Case Study: Oral Supplementation with the NAD+ Precursor Nicotinamide Mononucleotide (NMN)—Effects on Intracellular NAD+ and Triglycerides.

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ABSTRACT

NAD+ is a coenzyme that is essential in numerous metabolic reactions, the most important involving energy production. In the cellular respiration process, NAD+ is required for the production of ATP (adenosine triphosphate), the primary energy currency of cells. NAD+ transfers electrons from molecules including glucose during glycolysis and the citric acid cycle. These electrons are then transferred to the electron transfer chain, where NAD+ acts as an essential mediator in energy production, ensuring the efficient functioning of cells. NAD+ is also critically involved in DNA repair and healthy aging sirtuin enzymes.
Nicotinamide Mononucleotide (NMN) is the most direct biochemical precursor to NAD+ and thus supplementation of this molecule is an efficient method of increasing intracellular NAD+, which can improve cellular energetics and markers of aging. NMN may also lower triglycerides. In a study of intravenous dosing of 300 mg NMN in 10 healthy individuals, researchers discovered a significant reduction in serum triglycerides.
One concern with NMN is that when taken in an oral dose this molecule might be damaged or otherwise metabolized by stomach acid, pancreatic enzymes, or first pass hepatic enzymes. In other studies, we have shown that a liposomal powder preparation can protect other molecules, such as glutathione, from this type of degradation and significantly increase blood levels of the whole molecule.
We performed a small case study in which individuals were given 1000 mg of an oral liposomal NMN preparation (powder in a capsule) once after a baseline blood test. Serial triglyceride tests were performed hourly for five hours. Participants had an average of 15-percent decrease in triglycerides at hour five, compared to baseline. Another group was tested at baseline for intracellular NAD+ (Jinfinity Labs), then was given 1000 mg of a liposomal powder NMN daily for 15 days. An intracellular NAD+ test was then performed after 15 days. NAD+ levels increased 100 percent over this period.
This is the first case series that has demonstrated a rapid triglyceride-lowering effect of oral liposomal NMN (over 5 hours), along with a 100-percent increase in intracellular NAD+ over a 15-day period.

INTRODUCTION

NAD+ is a coenzyme that participates in numerous metabolic reactions, particularly those involved in energy production. It exists in two forms: NAD+ and NADH, which can interconvert in redox reactions. NAD+ is essential for cellular respiration and the generation of ATP (adenosine triphosphate), the primary energy currency of cells. In the process of cellular respiration, NAD+ accepts electrons from macromolecules like glucose during glycolysis and the citric acid cycle. These electrons are then transferred to the electron transport chain, where NADH is converted back to NAD+ while generating ATP. Thus, NAD+ acts as a critical mediator in energy production, ensuring the efficient functioning of cells.

In addition to its influence on energy production, NAD+ plays a significant role in DNA repair mechanisms. Enzymes involved in DNA repair, such as PARPs (poly ADP-ribose polymerases) use NAD+ as a substrate. NAD+ depletion has been linked to impaired DNA repair efficiency, leading to an

accumulation of DNA damage. This accumulation may contribute to aging and the development of various diseases.

NAD+ is also an essential cofactor in healthy aging mechanisms via its effects on sirtuin production. Sirtuins are a family of enzymes that regulate various cellular processes, including gene expression, DNA repair, and metabolism. NAD+ has been shown to activate sirtuins, which has demonstrated promising effects in animal and human studies.

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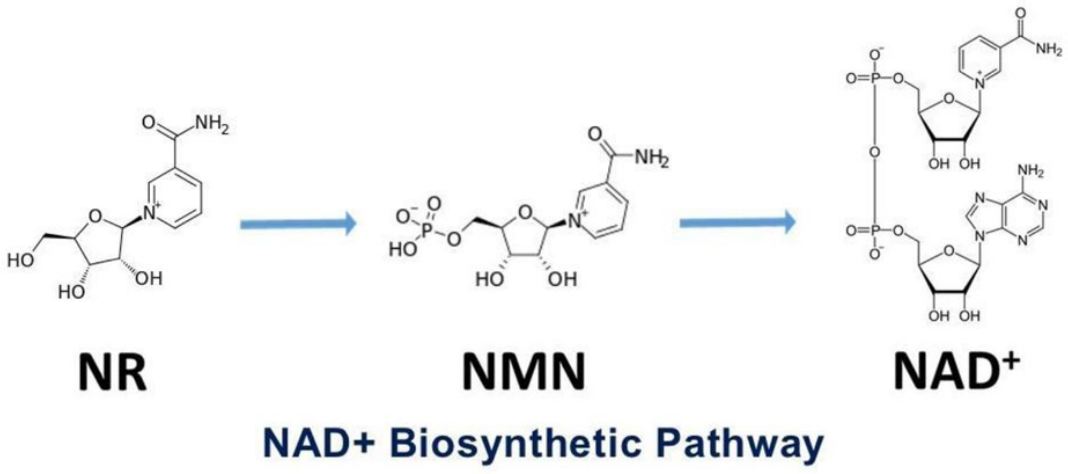
NMN is the immediate biochemical precursor to NAD+ in the body, and NMN supplementation has been demonstrated to increase NAD+ levels in animal and human studies. In a study published in 2019 in *Redox Biology*, a group of researchers demonstrated in aged mice at least a doubling of NAD+ levels after NMN supplementation. In an unpublished human study, 20 participants who took an NMN (plus cofactors) supplement had a significant increase in NAD+ and Sirtuin enzyme levels after 30 days, compared to baseline. Other human studies have shown significant increases in NAD+ following NMN supplementation. A study of trained runners who took a low dose (300 mg), medium dose (600 mg), or high dose (1200 mg) NMN supplement demonstrated significantly increased oxygen utilization compared to baseline levels.



Materials and Methods: This study is a case series of a liposomal Nicotinamide Mononucleotide (NMN) supplement and its effects on NAD+ levels and triglycerides. After a baseline blood triglyceride test, four individuals were given one gram (1,000 mg) of an oral liposomal capsule preparation, then serially tested hourly for five hours.

Another group of five individuals was tested at baseline for intracellular NAD+ (Jinfinity Labs), then was given one gram (1,000 mg) of a liposomal capsule preparation daily for 15 days. A second intracellular NAD+ test was done after 15 days.

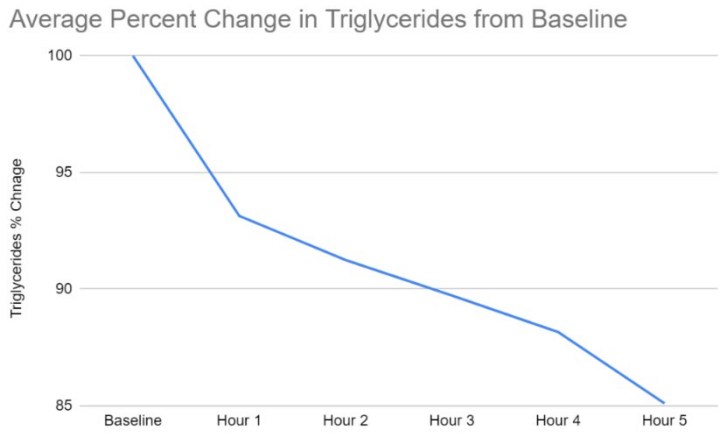
Inclusion Criteria: Healthy human individuals aged 18-65 years of age not currently taking an NMN, Nicotinamide Riboside (NR), or NAD+ supplement.

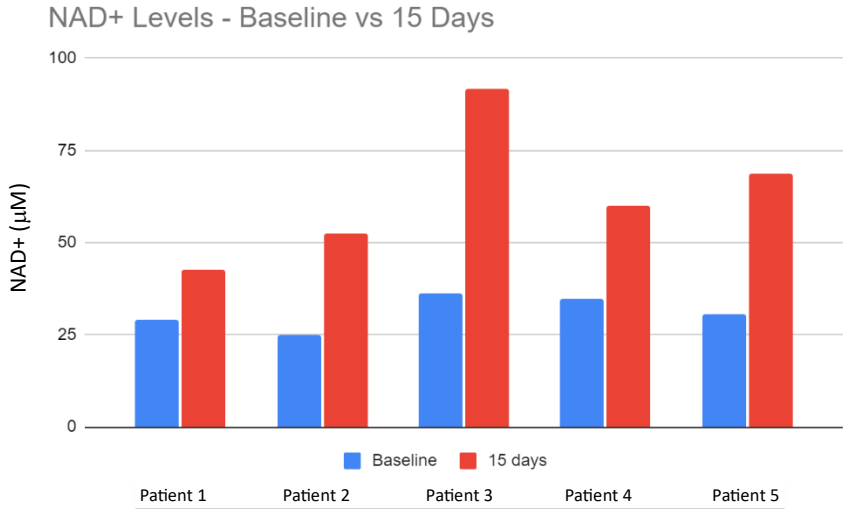
Exclusion Criteria: Pregnant or nursing, undergoing cancer treatment, or diagnosed with a mitochondrial disease.

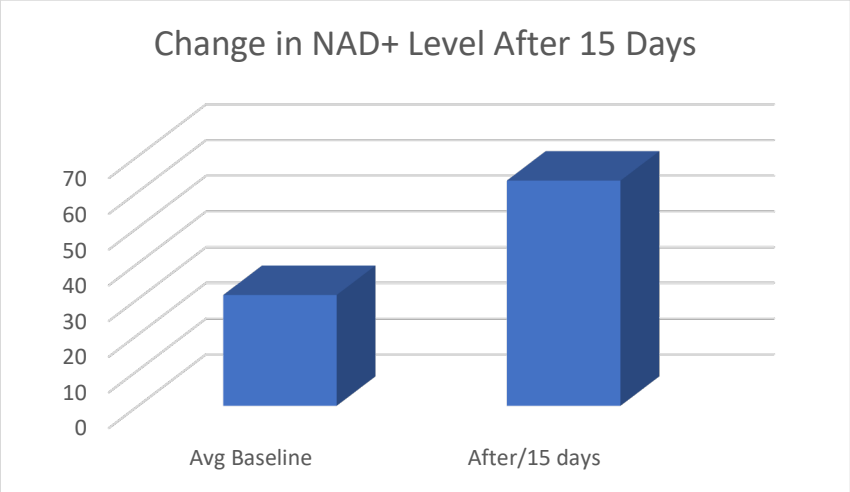
Primary and Secondary Endpoints: The primary endpoint is a change in the intracellular NAD+, which is an essential molecule involved in cellular energy production. The secondary endpoint is any change in blood triglycerides.

CONCLUSIONS

Participants in the first group (n=4) had an average of 15-percent decrease in triglycerides at hour five, compared to baseline. In the second group (n=5) NAD+ levels increased from an average of 31.04 μM to 63.08 μM, an increase of more than 100 percent over the 15-day supplementation period, compared to baseline. This is the first case series that has demonstrated a rapid triglyceride-lowering effect of oral liposomal NMN (over 5 hours), along with a 2X increase in intracellular NAD+ over a 15-day period.







REFERENCES

Tarantini S, Valcarcel-Ares MN, Toth P, et al. Nicotinamide mononucleotide (NMN) supplementation rescues cerebromicrovascular endothelial function and neurovascular coupling responses and improves cognitive function in aged mice. *Redox Biol*. 2019;24:101192. doi: 10.1016/j.redox.2019.101192.

Kimura S, Ichikawa M, Sugawara S, et al. Nicotinamide mononucleotide is safely metabolized and significantly reduces blood triglyceride levels in healthy individuals. *Cureus*. 2022;14(9): e28812. doi:10.7759/cureus.28812.

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 Feb;45(1):29-43. doi: 10.1007/s11357-022-00705-1.

Liao B, Zhao Y, Wang D, et al. Nicotinamide mononucleotide supplementation enhances aerobic capacity in amateur runners: a randomized, double-blind study. *J Int Soc Sports Nutr*. 2021 Jul 8;18(1):54. doi: 10.1186/s12970-021-00442-4.