AbinoNutra® NMN White Paper

NAD^+ Precursor for Healthy Longevity

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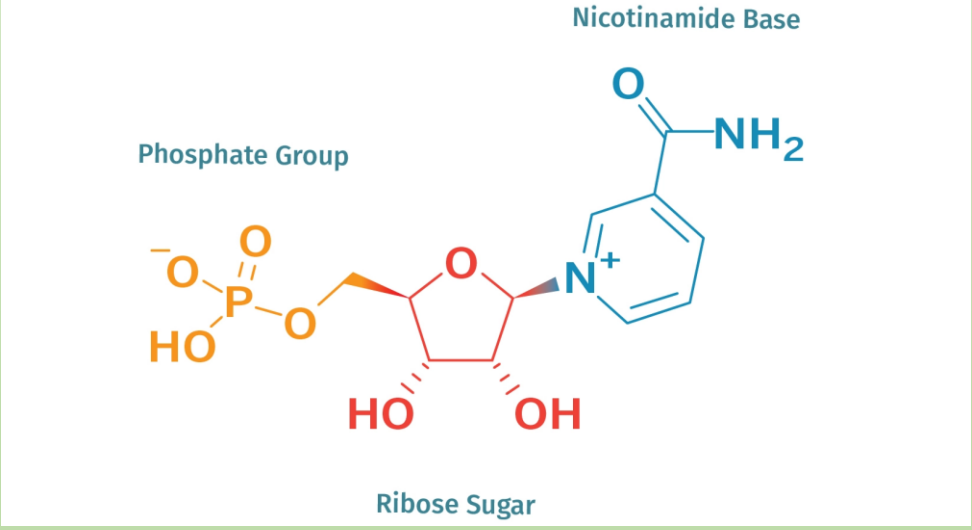
What is NMN?

- **β-Nicotinamide mononucleotide (NMN)** is a naturally occurring substance present in every living cell across all life forms.
- **NMN** belongs to a class of compounds known as nucleotides consisting of three key components: a phosphate group, a ribose sugar, and a nicotinamide base (see the image below).
- **NMN** is directly converted into nicotinamide adenine dinucleotide **(NAD^+)**, leading to elevated NAD^+ levels. For this reason, NMN is often referred to as an **NAD^+ precursor**.

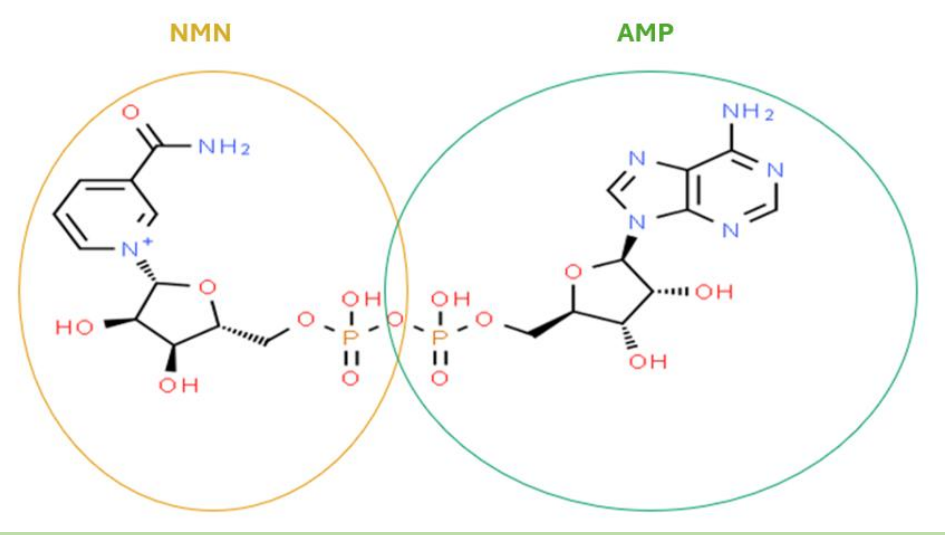


Reference:

What is NMN. (2024, December 5). Retrieved from https://www.nmn.com/what-is-nmn.

What is NAD⁺?

- **Nicotinamide adenine dinucleotide (NAD⁺)** is one of the most abundant and essential molecules in the human body, required for approximately 500 enzymatic reactions. Without NAD⁺, life would cease within minutes.
- **NAD⁺** plays a crucial role in energy metabolism, helping the body produce approximately 50–75 kg of ATP each day to meet its energy demands.
- **NAD⁺** also functions as a cell signaling molecule involved in DNA repair, epigenetic regulation, cellular senescence, and nearly all other hallmarks of aging.
- **NAD⁺** molecule consists of two nucleotides—nicotinamide mononucleotide (NMN) and adenosine monophosphate (AMP)—linked through their phosphate groups (see the image below).

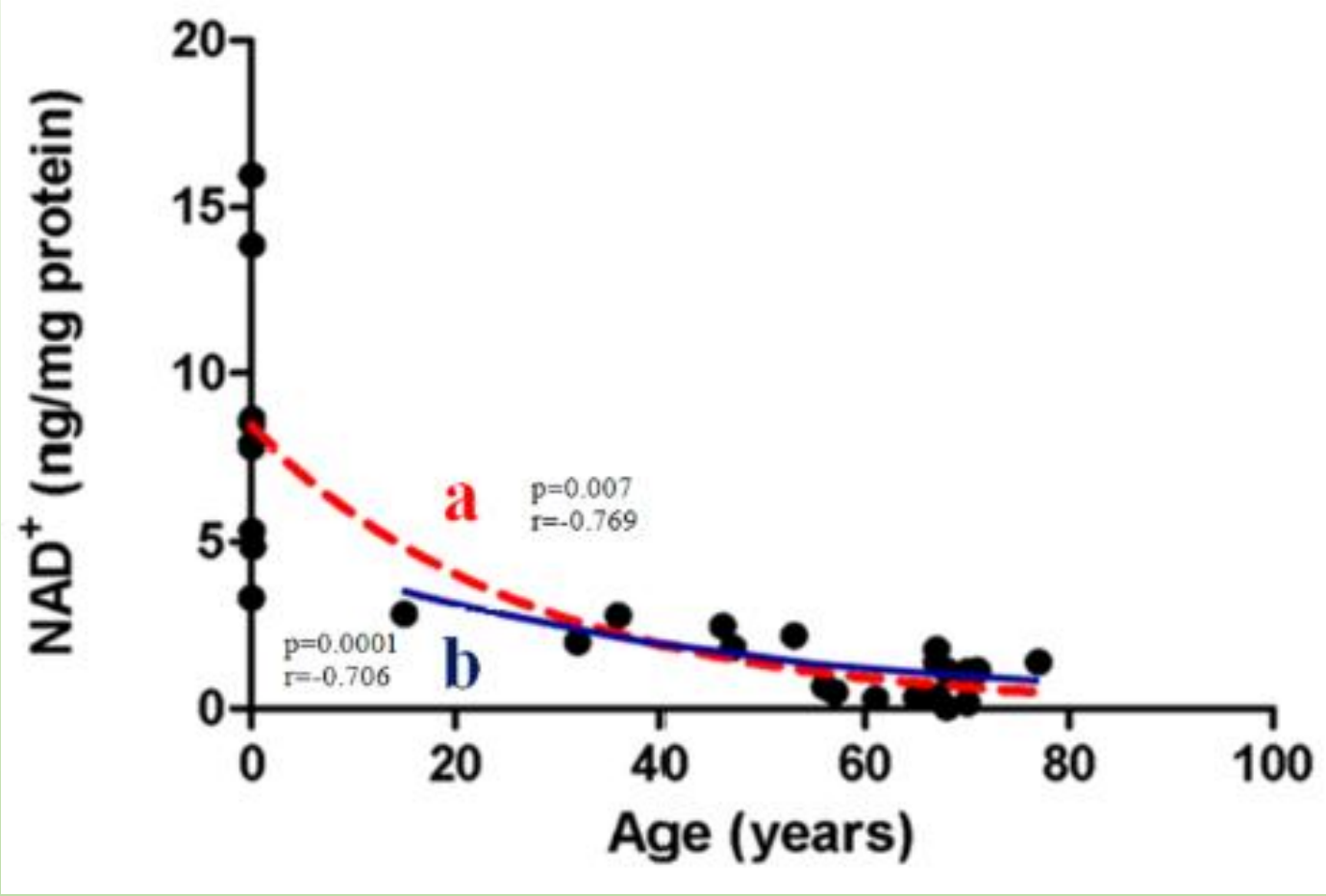


Reference:

What is NAD⁺?. (2020, October 20). Retrieved from https://www.nmn.com/precursors/what-is-nad.

Rajman L, Chwalek K, Sinclair DA. Therapeutic Potential of NAD-Boosting Molecules: The In Vivo Evidence. *Cell Metab.* 2018; 27(3): 529-547. DOI: 10.1016/j.cmet.2018.02.011

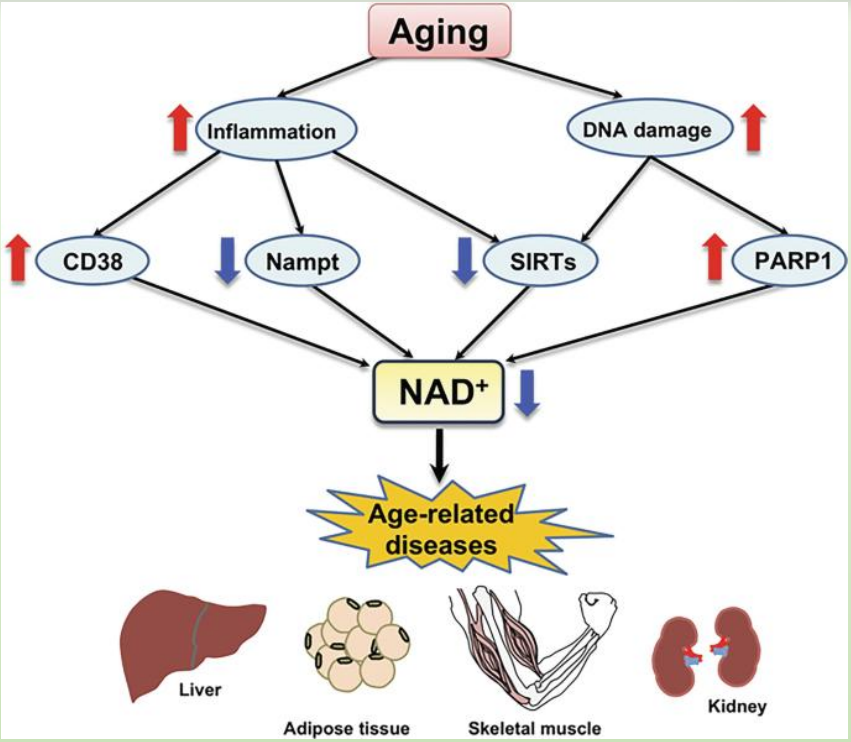
NAD^+ Levels Decline As We Age



Reference:

Massudi H, Grant R, Braidy N, Guest J, Farnsworth B, Guillemin GJ. Age-associated changes in oxidative stress and NAD^+ metabolism in human tissue. *PLoS One*. 2012; 7(7): e42357. DOI: 10.1371/journal.pone.0042357

The Biological Mechanism of NAD⁺ Decline and Aging

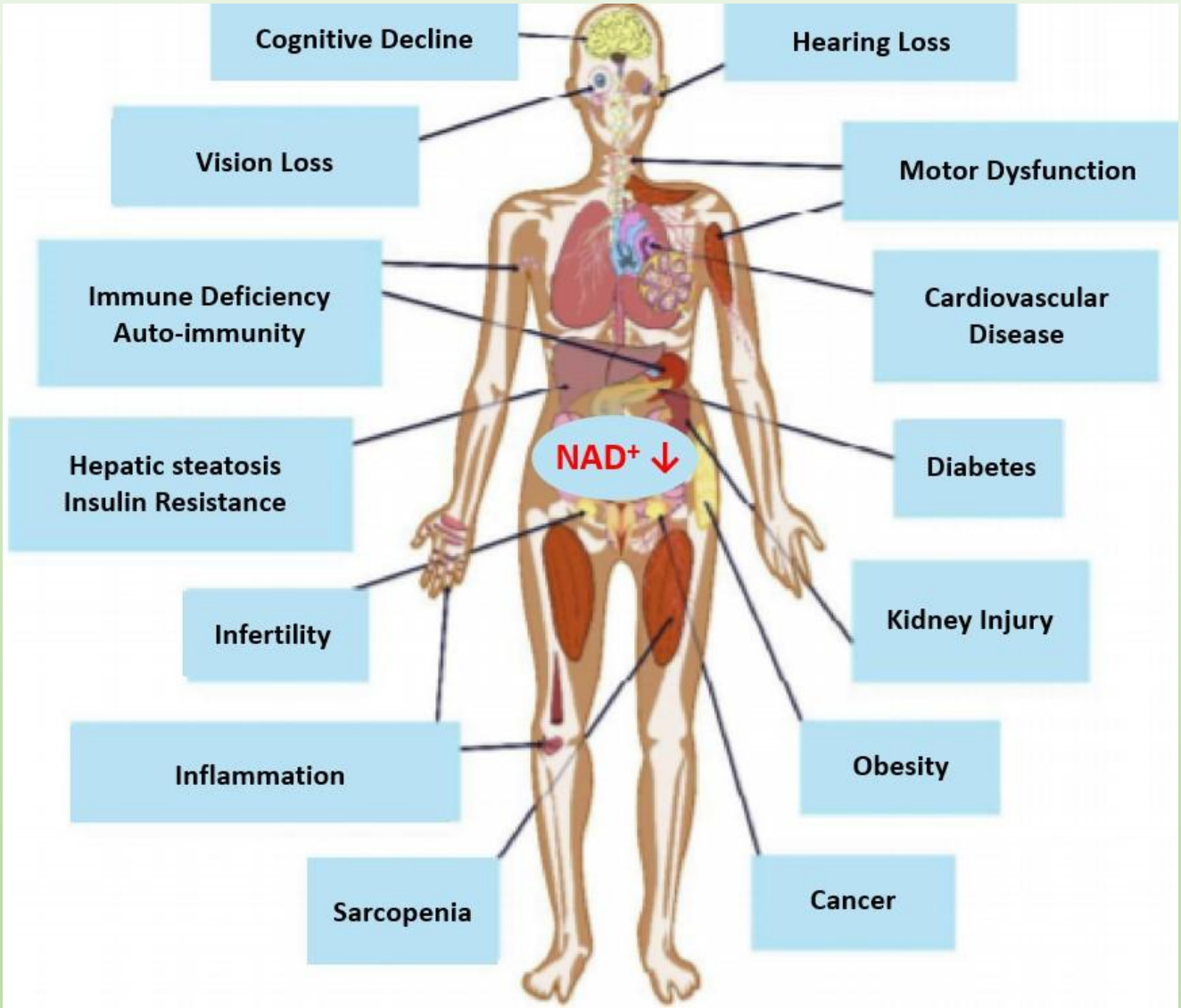


- As we age, stressors like **inflammation** and **DNA damage** become more prevalent. These stressors trigger NAD⁺ consuming enzymes, such as **PARP1** and **CD38**, to become hyperactive, rapidly draining the cell's NAD⁺ supply.
- The resulting decline in NAD⁺ levels limits the function of protective enzymes called sirtuins (**SIRTs**). This reduced sirtuin activity then accelerates the aging process by impairing **DNA repair**, shortening **telomeres**, causing **epigenetic changes**, etc. and ultimately contributing to age-related diseases.

Reference:

Palikhe S, Nakagawa T. (2022). NAD+ Metabolism in Aging. In: Mori N. (eds) Aging Mechanism II. Springer, Singapore. https://doi.org/10.1007/978-981-16-7977-3_8

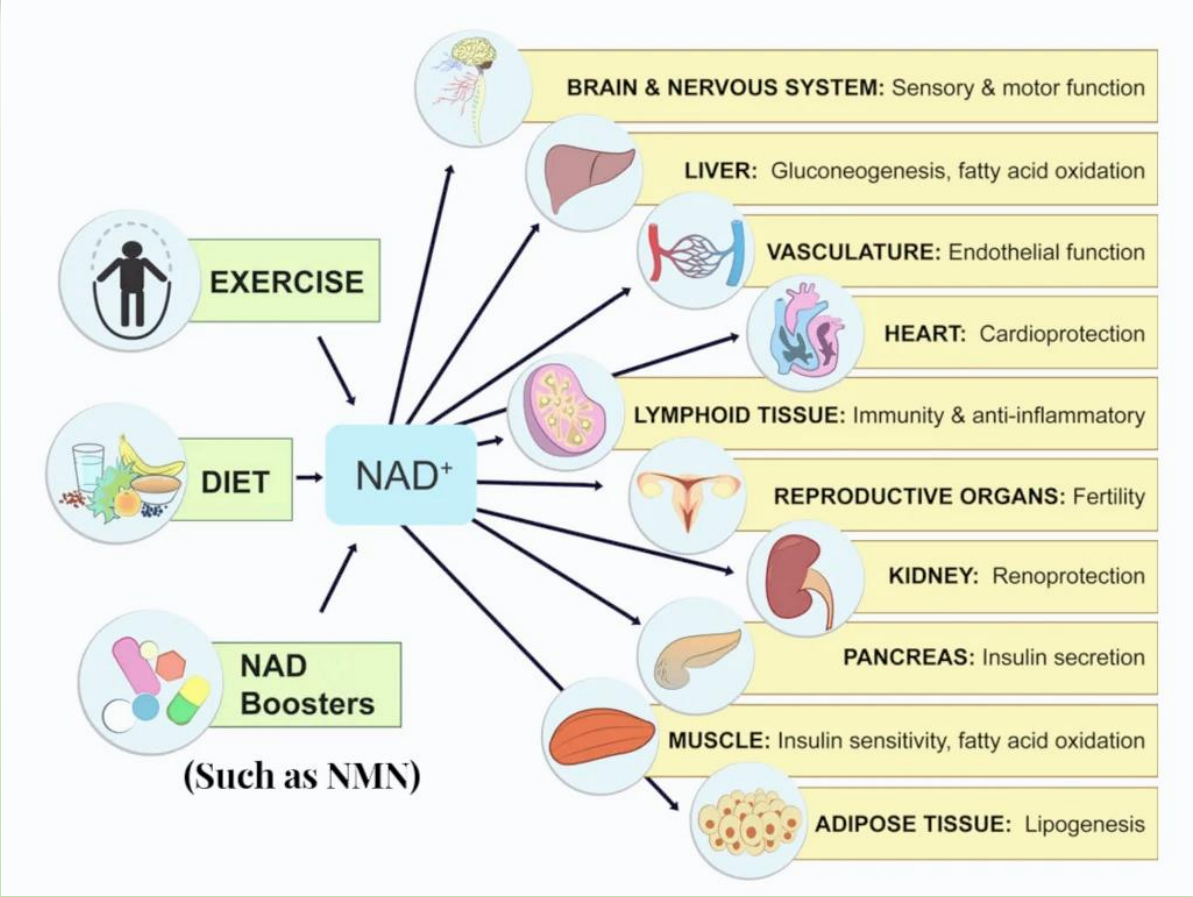
The Decline of NAD$^+$ Levels Linked to Various Age-related Diseases!



Reference:

Rajman L, Chwalek K, Sinclair DA. Therapeutic Potential of NAD-Boosting Molecules: The In Vivo Evidence. *Cell Metab.* 2018; 27(3): 529-547. DOI: 10.1016/j.cmet.2018.02.011

NAD^+ Rejuvenation Improves Age-Related Conditions in Cells and Animals

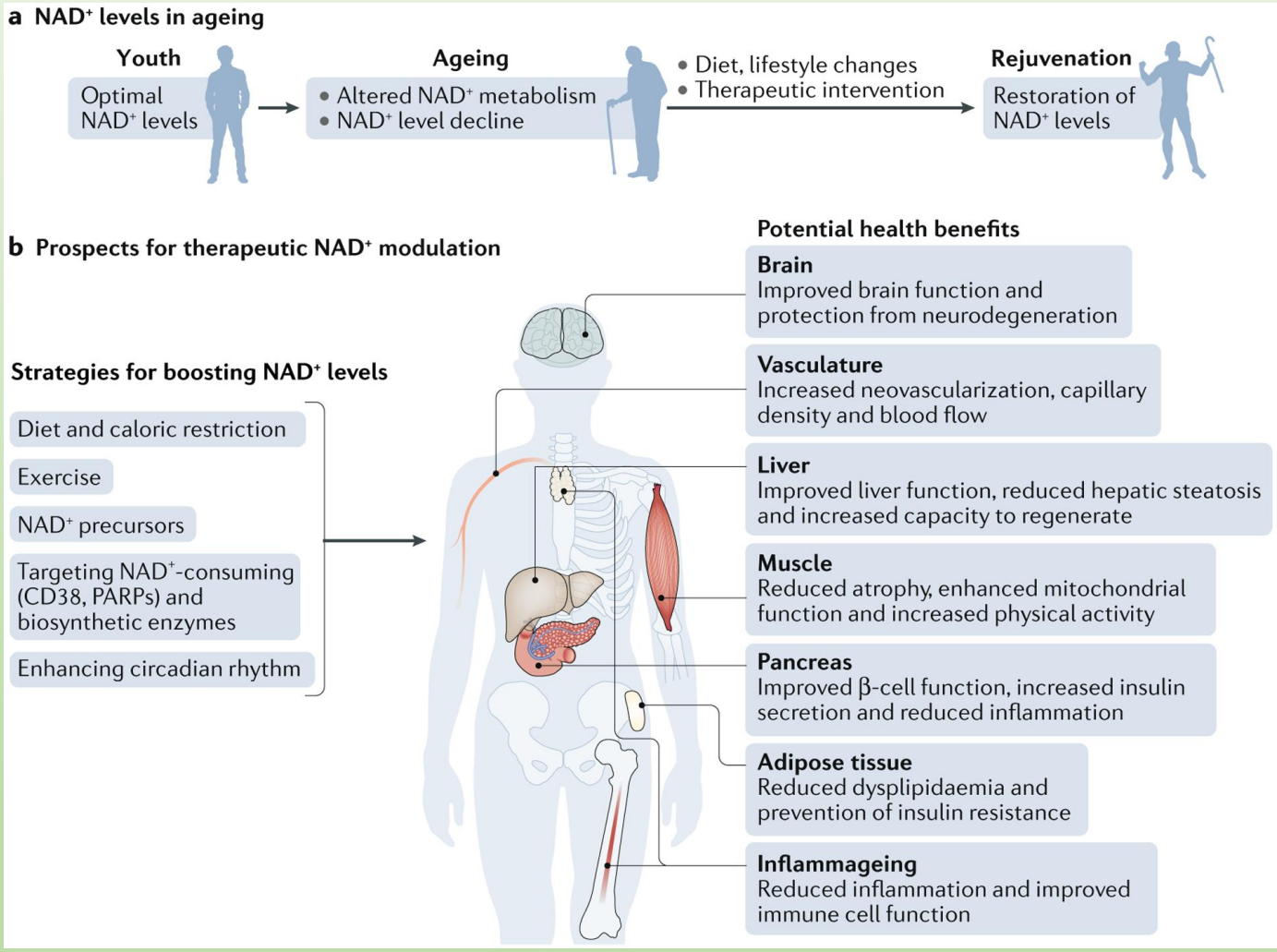


Preclinical studies on cells and animals (*in vitro* and *in vivo*) have shown that exercise, proper diet, and NAD^+ boosters (such as NMN) can elevate NAD^+ levels, which in turn promote cognitive function in the brain, gluconeogenesis in the liver, lipogenesis in adipose tissue, and more, as illustrated in the figure above.

Reference:

Rajman L, Chwalek K, Sinclair DA. Therapeutic Potential of NAD-Boosting Molecules: The In Vivo Evidence. *Cell Metab.* 2018 Mar 6;27(3):529-547. DOI: 10.1016/j.cmet.2018.02.011

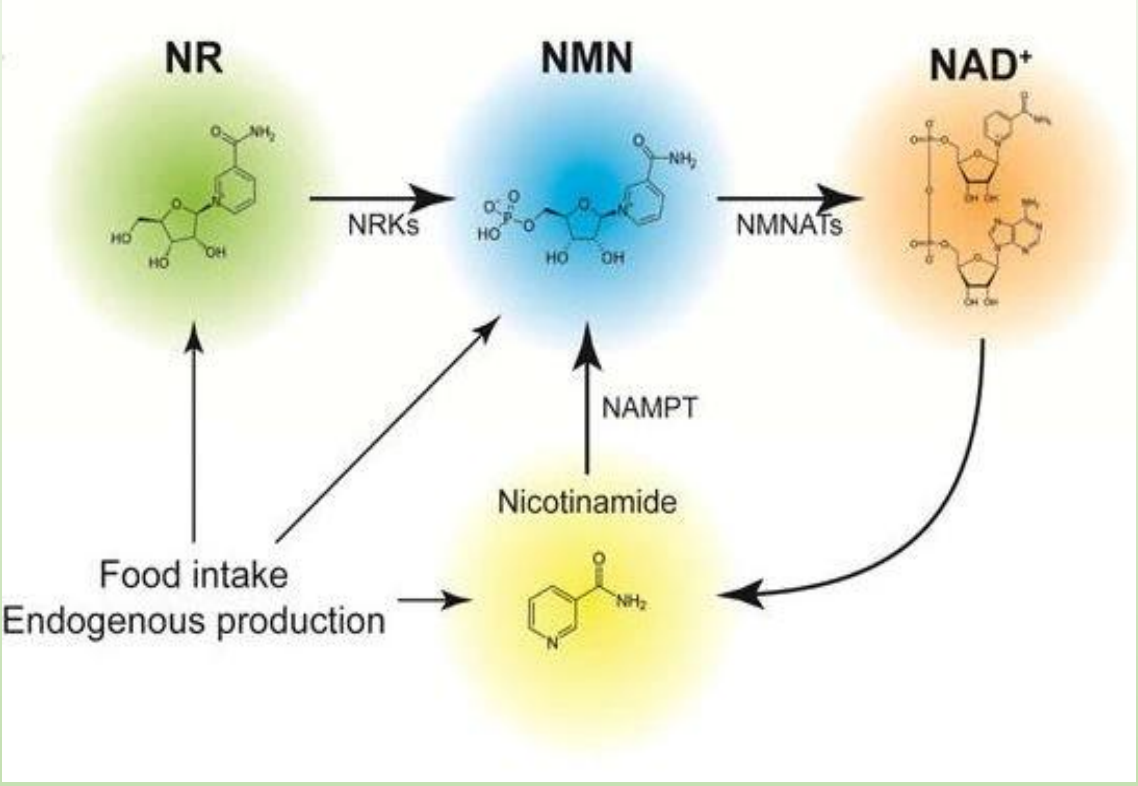
NAD^+ Rejuvenation Can Have Great Therapeutic Potential for Healthy Longevity as Many Preclinical Studies Have Found in Cells and Animals



Reference:

Covarrubias AJ, Perrone R, Grozio A, Verdin E. NAD+ metabolism and its roles in cellular processes during ageing. *Nat. Rev. Mol. Cell. Biol. 2021 Feb*;22(2):119-141. doi: 10.1038/s41580-020-00313-x

NMN is one of the Major Precursors of NAD^+ Biosynthesis

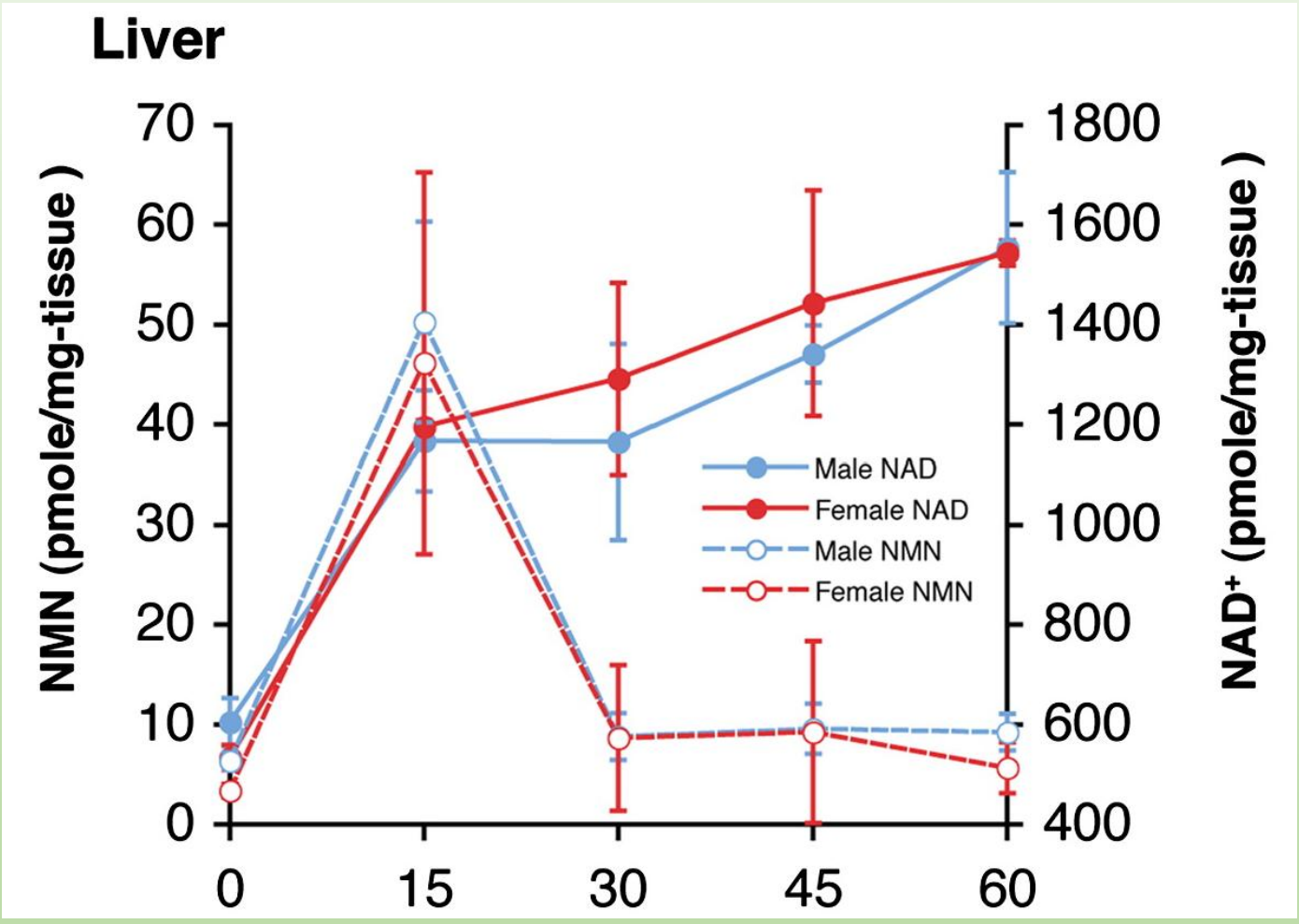


There are three biosynthetic pathways in cells that produce NAD^+: the **de novo**, **Preiss–Handler**, and **salvage** pathways. Among these, the **salvage pathway** (see the image above) is the primary route for NAD^+ production in mammals. **NMN (nicotinamide mononucleotide)** and **NR (nicotinamide riboside)** are key NAD^+ precursors that have been evaluated in more than 20 human clinical trials, demonstrating both their safety and their effectiveness in elevating NAD^+ levels.

Reference:

Yoshino J. Baur JA, Imai S. NAD^+ intermediates: The biology and therapeutic potential of NMN and NR. *Cell Metab*. 2018; 27(3): 513-528. doi: 10.1016/j.cmet.2017.11.002

NMN elevated NAD$^+$ levels ~3-folds and ameliorates age-related diseases in mice



Reference:

Yoshino J, Mills KF, Yoon MJ, Imai S. Nicotinamide Mononucleotide, a Key NAD+ Intermediate, Treats the Pathophysiology of Diet- and Age-Induced Diabetes in Mice. *Cell Metab.* 2011; 14(4): 528-536. DOI: 10.1016/j.cmet.2011.08.014

However, not all NMN are equally created when it comes to boosting human NAD^+

Summary for Human Clinical Trials on NMN Published Before 2024

The table below summarizes all NMN human clinical trials published before 2024. Among the 18 trials, 13 measured NAD^+ levels. Of these, 8 trials (green) reported a statistically significant increase in NAD^+ levels, while 5 trials (red) either were unable to detect NAD^+ or failed to show meaningfully significant increase in human NAD^+ levels.

These results clearly demonstrate that orally administered NMN can be effectively absorbed through the human intestine and significantly increase NAD^+ levels. However, differences in manufacturing processes may affect its effectiveness.

All of these human clinical trials demonstrate that NMN is safe and well tolerated at doses of up to 2 g per day.

Table. Human Clinical Trials on NMN Published Before 2024

Trial Description	Sponsor's Country	Publication	Dosages & Administration	Trial Duration	Trial Results	Safety & Tolerability
Open label, 10 healthy Jpn men of 40-60 yrs old.	Japan	*Endocr J.* 2020 Feb 28;67(2):153-160.	100, 250, & 500mg NMN, oral daily	Single dose	• Blood NAD level not reported. No plasma NMN was detected. • Plasma concentrations of 2-Py and 4-Py (NMN or NAD metabolites) were significantly and dose-dependently increased. • Sleep quality score and ophthalmic assessment showed no improved.	Safe & well tolerated.
RCT, 25 prediabetic and obese women of post menopause	USA	*Science.* 2021 Jun 11;372(6547) :1224-1229.	250mg NMN, oral daily	10 weeks	• NAD in peripheral blood mononuclear cell (PBMC) increased significantly. • Plasma and muscle 2-Py & 4-Py (NMN and NAD metabolites) increased, but NAD in muscle undetectable. • Muscle physical strength not improved. Muscle insulin sensitivity and signaling increased, but muscle physical function didn't improve.	Safe & well tolerated.
RCT, 48 armature Chinese athletes of 27-50 years old	China	*J Int Soc Sports Nutr.* 2021 Jul 8;18(1):54.	300, 600, 1200mg NMN, oral daily	6 weeks	• Combination of NMN and exercise improves aerobic capacity and muscle oxygen utilization compared to exercise alone in 600 & 1200mg groups. • But physical strength assessment showed no difference except single-leg stance for 600mg dose.	Safe & well tolerated.
Open label, 10 healthy Chinese men of 45-60 yrs old.	China	*Front Nutr.* 2021 Nov 29;8:756243	300mg NMN, oral daily	90 days	• Telomere length was significantly increased.	No adverse event observed
RCT, 108 healthy Jpn adults of >65 yrs old	Japan	*Nutrients.* 2022 Feb 11;14(4):755.	250mg NMN, oral daily	12 weeks	• Sleep quality, fatigue and physical performance were measured for NMN treatment (morning or afternoon) and placebo. • Only the afternoon NMN treated group was found improvement in lower limb function and drowsiness in older Jpn adults.	Safe & well tolerated.
RCT, 30 Healthy Jpn adults of 20-65 yrs old	Japan	*Front Nutr.* 2022 Apr 11;9:868640.	250mg NMN, oral daily	12 weeks	• Blood NAD significantly increased. • Blood levels of both NMN and NAD metabolites increased, but NMN was not detected.	Safe & well tolerated.
RCT, 42 healthy Jpn men of >65 years old	Japan	*NPJ Aging.* 2022 May 1;8(1):5.	250mg NMN, oral daily	12 weeks	• Blood NAD significantly increased. • Blood levels of both NMN and NAD metabolites increased. • Blood NMN and NR was increased significantly. • Some physical function assessments showed significant improvement.	Safe & well tolerated.
RCT, 66 healthy Indian adults of 40-65 yrs old	China	*Front Aging.* 2022 May 5;3:851698.	300mg NMN, oral daily	60 days	• Blood NAD level increased slightly but the increase is not statistically significant. • No significant improvement in physical function (6-minute endurance test) and overall health assessment (SF-35 Questionnaire survey). • No significant change in insulin residence test (HOMA-IR).	Safe & well tolerated.
Open label, 16 healthy postmenopausal women of 50-80 yrs old	Japan	*Glycative Stress Research* 2022 June 30; 9 (2): 33-41	300mg NMN, oral daily	8 weeks	• Blood NAD level was significantly decreased over baseline. • Blood NMN no change. • Some blood biomarkers significantly changed over baseline, such as HbA1c decrease, HDL-C increased, Adiponectin increased, DHEA-s increased, etc. • Skin conditions were significantly improved.	Safe & well tolerated.
RCT, 31 Healthy Jpn adults of 20-65 yrs old	Japan	*Sci Rep.* 2022 Aug 24;12(1): 14442.	1250mg NMN, oral daily	4 weeks	• Safety and tolerability assessment were assessed. • Ames test showed no increase in revertant mutant colonies. • All results in hematological, clinical biochemicals, urinary tests are within normal ranges. • Body composition and vital signs all normal. • No NMN treatment related adverse events.	Safe & well tolerated.

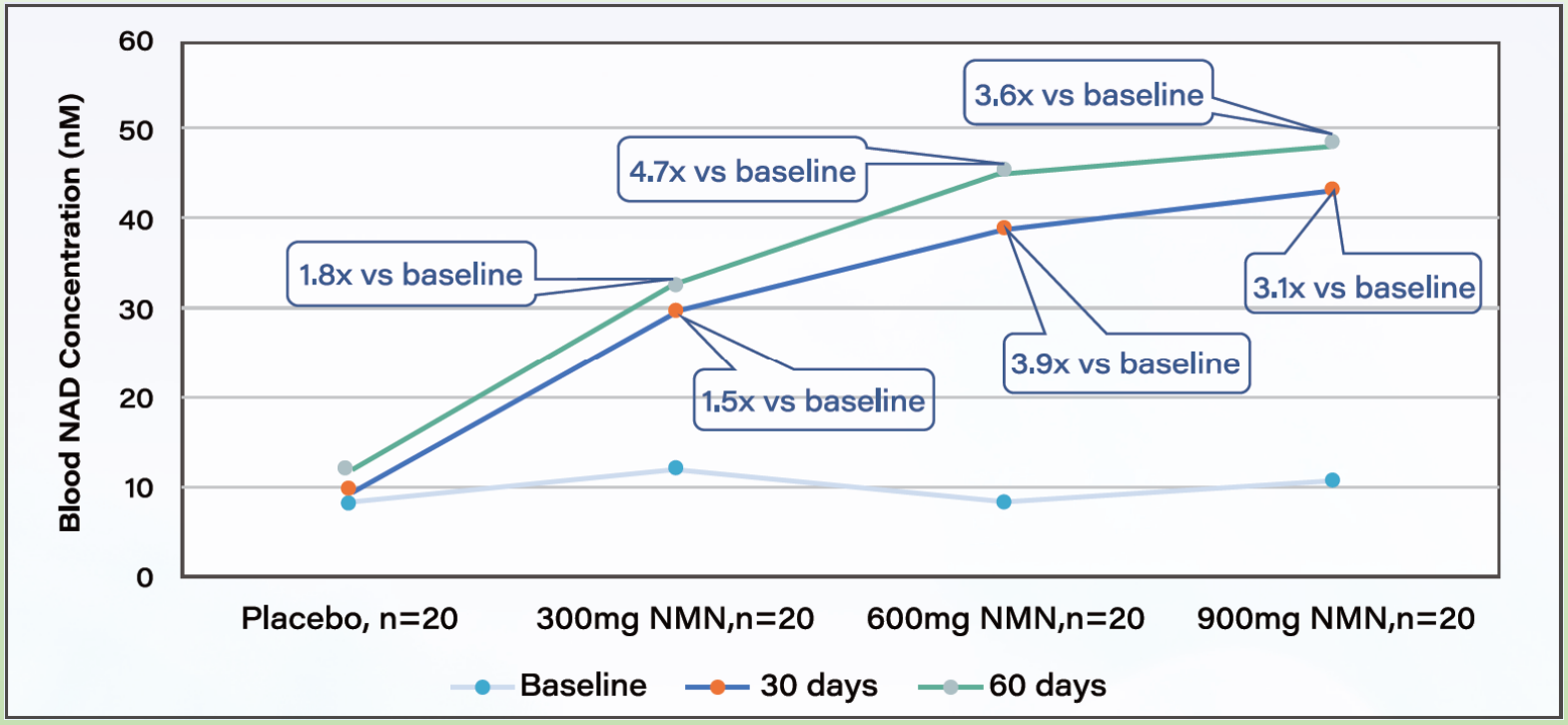
Trial Description	Sponsor's Country	Publication	Dosages & Administration	Trial Duration	Trial Results	Safety & Tolerability
Open label, 10 healthy Jpn adults of 20-70 years old	Japan	*Cureus*. 2022 Sep 5;14(9): e28812.	300mg NMN, single intravenous injection	Single dose	• Blood NAD significantly increased after the single injection. • No abnormal in vital signs and clinical lab parameters, except that TG was favorably decreased significantly. • No abnormal in blood biomarker test results for liver, pancreas, heart, and kidney. • No significant difference on immune biomarker levels in clinical blood tests.	Safe & well tolerated.
RCT, 32 obese adults of 55-80 yrs old	USA	*J Gerontol A Biol Sci Med Sci.* 2023 Jan 26;78(1):90-96.	1,000 & 2,000mg micro-crystalline NMN, oral daily	14 days	• Blood NAD^+ levels increased significantly and in a dose-dependent manner for the 1,000 mg and 2,000 mg daily doses, whereas doses below 1,000 mg did not consistently raise NAD+ levels. • Blood NMN levels also increased significantly and dose-dependently when comparing post-treatment to pre-treatment values. • Blood levels of NAD metabolites increased.	Safe & well tolerated.
RCT, 80 healthy Indian male & female of 40-85 yrs old	**USA**	*Geroscience*. 2023 Feb;45(1): 29-43.	300, 600, 900mg NMN, oral daily	60 days	• Blood NAD^+ levels in NMN-treated participants increased 1.5–4.7-fold compared to baseline at days 30 and 60, with the 600 mg daily dose showing the highest increase at day 60. • Physical performance, measured by the 6-minute walking test, improved significantly in a dose-dependent manner compared to placebo across all three NMN doses • Biological age was significantly younger than placebo at day 60 for all dosages. • Overall health, assessed via SF-36 scores, also improved significantly and dose-dependently for all three doses. The 600 mg daily oral dose was identified as the optimal dosage.	Safe & well tolerated.
RCT, 63 healthy male & female of 45-75 yrs old with existing low quality of sleep	China	*Am J Transl Med* 2022 Dec. 6(4):167-176	360mg NMN, oral daily	12 weeks	• The effect of NMN on sleep (insomnia) was assessed by Pittsburgh Sleep Quality Index (PSQI) and mobile smart bands sleet data. Total PSQI scores, sleep quality, sleep latency & daytime dysfunction were measure. • NMN supplementation significantly improves sleep quality.	Safety & tolerability not reported.
RTC, 36 healthy male & female of 40-59 yrs old	Japan	*Sci Rep.* 2023 Feb 16;13(1): 2786.	250mg NMN, oral daily	12 weeks	• Serum NAD, NMN, NAM concentrations and cardiovascular effect were assessed in this trial. • NAD and NMN concentrations were unable to be quantified. • Vascular health benefit was observed but not significant.	Safe & well tolerated.
RCT, 30 overweight & obese male & female of ≥45 yrs old	USA	*J Clin Endocrinol Metab*. 2023 Jul 14;108(8): 1968-1980.	2,000mg NMN, oral daily	28 days	• Blood NAD concentration, its metabolites & physiologic conditions were studied. • Blood NAD concentration increased >2-fold over baseline at both day 14 & 28. • Significantly cut weight at day 28 on these overweight and obese adults. • Significantly reduced diastolic blood pressure, total cholesterol, LDL, & non-HDL. • Muscle strength, muscle fatigue & aerobic capacity not significantly improved	Safe & well tolerated.
Open label, 11 healthy male & female of 20 – 65 yrs old	Japan	*Clin Nutr ESPEN.* 2023 Aug;56:83-86.	250mg NMN, oral daily	12 weeks	• Plasma NAD and NMN concentration significantly increased at the end of month 1, 2 & 3. • Postprandial blood insulin concentration increased significantly at the end of month 2 & 3.	Safe & well tolerated.
Open label, 21 mild essential hypertension male & female of 18-80 yrs old	China	*Signal Transduction and Targeted Therapy* 2023 Sep 8:353	800mg NMN, oral daily	6 weeks	• Hypertension adults have 44% lower blood NAD levels than healthy people. • NMN supplementation increased blood NAD levels of mild hypertension adults 43% higher than placebo. • NMN supplementation significantly reduced blood pressure at the end of 6-week trial and ameliorate vascular dysfunction of hypertension adults.	Safe & well tolerated.

Human Clinical Trials of AbinoNutra®NMN

Abinopharm, Inc., in collaboration with Professor Andrea Maier and the third-party clinical research organization ProRelix Research, conducted one of the largest and most successful human clinical trials on NMN (AbinoNutra®NMN) to date.

Another four human clinical trials on NMN (AbinoNutra®NMN) are currently underway in Taiwan, Japan, and Singapore.

NAD+ Increased Up to 4.7-Fold in 1st Human Clinical Trial of AbinoNutra®NMN



Reference:

Yi L, Maier AB, Tao R, Lin Z, Vaidya A, Pendse S, Thasma S, Andhalkar N, Avhad G, Kumbhar V. The efficacy and safety of β-nicotinamide mononucleotide (NMN) supplementation in healthy middle-aged adults: a randomized, multicenter, double-blind, placebo-controlled, parallel-group, dose-dependent clinical trial. *Geroscience*. **2023 Feb**;45(1):29-43.

Summary of the 1st Human Clinical Trial Results of AbinoNutra®NMN

Blood NAD Levels

Oral daily doses of 300, 600, 900mg:

- **Increased 1.5, 3.9 or 3.1 folds at day 30.**
- **Increased 1.8, 4.7 or 3.6 folds at day 60.**

Physical Strength

Oral daily doses of 300, 600, 900mg:

Physical strength improved significantly for all three dosages at both day 30 & 60 as assessed by 6-minute walking distance.

AbinoNutra®NMN Human Clinical Trial

Overall Health Assessment

Oral daily doses of 300, 600, 900mg:

Overall health improved significantly for all three dosages at day 60 as assessed by SF-36 questionnaire.

Biological Age

Oral daily doses of 300, 600, 900mg:

Biological ages were 4.1, 6.7 & 4.6 years younger respectively than the untreated at day 60.

Reference:

Yi L, Maier AB, Tao R, et al. The efficacy and safety of β-nicotinamide mononucleotide (NMN) supplementation in healthy middle-aged adults: a randomized, multicenter, double-blind, placebo-controlled, parallel-group, dose-dependent clinical trial. *Geroscience*. **2023**;45(1):29-43.

Media Coverages and Award Recognition for the First Human Clinical Trial Results of AbinoNutra®NMN

The renowned website dedicated to NMN and longevity news provided in-depth coverage of our human clinical trial on **AbinoNutra® NMN:** ***Link***

Lifespan.io featured both video and article coverage of our human clinical trial on **AbinoNutra® NMN:** *Link*

NutraIngredients.com covered our human clinical trial on **AbinoNutra® NMN**: *Link*

Longevity.Technology reported in detail our human clinical trial on **AbinoNutra® NMN:** *Link*

Our research paper on the human clinical trial of **AbinoNutra® NMN** was awarded 3rd Prize from American Aging Association (AGE)**:** *Link*

AbinoNutra®NMN Bulky Powder

Crystalline Granules

Crystalline Powder

- Unique Crystal Structure and Uniform Crystalline Particle Size For Maximum Human Absorption.
- Crystalline Granules and Powder: Formulation Choices for Capsules, Powder, Tablets and More.

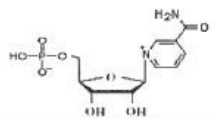
Quality of AbinoNutra® NMN Bulk Powder

Abinopharm, Inc.

CERTIFICATE OF ANALYSIS

Date of issue: 2023.08.08

Product Name: β-Nicotinamide Mononucleotide **Structure:** **Marking:200kg**



Molecular Formula: $C_{11}H_{15}N_2O_8P$
Molecular Weight: 334.22
CAS No: 1094-61-7
Batch No: 5206-2307040
Date of Manufacturing: June 24, 2023
Date of Retest: June 23, 2025

Test Item		Acceptance criteria	Result	Method
Appearance		White to almost white powder.	White powder	Visual method
Identification		IR: The IR spectrum of the sample conforms that of reference standard.	Complied	USP<197K>
		HPLC: The retention time of the main peak of the sample solution corresponds to that of Standard solution, as obtained in *purity* method.	Complied	In-house HPLC
Purity (g/100g)		≥99.0	99.8	In-house HPLC
Moisture (g/100g)		≤5.0	0.5	USP<921>
Sodium content (ICP-MS)(g/100g)		≤1	ND	ISO17294-2-2016
pH（100mg/ml solution in water）		2.0~4.0	3.2	USP<791>
Heavy metals	Pb (ICP-MS）(mg/kg)	≤0.5	ND	AOAC 2013.06
	As (ICP-MS）(mg/kg)	≤0.5	ND	
	Hg (ICP-MS）(mg/kg)	≤0.5	ND	
	Cd (ICP-MS）(mg/kg)	≤0.5	ND	
Residual protein (Bradford)(mg/kg)		≤100	15	USP<1057>
Nicotinamide (g/100g)		≤0.5	ND	In-house HPLC
Residual ethanol(mg/kg)		≤1000	195	USP <467>
Microbial	Total viable aerobic microbial counts, cfu/1g	≤750	conform	USP<2021>
	Yeasts and molds counts, cfu/1g	≤100	conform	USP<2021>
	Escherichia coli/10g	Not detected	ND*	USP<2022>
	Salmonella/10g	Not detected	ND*	USP<2022>
	Staphylococus aureus/10g	Not detected	ND*	USP<2022>
Particle size（μm）	D_{10}	Report	2 μm	ChP<0982>
	D_{50}	Report	65 μm	ChP<0982>
	D_{90}	Report	306 μm	ChP<0982>
Bulk density		Report	0.48g/ml	ChP<0993>
Conclusion		Conform to In-house Specification		

Note：*The results is for information only.
Certification prepared by: Grace Liu Title:QA Manager

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USA

Quality Test Report For Our AbinoNutra® NMN Ingredient

Purity = 99.8%

Unique crystals and uniform crystalline particle size help maximum human absorption

AbinoNutra® NMN Ingredient:

Premium Quality, Trusted by the Market

Abinopharm, Inc.

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