over 300,000 participants, a healthy sleep pattern was associated with a 15% lower risk of a reduced health span.¹⁸

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NMN

INTRODUCTION

Only recently have we begun to understand that the aging process itself is the primary driver for many chronic diseases. As a result, there has been growing effort to understand the mechanisms of aging and to find therapies that work to slow this process down and extend the "health span," the period of life characterized by the absence of severe disease with reasonably good health.1

Many mechanisms characterize the aging process, often referred to as the "hallmarks of aging," including cellular senescence, telomere attrition, mitochondrial dysfunction, dysregulated nutrient sensing, etc.² A substantial and growing body of evidence suggests that waning levels of nicotinamide adenine dinucleotide (NAD+), a metabolite with many different cellular functions, is intricately involved in the aging process. NAD+ decline with age has been described as a "major player in aging-related diseases." NAD+ is a coenzyme needed for at least 500 enzymatic reactions, many crucial to a cell's metabolism, and it also catalyzes electron transfer in metabolic reduction-oxidation (redox) reactions.⁴ In addition, NAD⁺ is essential to important signalling proteins known as sirtuins, and to poly(ADP-ribose) polymerases (PARPs), a family of 17 enzymes including PARP1 (also known as NAD+ ADP-ribosyltransferase 1), an enzyme that detects and repairs DNA damage. This partly explains the importance of NAD+ to optimal cellular functioning.5

A decline in NAD+ levels in both humans and experimental models of aging, as well as a decline in the proteins that require it for optimal function (including sirtuins and PARPs), have implicated this molecule as having an etiological role in many of the hallmarks of aging.6 Strategies to boost NAD+ levels have shown evidence of benefit for a wide range of age-related diseases in experimental models, including improved cognitive function, insulin secretion and sensitivity, hepatic function, and protection from cerebrovascular and cardiovascular disease.7 By targeting a key driving process for aging itself, the hope is that many age-related diseases may be prevented or delayed.

WHAT IS NMN?

Nicotinamide mononucleotide (NMN) is a bioavailable precursor to NAD+ that has been shown to increase cellular levels of NAD+ in human trials.8 Most cells cannot directly import NAD+ and must synthesize it *de novo* using tryptophan (known as the kynurenine pathway) or recycle other compounds to produce it. These compounds include NMN and other forms of vitamin B3, such as nicotinamide or nicotinic acid, with the majority of NAD+ production occurring through this process, known as the salvage pathway.

Most NAD⁺ precursors (including nicotinamide riboside (NR)) require several steps to be converted to NAD+ through enzymatic action that may be highly variable, potentially impairing NAD⁺ synthesis. For example, the enzyme NAMPT is rate-limiting for the conversion of nicotinamide (NAM) to NMN, and may be inhibited by aging, obesity, inflammation, and a high-fat diet. Given that NMN is only one chemical step away from NAD+ (as shown in the graphic below) and is not reliant on the enzyme NAMPT, it is an especially attractive candidate as an NAD+ booster.5,7



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In experimental models, supplementation with NMN has been associated with a wide range of benefits related to metabolism and cellular function. These benefits include suppression of weight gain, improved insulin sensitivity and plasma lipid profiles, enhancement of mitochondrial respiratory compatibility, and prevention of the decline of many physiological functions.9

Human trials of NMN supplementation have been encouraging. In a randomized and double-blind 10-week clinical trial, women with impaired glucose metabolism demonstrated signs of improved skeletal muscle insulin sensitivity and signalling, with an improvement similar to what would be observed with a 10% weight loss.¹⁰ In a six-week double-blind trial, healthy amateur runners had improved aerobic capacity compared to a placebo, an effect attributed to enhanced oxygen use by skeletal muscle.11 Trials with older adults have also demonstrated benefit; a double-blind controlled trial found that older adults receiving NMN (especially taken in the evening) reported reduced daytime drowsiness, as well as signs of improved muscle function (as assessed by a sit-to-stand evaluation) compared to a placebo.12 A second trial with men aged 65 or older found that in addition to increasing NAD+ levels, NMN supplementation improved muscle performance (as evaluated using gait speed and grip strength) compared to a placebo.13

Additionally, in a controlled trial with middle-aged adults, although no significant difference was found between NMN and a placebo, a trend toward reduced arterial stiffness was observed in a trial lasting only three months.14 Arterial stiffness has emerged as an independent risk factor for cardiovascular and metabolic diseases, which appears to precede the onset of these diseases.15

MECHANISM OF ACTION

The benefits of NMN are likely to be mediated entirely by its effects on NAD+, which itself has diverse metabolic and physiological actions. Sirtuins, for example, have many cardiac and metabolic effects, including upregulation of mitochondrial biogenesis, protection against atherosclerosis, improved endothelial function, enhanced insulin sensitivity, reduced inflammaging, etc.¹⁶ Sirtuins impact inflammation, cell growth, circadian rhythms, energy metabolism, neuronal function, and stress resistance, playing a role in nearly all cellular functions.7

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ASSESSMENT

No specific contraindications have been described for NMN. It has an excellent safety profile in published clinical trials with both younger and older populations.

GENERAL RECOMMENDATIONS AND DOSING

The recommended adult dose of NMN is 1 capsule 2 times per day, consistent with the clinical trial dosing of 250-300 mg per day used in most trials. Higher doses (600-1200 mg per day) were used among younger adults to improve aerobic capacity.

SUMMARY

NMN has significant promise as an NAD+ booster as it can increase levels of this metabolite, which has been clearly linked to many critical physiological functions that influence cellular metabolism and repair. Initial controlled trials suggest it not only increases NAD+ levels, but also reflects the clinical improvements expected from increased NAD+ availability.

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