



DOSSIER · SUBSTANCE

NAD Precursors (NMN, NR)

NAD precursors such as **nicotinamide mononucleotide (NMN)** and **nicotinamide riboside (NR)** are being studied as potential modulators of **NAD⁺ metabolism**. The human evidence base is limited, though controlled trials are available. Research focuses on **metabolism, safety, and inflammatory markers**, while other applications lack robust data.

1,232

STUDIES IN
TOTAL

223

IN HUMANS

71

OF WHICH
CONTROLLED

300

IN ANIMALS

140

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-17

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

NAD precursors (NMN, NR) at a glance

ORIGIN:

NAD precursors such as nicotinamide mononucleotide (NMN) and nicotinamide riboside (NR) are chemical compounds converted in the body into nicotinamide adenine dinucleotide (NAD+).

EVIDENCE BASE:

1,145 evaluated publications · 64 controlled human studies · 139 observational studies · 70 review articles · 285 animal studies · 112 cell culture studies

STRONGEST EVIDENCE:

- **Metabolism** NMN increases NAD+ levels in the blood in a dose-dependent manner but shows no significant effects on insulin resistance (HOMA-IR), physical performance, or subjective health in short-term studies. NMN's bioavailability is established, though direct metabolic effects remain to be confirmed.
- **Inflammation** NR raises cerebral NAD+ levels and reduces inflammatory cytokines in serum and cerebrospinal fluid in preclinical studies; whether these effects occur in humans has not yet been examined. Small human trials provide initial evidence of associations with mild improvements in neurodegenerative processes. Preclinical studies and small human trials showed reductions in inflammatory markers in neuronal extracellular vesicles and in NAFLD, albeit with high interindividual variability.
- **Musculoskeletal system** NMN increases blood NAD+ levels and nominally improves gait speed and grip strength in older men, though without significant effects on body composition. Data suggest potential muscular effects but are inconsistent.
- **Heart and circulation** A single study with NMN (600 mg/day) improved aerobic capacity (VO₂peak) in healthy adults, while lower dosages showed no effects. The study indicates a potential dose-dependent enhancement of cardiovascular performance, though molecular mechanisms were not assessed.
- **Safety and tolerability** NR and NMN are well tolerated in controlled studies, with no serious adverse events.

LIMITATIONS:

- The methodological quality of human studies is heterogeneous: many are small, non-randomised, or open-label, with varying dosages and measurement methods, complicating cross-study comparisons.
- Evidence of efficacy is often limited to surrogate parameters such as NAD+ levels or inflammatory markers, while clinical endpoints like disease progression or quality of life are rarely assessed.
- Long-term studies are lacking, and the translatability of preclinical findings (animal and cell studies) to humans remains to be established, as NAD+ metabolism and ageing processes are species-specific. Human relevance of these findings is not yet confirmed.

INTERPRETATION:

NAD precursors such as NMN and NR demonstrably increase NAD+ levels and show potential effects on inflammatory markers, muscular function, and cardiovascular performance, though without consistent clinical efficacy in short-term human studies.

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1. What NAD Precursors Are

NAD precursors are chemical compounds converted in the body into **nicotinamide adenine dinucleotide (NAD+)**. NAD+ is a central **coenzyme** in redox reactions and plays a key role in **energy metabolism, DNA repair, and cellular ageing**. NMN and NR are two of the most well-known precursors that can be supplemented orally. Both are recycled into NAD+ via the **salvage pathway**. Natural sources of NAD precursors include milk, yeast, and certain vegetables, though in significantly lower quantities than those found in supplements.

Bioavailability and metabolism are critical to understanding the evidence base. NMN and NR are absorbed and metabolised differently. NR is directly converted into NMN via specific **nicotinamide riboside kinases (NRK1/2)**, whereas NMN must first be cleaved into NR to cross the cell membrane.

Measuring NAD+ levels in blood or tissue is methodologically challenging and varies between studies. Additionally, evidence suggests that **efficacy** may depend on the **baseline NAD+ metabolic state**, which could explain individual differences in study outcomes.

2. What the Studies Show in Detail

The key human studies and most important reviews—by application area, including population, duration, preparation, measured parameters, and results, as reported in the original publications. Numbers are included only where the study specifies them.

Distribution of **controlled human studies** by application area—the numbers are not additive, as a single study may cover multiple areas:

APPLICATION AREA	CONTROLLED STUDIES
Metabolism	31
Safety and tolerability	27
Musculoskeletal system	18
Inflammation	12

APPLICATION AREA	CONTROLLED STUDIES
Cognition and mental health	9
Heart and circulation	8
Fatigue and stress	7
Absorption and availability	6

Inflammation

Cerebral NAD+ levels were measured using ³¹phosphorus magnetic resonance spectroscopy, NAD+ metabolites in cerebrospinal fluid, and cerebral metabolic activity via ¹⁸fluorodeoxyglucose positron emission tomography. NR significantly increased cerebral NAD+ levels, though with high interindividual variability. In participants with NAD+ elevation, changes in cerebral metabolism were observed, associated with mild clinical improvement (no quantitative data provided). Additionally, inflammatory cytokines in serum and cerebrospinal fluid decreased, though these findings are based on laboratory parameters and do not demonstrate neuroprotection in humans. Limitations included the short intervention duration and the small, homogeneous population, which precludes generalisation to other neurodegenerative diseases or advanced stages. The study provides preliminary evidence suggesting a potential neuroprotective effect of NR that requires validation in larger studies with clinical endpoints ¹.

The primary endpoint was insulin sensitivity; secondary analyses included NAD+ metabolites in skeletal muscle, body composition, and inflammatory markers. NR significantly increased NAD+ synthesis markers (nicotinic acid adenine dinucleotide, methylnicotinamide) in muscle and reduced body fat mass (increase in fat-free mass by 1.34 ± 0.50%, p = 0.02). While inflammatory parameters were not directly measured, changes in the NAD+ metabolome suggest a potential link to inflammation, though this remains speculative without targeted inflammatory diagnostics. Limitations included the small sample size and the lack of specific inflammatory marker assessment. The results indicate that NR may have metabolic effects, while its potential inflammation-modulating properties require confirmation in larger studies with dedicated inflammatory endpoints ⁵.

A randomised, placebo-controlled crossover study (2023) involving 22 healthy older adults (age not specified) tested 500 mg of NR twice daily over 6 weeks. NAD+ levels and inflammatory markers in neuronally enriched plasma extracellular vesicles (NEVs) were measured. NR significantly increased NAD+ levels in NEVs and reduced concentrations of Aβ42, phosphorylated JNK (pJNK), and pERK1/2—kinases associated with insulin resistance and neuroinflammation. Changes in NAD(H) correlated with those in the insulin-Akt signalling pathway as well as pERK1/2 and pJNK. The study provides initial evidence in humans of a potential anti-inflammatory effect of NR in a neuronal context, though NEVs only allow indirect conclusions about cerebral processes, and no clinical endpoints were assessed. Additionally, data on long-term effects and dose-response relationships are lacking ¹².

In a 6-month, randomised, double-blind, placebo-controlled study (2023) involving 111 NAFLD patients (age not specified), a combination of NR and pterostilbene (NRPT) was tested at two dosages (1× and 2× the recommended daily dose). The primary endpoint was hepatic fat fraction, with secondary endpoints including liver enzymes (ALT, GGT) and toxic lipids (ceramides). NRPT significantly reduced ALT and GGT in the 1×-dose group (no quantitative data provided), while the 2× dose showed no additional effects. Ceramide 14:0 decreased significantly in the 1×-dose group (p < 0.05 vs. placebo). The study suggests a dose-dependent effect of NRPT in NAFLD, though the absence of an NR-only group prevents attribution of effects to NR alone. Limitations also included the lack of analysis of specific inflammatory markers such as CRP or cytokines ¹⁵.

HYPOTHESIS

The available studies suggest that **NAD precursors** such as NR may exert anti-inflammatory effects in various tissues (CNS, muscle, liver). The mechanisms likely involve modulation of the NAD+ metabolome, activation of sirtuins, and reduction of pro-inflammatory signalling pathways (e.g., JNK/ERK). However, systematic investigations into dose-response relationships, long-term effects, and applicability to other inflammatory diseases (e.g., rheumatoid arthritis) stand out as the next research questions.

Metabolism

Primary endpoints were insulin sensitivity (hyperinsulinaemic-euglycaemic clamp) and substrate metabolism (indirect calorimetry, labelled substrates). NR had no effect on insulin sensitivity, resting energy expenditure, or hepatic fat fraction. However, a slight increase in lean body mass was observed in the NR group (no quantitative data provided), while fat oxidation remained unchanged. The study demonstrates that NR does not induce acute metabolic improvements in obese men, though longer intervention periods or higher dosages may be necessary. Limitations included the lack of NAD+ level measurements or muscle biopsies, which would have allowed insights into intracellular mechanisms ².

In a randomised, multicentre, double-blind, placebo-controlled study (2023), 80 healthy middle-aged adults (age not specified) received daily doses of 300 mg, 600 mg, or 900 mg of β-nicotinamide mononucleotide (NMN) or placebo for 60 days. The primary endpoint was the increase in blood NAD+ concentration, with secondary endpoints including physical performance (6-minute walk test), biological age (Aging.AI 3.0), insulin resistance (HOMA-IR), and subjective health (SF-36). NMN significantly increased NAD+ levels in a dose-dependent manner (p ≤ 0.001 vs. placebo and baseline), with the 900 mg dose showing the strongest effect. No significant changes were observed in HOMA-IR, physical performance, or SF-36. The study confirms the bioavailability of NMN but shows no direct metabolic or functional effects. Limitations included the short duration and the lack of muscle or liver NAD+ level measurements, which would be relevant for interpreting metabolic effects ⁴.

The primary endpoint was mitochondrial function in skeletal muscle (respiratory capacity, protein abundance). NR had no effect on mitochondrial respiration, content, or morphology. However, the protein abundance of nicotinamide phosphoribosyltransferase (NAMPT) in muscle decreased significantly (p < 0.05), while NAD+ metabolites remained unchanged. The study refutes the hypothesis that NR improves mitochondrial function in insulin resistance but reveals an unexpected regulation of NAMPT. Limitations included the lack of NAD+ level measurements in other tissues (e.g., liver) and the short intervention duration ⁶.

The primary endpoint was tolerability, with secondary analysis of NAD+ metabolites in blood. NMN was well tolerated, with no significant changes in clinical laboratory parameters. The study confirms the short-term safety of NMN but provides no data on metabolic effects or long-term tolerability. Limitations included the small sample size and the lack of functional endpoint assessments (e.g., insulin sensitivity) ¹³.

HYPOTHESIS The studies suggest that NAD precursors such as NR and NMN increase NAD⁺ levels in blood and muscle but show no consistent metabolic effects (e.g., insulin sensitivity, fat oxidation). Higher dosages, longer intervention periods, or more specific populations (e.g., older adults with NAD⁺ deficiency) may be required to observe clinically relevant metabolic effects. Additionally, systematic comparisons between NR and NMN and data on tissue-specific NAD⁺ levels are lacking.

Musculoskeletal System

Primary endpoints were the pharmacokinetics of NR and NAD⁺ levels in whole blood. The study confirms the bioavailability of NR but provides no data on muscular NAD⁺ levels or functional parameters. Limitations included the open-label design and small sample size ³.

A randomised, double-blind, placebo-controlled study (2022) tested 250 mg of NMN daily for 6 or 12 weeks in healthy older men (age not specified). Primary endpoints were NAD⁺ levels in blood and muscular function (gait speed, grip strength). NMN significantly increased NAD⁺ levels ($p < 0.05$) and nominally improved gait speed ($p = 0.07$) and left-hand grip strength ($p = 0.04$), though with no significant effects on body composition. The study suggests a potential improvement in muscle performance, albeit with small effect sizes and without controlling for physical activity. Limitations included the lack of muscle biopsies or mitochondrial function assessments ⁷.

HYPOTHESIS The available data indicate that NAD precursors such as NR and NMN increase NAD⁺ levels in blood and possibly in muscle but show no consistent effects on muscular function. The observed improvements (e.g., gait speed) may be attributable to indirect mechanisms such as enhanced mitochondrial efficiency or neuromuscular signalling pathways.

Heart and Circulation

The primary endpoint was aerobic capacity (VO₂peak) in cardiopulmonary exercise testing. NMN at 600 mg and 1,200 mg daily significantly increased VO₂peak ($p < 0.05$ vs. placebo), while the 300 mg dose showed no effects. The study suggests a dose-dependent improvement in exercise performance, though without assessment of NAD⁺ levels or molecular mechanisms. Limitations included the short duration and the lack of long-term effect or safety parameter assessments ⁸.

HYPOTHESIS The study showed that NMN may improve cardiovascular performance in healthy adults, possibly through enhanced mitochondrial efficiency or reduced oxidative stress. However, data on clinical endpoints (e.g., heart failure) and long-term effects are lacking. Additionally, it remains unclear whether the observed effects are due to a direct action of NMN or improved training adaptation.

Gut and Microbiome

Primary endpoints were β -cell function, α -cell function, and secretion of incretin hormones (GLP-1, GIP). NR had no effect on glucose, insulin, or C-peptide levels, β -cell function, or incretin hormones. The study refutes the hypothesis that NR influences endocrine pancreatic function or incretin secretion in obesity. Limitations included the lack of NAD⁺ level measurements in the gut or microbiome analyses, which would have allowed insights into potential indirect effects ⁹.

The primary endpoint was safety, with secondary measurement of NAD⁺ levels in blood. NRPT tended to increase NAD⁺ levels, with only the 500/100 mg dose showing a significant increase (47%, $p = 0.04$). The study showed the short-term safety of NRPT in AKI but provides no data on clinical outcomes or microbiome effects. Limitations included the short duration and small sample size ¹⁷.

HYPOTHESIS The available data from a controlled trial suggest that NR has no direct effects on endocrine pancreatic function or incretin secretion. However, indirect effects via the microbiome or gut barrier may play a role, which should be systematically investigated in future studies.

Safety and Tolerability

The primary endpoint was safety, with secondary assessment of NAD⁺ metabolites in blood and urine, as well as clinical parameters (MDS-UPDRS). NR was well tolerated, with no moderate or severe adverse events. Blood NAD⁺ levels increased up to fivefold ($p < 0.001$), while changes in MDS-UPDRS scores were observed but may have been influenced by a shorter interval since the last levodopa dose. The study showed the safety of high-dose NR in Parkinson's patients but lacks long-term data or comparisons with lower dosages ¹⁰.

Primary endpoints were the pharmacokinetics and pharmacodynamics of NMN. The study reports the bioavailability and safety of MIB-626 but provides no data on clinical endpoints or long-term effects ¹⁶.

The primary endpoint was safety, with secondary assessment of NAD⁺ levels in blood and mitochondrial function in peripheral blood mononuclear cells. NR doubled blood NAD⁺ levels and showed correlations with improved mitochondrial respiration *in vitro* (basal: $R^2 = 0.413$, $p = 0.003$; maximal: $R^2 = 0.434$, $p = 0.002$) and reduced NLRP3 expression ($R^2 = 0.330$, $p = 0.020$). The study reports the safety of NR in heart failure but provides no clinical endpoints or long-term data on mitochondrial function or inflammation in humans ³⁶.

Fatigue and Stress

A randomised, double-blind, placebo-controlled study (2022) investigated the effects of 250 mg NMN daily over 12 weeks in 108 older Japanese adults (age not specified). Primary endpoints included sleep quality (Pittsburgh Sleep Quality Index), fatigue ("Jikaku-sho shirabe"), and physical performance (e.g., 5-times sit-to-stand test). NMN improved physical performance (5-STs) and reduced daytime fatigue, particularly when taken in the afternoon (effect sizes $d = 0.72$ and 0.64 , respectively). The study suggests a time-dependent effect of NMN, though it did not measure NAD⁺ levels or molecular mechanisms. A limitation was the lack of control for physical activity or diet ¹¹.

HYPOTHESIS The study indicates that NMN may improve physical performance and fatigue in older adults, potentially by enhancing mitochondrial efficiency or reducing oxidative stress. However, data on long-term effects and generalisability to other populations (e.g., chronic fatigue syndrome) are lacking.

Cognition and Mental Health

No controlled human studies with specific endpoints exist for the domain of *cognition and mental health*. Review articles suggest a neuroprotective potential of NAD precursors such as NMN or NR *in preclinical models*, based on data related to Alzheimer's disease, ischaemia-reperfusion injury, and retinal degeneration. Postulated mechanisms include increasing NAD⁺ levels, activating sirtuins, and reducing oxidative stress.

Overall Picture

Available studies on NAD precursors such as nicotinamide riboside (NR) and nicotinamide mononucleotide (NMN) consistently show that these compounds increase NAD⁺ levels in blood and muscle; increases in the central nervous system have so far been measured in preclinical models, and effects in humans have not been investigated. However, effects on clinical endpoints are heterogeneous and depend on the population, dosage, and duration of intervention. The strongest evidence for effects exists for inflammatory markers (e.g., reduction of cytokines in Parkinson's disease or NAFLD) and metabolic parameters (e.g., increased lean mass), though with small effect sizes and high interindividual variability.

Significant gaps remain in the systematic assessment of long-term effects, dose-response relationships, and tissue-specific NAD⁺ levels. Additionally, studies in specific patient groups (e.g., diabetes, heart failure, neurodegenerative diseases) with clinically relevant endpoints are lacking. Most studies are short (4–12 weeks) and use surrogate markers (e.g., NAD⁺ metabolites), while hard endpoints (e.g., mortality, hospitalisation rates) are not investigated. Larger, long-term studies with clearly defined clinical endpoints are required for a definitive evaluation of the therapeutic potential of NAD precursors.

Methodology of the Evidence Base

The controlled human trials predominantly comprise randomised, placebo-controlled, double-blind trials (RCTs) with small to medium sample sizes (n = 8–111); the remaining human studies are observational or exploratory. Typical intervention durations range from 4 weeks to 6 months, with most studies lasting 6–12 weeks. Primary endpoints often include safety parameters (e.g., adverse events) or surrogate markers (e.g., NAD⁺ levels, inflammatory markers), while clinical endpoints (e.g., insulin sensitivity, physical performance) are less frequently assessed. Systematic gaps exist in the evaluation of long-term effects (> 6 months), comparability of different NAD precursors (NR vs. NMN), and investigation of specific patient groups (e.g., older adults with NAD⁺ deficiency). Furthermore, tissue-specific analyses (e.g., muscle or liver biopsies) that could provide insights into intracellular mechanisms are often lacking. Most studies are exploratory and not designed to validate clinical effects.

NAD⁺ Increase ≠ Clinical Benefit

A central issue in

NAD PRECURSOR

research is the **equating of NAD⁺ levels with clinical efficacy**. Many studies merely measure the **increase in NAD⁺ in blood or tissue** and infer potential health benefits from this. However, **elevated NAD⁺ levels** are a **biochemical marker**, not proof of **functional improvement**. Even in controlled studies examining **metabolic parameters** such as insulin resistance or muscle metabolism, the effects are **inconsistent**. Some studies show **no change** despite NAD⁺ increases, while others report **minor improvements** that may be of limited clinical relevance.

The

FOCUS ON SURROGATE PARAMETERS

also obscures the fact that **causal relationships** between NAD⁺ metabolism and disease progression are **not sufficiently established**. For example, **Parkinson's disease** is often cited as a potential application, yet the **NADPARK study** and the **NR-SAFE study** demonstrate **safety and NAD⁺ increases** but **no significant improvement** in motor symptoms. A similar pattern is observed for **cognitive parameters**: some studies report **changes in biomarkers**, but whether this affects **actual cognitive performance** remains unclear. The **overinterpretation of laboratory findings** without clinical correlates is a recurring issue in this field of research.

3. How Robust the Research Is

Research on **NAD precursors** spans basic science, animal studies, and human trials. Among human studies, controlled trials are available, while the remainder are observational or focused on safety. The **most extensively studied applications** are **metabolism, safety, and the musculoskeletal system**. Cognition, cardiovascular health, and fatigue follow with significantly fewer studies. The **most cited controlled trials** address **Parkinson's disease (NADPARK study)**, **insulin resistance**, **bioavailability**, and **muscle metabolism**. Review articles on **ageing and neurodegenerative diseases** often encompass multiple interventions, including NAD precursors and other compounds, and are frequently based on **animal models or cell cultures**.

The **methodological quality** of human studies is heterogeneous. Many are **small, non-randomised, or open-label**. Even in controlled trials, **dosages, measurement methods, and endpoints** vary, complicating comparisons. **Safety data** are robust, but **evidence of efficacy** often remains limited to **surrogate parameters** such as **NAD⁺ levels or inflammatory markers**. **Clinical endpoints** such as disease progression or quality of life are rarely assessed. Furthermore, **long-term studies** extending beyond brief periods are lacking. The **translatability** of animal and cell studies to humans is limited, as these findings are preclinical and require further validation in human trials.

4. Common Claims — and What the Data Show

STATEMENT	EVIDENCE BASE
NAD precursors as anti-ageing agents	The available data is limited to short-term studies with surrogate parameters . Long-term effects on ageing processes or life expectancy have not been i
Use in neurodegenerative diseases	Controlled studies show no significant improvement in clinical symptoms, but merely changes in biomarkers .
Improvement of physical performance	Individual studies report minor effects on endurance or muscle metabolism, but no consistent results .
Effects on cardiovascular diseases	Research is limited to animal models and mechanistic studies . Human studies with clinical endpoints are lacking .

5. Fact Sheet: Molecule and Charge

NAD precursors (NMN, NR) are not single molecules but a **mixture** — there is no single molecular formula or fixed molecular mass. What can be described are functional groups, charge behaviour, and redox properties; these are the focus of the next section.

6. Charge, Electrons, and Radicals

NAD precursors such as NMN and NR participate in redox processes. In human tissue, they reduce reactive oxygen species (ROS). NMN lowered ROS in ovarian tissue and skin cells (HEKa, HaCaT) ^{27 28}. In UVB-exposed HaCaT cells, NR in combination with other substances reduced ROS by 22.0% ³⁰. The effect on ROS has not been directly measured electrochemically in controlled human studies but has been observed as a secondary effect. NAD+ itself protects against ROS and supports mitochondrial function ^{25 26}.

The electrochemical properties of NAD precursors have not been directly investigated in humans. In tissue and cell models, NMN and NR exhibit dose-dependent effects on ROS levels without affecting cell viability alone ²⁹. Animal and tissue studies suggest a role in electron transfer, as NAD+ functions as a coenzyme in redox reactions ²⁵. Whether NMN or NR act as radical scavengers themselves or indirectly via NAD+ elevation remains unclear.

7. Interactions with Other Substances

Substances from this platform that have been **jointly** investigated or discussed with this compound in human studies and review articles—whether in combination, comparison, or via a shared mechanism of action. The number indicates studies in which both appear.

SUBSTANCE	JOINT STUDIES	OF WHICH CONTROLLED IN HUMANS
Chronic inflammation	61	12
Stress, cortisol and inflammation	43	2
Resveratrol	10	5
Gut microbiome	9	1
Coenzyme Q10	5	3
Turmeric and curcumin	3	1
Butyrate (butyric acid)	3	1
L-Carnitine	3	1
Urolithin A	2	0

Data on interactions between NAD precursors such as NMN or NR and pharmaceuticals or nutrients are limited. One study investigated NR in combination with pterostilbene (NRPT) in adults with NAFLD over six months without reporting specific interactions ¹⁵. Observations suggest that NR increases the concentration of NAD+ precursors such as nicotinic acid riboside (NAR) and nicotinic acid mononucleotide (NAM) in skeletal muscle, indicating altered metabolism ³¹. Additionally, a synergistic effect of NR with IFN-β in sepsis via SIRT1 activation has been described, suggesting potential interactions with immunomodulatory substances ³³. In vitro, NMN was tested in combination with palmitate in β-cells to assess effects on cell function ³⁴.

Evidence of enzyme interactions arises from the observation that NR, in combination with PARG inhibition (PARGi), leads to hyperaccumulation of poly(ADP-ribose) (PAR), indicating activation of PARP1³². Furthermore, regulation of mitochondrial functions via the AMPK-SIRT1-PGC1 α signalling pathway has been described, implying interactions with other substances affecting this pathway. One study shows that SIRT5 interacts with argininosuccinate lyase (ASL) and regulates its post-translational modification (e.g., glutarylation), suggesting possible interactions with amino acid metabolic pathways. Further investigations into binding affinities or potentiating/attenuating effects are required.

8. Overdose, Tolerability, and Limits

Data on overdose, toxicity, and upper limits of NAD precursors (NMN, NR) from controlled human studies are limited. NR has been tested at doses of up to 3000 mg per day over four weeks without serious adverse effects being reported. A study with 1500 mg NR twice daily (3000 mg/day) in Parkinson's patients showed no increased toxicity, supporting the expansion of the dosage range in Phase II studies^{10 10}. Laboratory parameters such as ALT levels improved in a group taking NRPT, suggesting potential hepatoprotective effects without direct evidence of toxicity¹⁵.

Adverse effects reported in available studies are limited to mild gastrointestinal symptoms observed with NR or NRPT administration¹⁷. In a comparative study with intravenous administration, NR exhibited fewer and milder side effects than NAD⁺ during infusion, with no subsequent adverse events³⁵. Contraindications cannot be explicitly derived from the available data, as study populations included specific conditions (e.g., Parkinson's, AKI, cognitive impairment) and no systematic assessment was conducted for certain pre-existing conditions. Further research would be necessary to clarify potential interactions with medications or contraindications in cases of impaired liver or kidney function.

9. The Most Robust Studies

Ranked by evidential strength, not by prominence. The full evaluation includes significantly more studies; only the most reliable are listed here.

Controlled Human Studies

- ¹ The NADPARK study: A randomised phase I trial of nicotinamide riboside supplementation in Parkinson's disease (2022)
- ² A randomised placebo-controlled clinical trial of nicotinamide riboside in obese men: safety, insulin sensitivity, and lipid-mobilising effects (2018)
- ³ An open-label, non-randomised study of the pharmacokinetics of the nutritional supplement nicotinamide riboside (NR) and its effects on blood NAD⁺ levels (2017)
- ⁴ The efficacy and safety of β -nicotinamide mononucleotide (NMN) supplementation in healthy middle-aged adults: a randomised, multicentre, double-blind, (2023)
- ⁵ Nicotinamide riboside supplementation alters body composition and skeletal muscle acetylcarnitine concentrations in healthy obese humans (2020)
- ⁶ Nicotinamide riboside does not alter mitochondrial respiration, content, or morphology in skeletal muscle from obese and insulin-resistant men (2020)
- ⁷ Chronic nicotinamide mononucleotide supplementation elevates blood nicotinamide adenine dinucleotide levels and alters muscle function in healthy older adults (2022)
- ⁸ Nicotinamide mononucleotide supplementation enhances aerobic capacity in amateur runners: a randomised, double-blind study (2021)
- ⁹ Effects of nicotinamide riboside on endocrine pancreatic function and incretin hormones in non-diabetic men with obesity (2019)
- ¹⁰ NR-SAFE: a randomised, double-blind safety trial of high-dose nicotinamide riboside in Parkinson's disease (2023)
- ¹¹ Effect of 12-week intake of nicotinamide mononucleotide on sleep quality, fatigue, and physical performance in older Japanese adults: a randomised, double-blind study (2022)
- ¹² Oral nicotinamide riboside raises NAD⁺ and lowers biomarkers of neurodegenerative pathology in plasma extracellular vesicles enriched for neuronal origin (2023)
- ¹³ Safety evaluation of oral β -nicotinamide mononucleotide administration in healthy adult men and women (2022)
- ¹⁴ Nicotinamide adenine dinucleotide metabolism and arterial stiffness after long-term nicotinamide mononucleotide supplementation: a randomised, double-blind study (2023)
- ¹⁵ Nicotinamide riboside and pterostilbene reduce markers of hepatic inflammation in NAFLD: a double-blind, placebo-controlled clinical trial (2023)
- ¹⁶ MIB-626, an oral formulation of a microcrystalline unique polymorph of β -nicotinamide mononucleotide, increases circulating nicotinamide adenine dinucleotide levels (2023)
- ¹⁷ Nicotinamide riboside with pterostilbene (NRPT) increases NAD⁺ in patients with acute kidney injury (AKI): a randomised, double-blind, placebo-controlled study (2020)
- ¹⁸ Randomised crossover clinical trial of coenzyme Q10 and nicotinamide riboside in chronic kidney disease (2023)
- ¹⁹ Nicotinamide riboside as a neuroprotective therapy for glaucoma: study protocol for a randomised, double-blind, placebo-controlled trial (2022)
- ²⁰ Effect of nicotinamide riboside on airway inflammation in COPD: a randomised, placebo-controlled trial (2024)
- ²¹ Ingestion of β -nicotinamide mononucleotide increased blood NAD levels, maintained walking speed, and improved sleep quality in older adults in a double-blind study (2024)
- ²² Effect of the Mediterranean diet supplemented with nicotinamide riboside and pterostilbene and/or coconut oil on anthropometric variables in amyotrophic lateral sclerosis (2023)
- ²³ Towards personalised nicotinamide mononucleotide (NMN) supplementation: nicotinamide adenine dinucleotide (NAD) concentration (2024)
- ²⁴ Nicotinamide riboside supplementation is not associated with altered methylation homeostasis in Parkinson's disease (2023)

10. Summary

What is established: NAD precursors such as NMN and NR demonstrably increase NAD⁺ levels in blood and muscle, as confirmed by controlled human studies; for brain tissue, the findings so far come from preclinical work, and an effect in humans has not been investigated. The safety of both precursors is well documented in short-term studies, with no serious adverse events reported. In specific applications, effects on surrogate parameters are observed: NR reduces inflammatory cytokines in the CNS and in NAFLD, while NMN dose-dependently improves aerobic capacity in healthy adults. The bioavailability of both compounds is established, though without consistent clinical effects on metabolic parameters such as insulin sensitivity or fat oxidation.

HYPOTHESIS NAD precursors may exert anti-inflammatory effects in various tissues, likely through modulation of the NAD⁺ metabolome and activation of sirtuins. The observed improvements in muscular function (e.g., gait speed) and cardiovascular performance suggest indirect mechanisms such as enhanced mitochondrial efficiency or neuromuscular signalling pathways. However, the effects are often small and vary interindividually, indicating a dependence on baseline NAD⁺ metabolism. Furthermore, systematic comparisons between NR and NMN, as well as data on tissue-specific NAD⁺ levels, are questions that still await investigation.

What a study should clarify: Future research should focus on long-term studies with clinical endpoints (e.g., disease progression, quality of life) to validate the transferability of surrogate parameters. Systematic investigations into dose-response relationships, particularly in comparisons between NR and NMN, are necessary to identify optimal dosages and target populations. Additionally, tissue-specific NAD⁺ levels (e.g., liver, muscle, CNS) should be assessed to better understand the mechanisms underlying the observed effects. The role of the microbiome and gut barrier in the action of NAD precursors should also be explored, as indirect effects on metabolism and inflammatory regulation are plausible. Finally, studies in homogeneous populations (e.g., patients with sarcopenia, neurodegeneration, or metabolic syndrome) are required to test the applicability of the results to clinically relevant groups.

11. What Remains Unclear

- **Long-term effects:** Are there **cumulative effects or risks** after years of intake?
- **Individual differences:** Why do some subjects respond to NAD precursors while others do not?
- **Combination therapies:** Can NAD precursors act **synergistically** with other substances, for example in metabolic disorders?

12. Further Paths

Topics, mechanisms and chains in which this substance appears — for those who want to look beyond the substance.

- Interaction network

Frequently Asked Questions

Are NMN and NR equally effective?

The **bioavailability and metabolism** of NMN and NR differ. NR is directly converted to NMN via **NRK1/2**, whereas NMN must first be cleaved. Studies show **varying effects** on NAD⁺ levels and metabolic parameters, but **no clear advantage** of either substance has been established. The choice depends on **individual tolerability and objectives**, not on proven superiority.

Can NAD precursors reduce inflammation?

Some controlled trials show **changes in inflammatory markers**, but **no clinically relevant reduction** in inflammatory processes. The evidence is **still developing and inconsistent**. Furthermore, studies specifically targeting **chronic inflammation** are lacking. The **applicability** of laboratory findings to humans is **not assured**.

Are NAD precursors beneficial for healthy individuals?

The **majority of studies** have been conducted in **individuals with metabolic disorders or overweight**. For **healthy individuals**, there is **no robust evidence** of a **preventive or performance-enhancing benefit**. While **safety data** are positive, **long-term effects** remain unknown. A **general recommendation** cannot be derived from the current evidence base.

Sources

- 1 The NADPARK study: A randomized phase I trial of nicotinamide riboside supplementation in Parkinson's disease
Brakedal B, Dölle C, Riemer F, Ma Y, Nido GS, Skeie GO et al. · 2022
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