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Report

Real-world User-reported Benefits of a Multi-ingredient NMN-based Supplement Targeting Age-related Decline: A Brief Report

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Abstract

The age-related decline in nicotinamide adenine dinucleotide (NAD^+) contributes to mitochondrial dysfunction and oxidative stress, which may be mitigated by supplementation with NAD^+ precursors such as nicotinamide mononucleotide (NMN). This retrospective observational study evaluated user-reported outcomes of a multi-ingredient supplement (NMN, hydroxytyrosol, ergothioneine, resveratrol, and vitamin D_3) using 196 self-reported experiences collected from the Wonderfeel Biosciences online platform (April 2022–September 2024). Among 196 analyzed users, 131 (66.8%) reported positive effects, primarily in the nervous (81%), integumentary (11%), muscular (4%), skeletal (2%), digestive (2%), and endocrine (1%) systems, while 31.6% noted neutral effects and 1.5% reported non-causal adverse events. These findings align with known mechanisms of NAD^+ restoration and oxidative stress mitigation, suggesting complementary biological pathways. Although this real-world evidence highlights perceived improvements in energy, cognition, sleep, and skin health, the study's limitations—including self-reported data, lack of demographic controls, and absence of biomarkers—necessitate confirmation through the prospective controlled clinical trial scheduled to commence in late 2025.

Keywords

Nicotinamide Mononucleotide, Hydroxytyrosol, Ergothioneine, Resveratrol, Vitamin D_3, Real-world Setting, Self-reported

1. Introduction

The coenzyme nicotinamide adenine dinucleotide (NAD^+) plays a fundamental role in cellular metabolism, particularly in energy production through oxidative phosphorylation [1]. Beyond its metabolic functions, NAD^+ regulates enzymatic pathways involved in DNA repair, signal transduction, and cellular senescence [2]. During aging, NAD^+ levels decline due to a combination of increased consumption and diminished biosynthesis [3]. Age-related activation of NAD^+-consuming enzymes such as cluster of differentiation 38 (CD38) and poly (ADP-ribose) polymerases (PARPs) contributes significantly to this depletion [4-6]. CD38 activity rises with age, accelerating NAD^+ hydrolysis, while PARPs are activated by accumulated DNA damage, further depleting cellular NAD^+ reserves. Mitochondrial dysfunction and oxidative stress also impair NAD^+ homeostasis, exacerbating its decline and disrupting cellular function [7].

To restore NAD^+ levels, two primary strategies have been explored: the inhibition of NAD^+-consuming enzymes, such

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as CD38 or PARPs [8], and the supplementation of NAD^+ precursors, including nicotinamide mononucleotide (NMN) or nicotinamide riboside (NR), which enter the salvage pathway to replenish intracellular NAD^+ [9]. However, these approaches have limitations. Enzyme inhibition may lose efficacy as enzymatic activity increases with age, and precursor supplementation may be insufficient in the context of mitochondrial stress or impaired biosynthesis pathways. These limitations highlight the potential value of synergistic interventions that combine NAD^+ precursors with antioxidants and mitochondrial-supportive agents to both reduce NAD^+ consumption and enhance its regeneration.

Our research team at Wonderfeel Biosciences (California, USA) developed a multi-ingredient formulation containing NMN at a daily dose of 900 mg, which has been shown to elevate NAD^+ levels without adverse effects compared to lower doses such as 300 mg [10]. This formulation includes resveratrol (100 mg daily), which functions as a sirtuin activator and antioxidant, and has demonstrated anti-apoptotic and mitochondria-enhancing properties in preclinical studies [11]. When combined with NMN, resveratrol has been shown to improve tissue-specific NAD^+ levels [11]. Hydroxytyrosol (20 mg daily), derived from olive extract, contributes cardiovascular and anti-inflammatory effects, particularly in reducing lipid peroxidation [12]. Ergothioneine (4 mg daily) provides neuroprotection, and vitamin D_3 (20 mcg daily) supports immune function, oxidative stress reduction, and may enhance NMN uptake [13, 14].

Although each of these compounds has been independently studied, their combined effects have not been evaluated in controlled clinical trials. Preclinical models support potential synergy, with NMN and resveratrol co-administration increasing NAD^+ levels in cardiac and muscle tissue [11], while hydroxytyrosol and ergothioneine reduce oxidative stress through complementary mechanisms [12, 13, 15]. Vitamin D_3 may further support NMN activity by enhancing cellular uptake under oxidative stress [14]. No antagonistic interactions among these ingredients have been reported, and the formulation was designed to minimize mechanistic overlap [16]. Nonetheless, the absence of head-to-head clinical comparisons remains a limitation.

This preliminary report aims to retrospectively analyze for the first time the self-reported experiences with a multi-ingredient supplement that included NMN, hydroxytyrosol, ergothioneine, resveratrol and vitamin D_3, after its introduction to the market.

2. Materials and Methods

This observational, retrospective analysis was based on unsolicited, voluntary user feedback posted on the official Wonderfeel Biosciences website between April 2022 and September 2024 and available at https://getwonderfeel.com/product/wonderfeel-youngr-nmn/#product-reviews

All user feedback related to the NMN-multi-ingredient supplement was publicly available, de-identified, and anonymized at the time of data extraction, eliminating the need for informed consent or ethics committee review. No direct solicitation or compensation was provided for these user submissions, and no identifiable demographic information (such as age or sex) was available.

The effects were further grouped by affected physiological systems using a pre-established framework based on clinical taxonomy to ensure consistency and reduce classification bias. A descriptive statistical approach was applied. Frequencies and proportions were calculated for each sentiment category (positive, neutral, negative), as well as for the distribution of effects across body systems. Data were presented as absolute counts and percentages and were organized and tabulated via Microsoft Office 2024 Excel version 16.91.

To reduce classification bias, two independent physician reviewers (L. F. C. and A. S.) assessed the categorization of effects. Discrepancies were resolved through discussion until consensus was achieved.

No inferential statistics (e.g., p-values, confidence intervals) were applied, as the dataset was not derived from a controlled, randomized population and lacked adequate demographic granularity. Given the self-selected nature of the sample and the absence of a control group, the findings are hypothesis-generating only and should not be interpreted as demonstrating causality or clinical efficacy.

3. Results

The anonymous voluntary comments came from 196 users, who were classified as positive (n: 131, 66.8%), neutral (n: 62, 31.6%), and negative (n: 3, 1.5%).

Table 1. *Positive reports into six body systems.*

Systems			Results		
	n	%		n	%
Nervous	106	81			
			Increased Overall Energy Levels	59	45

Systems			Results		
	n	%		n	%
			Improve Sleep	21	16
			Elevated Clarity	11	8
			Sharper Focus	8	6
			Uplifted Mood	3	2
			Improved Memory	2	2
			Reduced Pain	1	1
			Faster Hangover Recovery	1	1
Integumentary	14	11			
			Healthier Skin	11	8
			Thicker Hair	2	2
			Better-looking Nails	1	1
Muscular	5	4			
			Improved Physical Performance	5	4
Skeletal	3	2			
			Reduced Pain in Joints	2	2
			Improved Bones	1	1
Digestive	2	2			
			Improved Digestion	1	1
			Reduced Inflammation	1	1
Endocrine	1	1			
			Efficient Weight Management	1	1
Total Responses	131	100		131	100

The positive reports were classified into six body systems, namely, nervous, intergumentary, muscular, skeletal, digestive, and endocrine systems, as shown in Table 1.

The analysis of the effects with the highest percentage was as follows:

3.1. Nervous System (n=106, 81%)

1) Increased overall energy levels (45%) are correlated with the role of NMN in mitochondrial ATP synthesis via NAD^+-dependent pathways [8].
2) Improved Sleep (16%): May reflect systemic reductions in oxidative stress and mitochondrial support mediated by the combined effects of NMN and antioxidant ingredients [12].
3) 3 Elevated Clarity (8%) & Sharper Focus (6%): Aligns with resveratrol's activation of Sirtuin 1, enhancing cerebral blood flow [10].

3.2. Integumentary System (n=14, 11%)

Healthier skin (8%): Hydroxytyrosol inhibits collagen-degrading matrix metalloproteinases [12], whereas ergothioneine protects against UV-induced damage [14].

3.3. Muscular System (n=5, 4%)

Improve physical performance (4%): NMN enhances fatty acid oxidation and glucose metabolism in muscle [8].

3.4. Skeletal System (n=3, 2%)

Reduced pain in joints (2%) and improved bones (1%): Vitamin D_3 supports calcium homeostasis, and hydroxytyrosol reduces inflammation [15].

3.5. Digestive System (n=2, 2%)

Improving digestion (1%): Resveratrol modulates the diversity of the gut microbiota [10].

3.6. Endocrine (n:1, 1%)

Efficient weight management (1%): NMN activates adipose tissue thermogenesis via Sirtuin 3 [9].

Extra space

The 62 neutral effects were divided into 32 users (52%) who reported effects unrelated to their health status (e.g., delivery times of the supplement, cost) and 30 users (48%) who reported no changes. Negative effects were associated with three adverse events (n=3; 1.5%), including increased blood pressure, gastrointestinal disturbances, and insomnia. The evaluation of these adverse events did not reveal causality based on temporal patterns and limited mechanistic plausibility [17].

4. Discussion

Our observational analysis of 196 users underscores the positive perceived benefits associated with a multi-ingredient supplement that combines NMN, resveratrol, hydroxytyrosol, ergothioneine, and vitamin D_3. These benefits, reported by approximately two-thirds of users, appear to arise from synergistic biological pathways involving NAD^+ optimization [11], oxidative stress mitigation [15], and immunometabolic regulation [18].

The combined actions of NMN and resveratrol are known to enhance intracellular NAD^+ levels and activate sirtuins, leading to improved mitochondrial efficiency and DNA repair mechanisms. Hydroxytyrosol and ergothioneine contribute to reducing lipid peroxidation and mitochondrial reactive oxygen species, thus complementing the NAD^+ recycling pathways influenced by NMN. Additionally, vitamin D_3 supports immune modulation and calcium homeostasis, and may potentiate antioxidant defenses in cellular environments affected by oxidative stress. These overlapping and complementary mechanisms likely explain the diversity of physiological improvements reported by users.

The findings align with a growing body of evidence suggesting that multi-ingredient supplements can help address nutritional deficits common in modern diets, particularly among older adults. Such formulations may offer a more comprehensive strategy to counteract age-associated NAD^+ decline, oxidative imbalance, and related physiological impairments, especially in individuals with limited access to nutrient-dense foods or those experiencing early signs of metabolic dysregulation.

However, this real-world evidence must be interpreted within the context of several important limitations. The data were derived from subjective user feedback, which is inherently prone to recall bias, self-selection, and placebo effects. The absence of demographic data, such as age, sex, or baseline health status, limits the ability to stratify responses or detect differential effects across subgroups. Furthermore, the lack of accompanying biomarker data prevents direct correlation between reported outcomes and objective measures of NAD^+ status, oxidative stress, or systemic inflammation.

Despite these limitations, the spontaneous and consistent nature of the user responses provides valuable insights into the real-world application of this supplement. A prospective, randomized controlled clinical trial is scheduled to begin in the second half of 2025, and will be essential for confirming efficacy, establishing causality, and exploring mechanistic interactions among the supplement's active ingredients. Continued investigation into the physiological impact of NMN and its synergistic partners will help refine our understanding of how multi-ingredient interventions may contribute to healthspan and healthy aging.

5. Conclusion

This retrospective observational analysis highlights consistent, user-reported improvements across several physiological systems following the use of a multi-ingredient supplement containing NMN, resveratrol, hydroxytyrosol, ergothioneine, and vitamin D_3. These findings align with mechanistic insights from preclinical studies and suggest potential synergies in supporting mitochondrial function, reducing oxidative stress, and optimizing NAD^+ metabolism. However, due to the self-selected and subjective nature of the data, absence of standardized outcomes, and lack of demographic stratification, the results should be interpreted cautiously. Future randomized, controlled clinical trials are essential to establish causality, validate efficacy, and explore the mechanistic interactions of these combined ingredients.

Abbreviations

NAD^+	Nicotinamide Adenine Dinucleotide
NMN	Nicotinamide Mononucleotide
DNA	Deoxyribonucleic Acid
CD38	Cluster of Differentiation 38
mg	Milligrams
mcg	Micrograms
PARPs	Poly (ADP-ribose) Polymerases
NR	Nicotinamide Riboside
ATP	Adenosine Triphosphate
CFR	Code of Federal Regulations

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Author Contributions

Luis Fernando Cifuentes: Conceptualization, data curation, research, methodology, and writing the original draft.

Andrew Salzman: Supervision, validation, and writing review and editing.

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Ethics Statement

This study analyzed anonymous user comments voluntarily submitted to the Wonderfeel Biosciences public platform. No personal identifiers were collected, nor were any interventions performed. Under 45 CFR 46.104, this research is classified as “non-human subjects research". Because no personal identifiers were collected and participation was entirely voluntary, formal ethics approval and individual consent were not required under clinical research guidelines. Data was aggregated and analyzed according to the principles of data minimization and privacy.

Data Availability Statement

The anonymized dataset supporting this study’s is available at https://getwonderfeel.com/product/wonderfeel-youngr-nmn/#product-reviews

Conflicts of Interest

The authors, Luis Fernando Cifuentes and Andrew Salzman, are employees in the research and development department at Wonderfeel Biosciences, the company that produces the multi-ingredient (NMN, hydroxytyrosol, ergothioneine, resveratrol, and vitamin D_3) supplement. While both authors are involved in the development and research related to the product, the study was conducted independently, and the founders had no role in the study design, data collection, analysis, interpretation, manuscript writing, or the decision to publish these findings. The authors have made every effort to ensure objectivity and transparency in reporting the results.

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