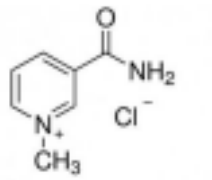
1-MNA

1-MNA, short for 1-methyl nicotinamide, is a natural compound produced in the body through the breakdown of niacin, a form of vitamin B3. Researched extensively for its safety profile, 1-MNA supplementation aims to safely restore NAD levels, optimize cellular redox pathways, and combat age-related diseases comprehensively.



1-MNA Benefits:

- Safely Increase NAD levels and block NNMT
- Improve Cell Energy Metabolism
- Anti-Inflammatory and Anti-Thrombotic properties
- Positive effect on Vascular Endothelium

1-MNA effectively restores healthy nicotinamide adenine dinucleotide (NAD) levels by inhibiting the nicotinamide N-methyltransferase (NNMT) enzyme. Additionally, it enhances the longevity activity of Sirtuin 1 (SIRT1) and Nuclear factor erythroid 2-related factor 2 (NRF2), reduces oxidative stress, and blocks inflammation by inhibiting Nuclear factor kappa beta (NF-κB).
(For a deep dive on 1-MNA's role in NAD regulation, see next page.)

Sources of 1-MNA

1-MNA is a compound naturally produced in our bodies, primarily in the liver, as it's a byproduct of nicotinic acid and nicotinamide metabolism. While it's also found in vitamin B3-rich foods, dietary sources contribute minimally to the total amount of 1-MNA present in the human body. In fact, around 60% of the niacin we consume is transformed into
1-MNA, as cited by Menon et al., 2007.

Some foods that are notable for their 1-MNA content, as reported
by Taguchi et al., 1986, include:

- Undaria pinnatifida (Wakame seaweed): 3.2 mg per 100g
- Green tea leaves: 3.0 mg per 100g
- Chicken gizzards: 2.4 mg per 100g
- Celery: 1.6 mg per 100g
- Chinese black mushrooms: 1.3 mg per 100g.

1-MNA Safety

Research has consistently shown that 1-MNA is both safe and well-tolerated in humans. The European Food Safety Authority (EFSA) has conducted a thorough assessment of 1-MNA's safety, confirming its safe usage.

Video Resources

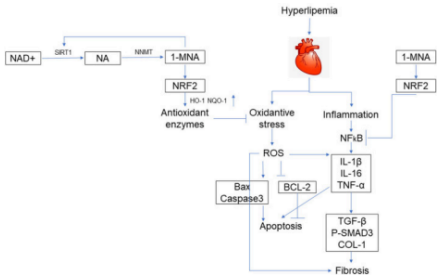
Elizabeth Yurth, MD spoke about 1-MNA as part of a comprehensive lecture on NAD and the potential risks of current methods of increasing NAD levels, including other precursors and infusions. We suggest you watch the entire video, about 40 minutes, but if you want to watch only the 1-MNA section, please skip to 27:55. SSRP Institute Peptide World Congress (2023)- Dr. Elizabeth Yurth Lecture - NAD+ Exposed

Additionally, here is a short 6-minute video overviewing 1-MNA's impact on metabolism, inflammation, and disease prevention. Understanding 1-MNA - Short Video

The Role of 1-MNA in NAD Regulation

The recent publication in Nature Medicine, *A terminal metabolite of niacin promotes vascular inflammation and contributes to cardiovascular disease risk,* highlighted some of the risks associated with ingesting large amounts of niacin and related precursors. So how does this relate to 1-MNA?

NAD is crucial for energy production in the body's cells. However, as we age, NAD levels decline. When NAD is depleted by enzymes such as CD38 and NNMT creating a low NAD state, the body tries to help by making 1-MNA. 1-MNA turns off NNMT to enable the replenishment of NAD. 1-MNA can also act as a substitute for NAD in a way by acting to turn on SIRT in these low NAD states. Additionally, it can be anti-inflammatory by reducing the NLRP3 inflammasome and turning off NF kappa beta (and as such can help improve long-COVID, heart disease and general inflammation).



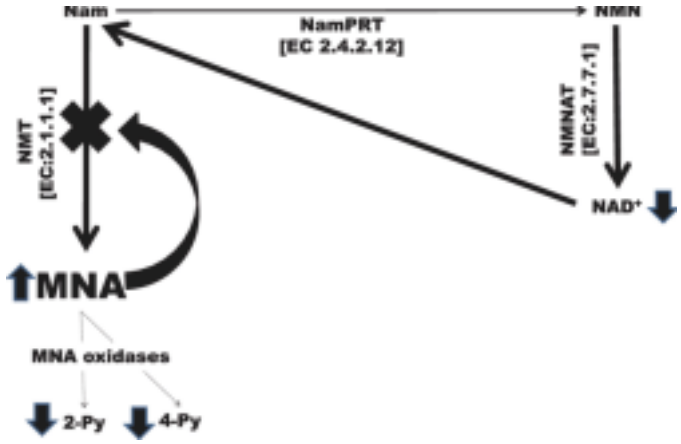
https://www.frontiersin.org/articles/10.3389/fcvm.2021.721814/full

When there is too much NAD in the system, the body will look to return to homeostasis by upregulating the NNMT enzyme. High NNMT levels are found in most disease states. NNMT degrades NAD into the metabolites N-Me-2PY and N-Me-4PY. These pyridones 2PY and 4PY have been linked to cardiovascular disease (illustrated in the Nat Med study and earlier studies) as well as kidney disease.

Regulating the amount of 2PY and 4PY is critical to proper NAD metabolism. Research has indicated that 2PY in particular appears to have a hormetic effect - a little 2PY is anti-inflammatory, antimicrobial, and linked to lower cancer, while too much has the opposite effect. 4PY appears to be the more worrisome.

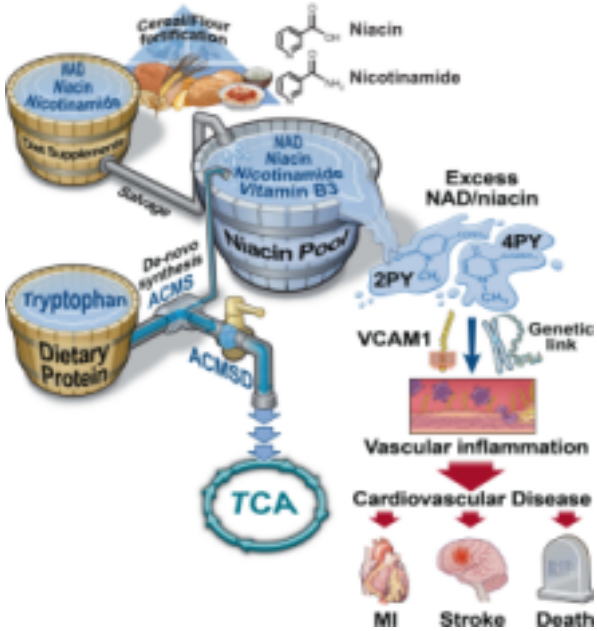
According to the Nat Med study, 4PY was strongly linked to the development of heart attack, stroke, and other cardiac events. More specifically, people with elevated levels of 4PY were around 60% more likely, on average, to have these cardiac events compared to people with lower levels.

1-MNA is a modulator of this system. When 1-MNA levels are high enough and there is enough 2PY, MNA oxidases are turned off to avoid making too much 2PY or 4PY. 1-MNA at low doses does not increase 4PY levels enough to negatively affect the endothelium and allows 1-MNA to maintain its anti-inflammatory effects. According to available data and experimental results, 1-MNA dosed up to 1000mg still had a negligent impact on 4PY levels and did not affect the biological benefits of 1-MNA. It is only with very large doses of 1-MNA caused up the chain (niacin, NMN, etc.) that the negative effects of 4PY begin to present.



https://www.researchgate.net/figure/Mechanism-for-maintenance-of-cellular-NAD-1-concentration-by-MNA-When-NAD-1_fig4_324832352

When pumping the system full of NAD and its precursors, NNMT stays turned on as there is never enough 1-MNA to keep things in check. More and more 2PY and 4PY are formed pushing the cell out of homeostasis and into dysregulation. It is for this reason that looking strictly at NAD serum levels can be misleading. Continuing to fill up the NAD bucket keeps serum levels nice and high, but it does not "plug the leak" and can lead to negative, downstream effects.



https://www.nature.com/articles/s41591-023-02793-8

Yes, people will report feeling an immediate boost of energy when you flood the system with NAD (i.e. via an infusion or large dose of niacin). This is due to the quick burst of ATP from the NAD, but is also in part an effect of a senescent cell cascade caused by the homeostatic imbalance - essentially an adrenaline rush as the body works to clear out this increased senescent burden. Much like giving insulin to a Type-2 diabetic does not fix the pathology of the diabetes; pumping NAD into the serum does not fix the disease state nor the fact that the mitochondria are not efficiently pumping out adequate NAD (which in turn is not getting to the Kreb cycle and then not getting enough NADH to supply the mitochondria for the proton motive forces needed for all the amazing cell signaling that follows). 1-MNA is an alternative to niacin, NAD, or its precursors, because it works further down the chain. It can build NAD safely as it turns off NNMT and guides the cell back into homeostasis. The NAD bucket stays full, while also giving the body the added benefits of 1-MNA itself.

1-MNA Research Studies

Below are a few other research articles on 1-MNA's influence on *Longevity, Cardiovascular, Obesity & Diabetes, and Inflammation.*

Longevity :

Hong S, Moreno-Navarrete JM, Wei X, Kikukawa Y, Tzameli I, Prasad D, Lee Y, Asara JM, Fernandez-Real JM, Maratos-Flier E, Pissios P. Nicotinamide N-methyltransferase regulates hepatic nutrient metabolism through Sirt1 protein stabilization. Nat Med. 2015, 21: 887-94.

Abstract

Full Study

Cardiovascular :

Song Ziguang, Zhong Xiao, Li Mingyang, Gao Pingping, Ning Zhongping, Sun Zhiqi, Song Xiang. *1-MNA Ameliorates High Fat Diet-Induced Heart Injury by Upregulating Nrf2 Expression and Inhibiting NF-κB in vivo and in vitro*. *Frontiers in Cardiovascular Medicine*, 8, 2021

Abstract

Full Text

Obesity & Diabetes :

Zhang J, Chen Y, Liu C, Li L, Li P. N1-Methylnicotinamide Improves Hepatic Insulin Sensitivity via Activation of SIRT1 and Inhibition of FOXO1 Acetylation. J Diabetes Res. 2020 Mar 23;**2020**:1080152.

Abstract

Full Text

Cancer Prevention :

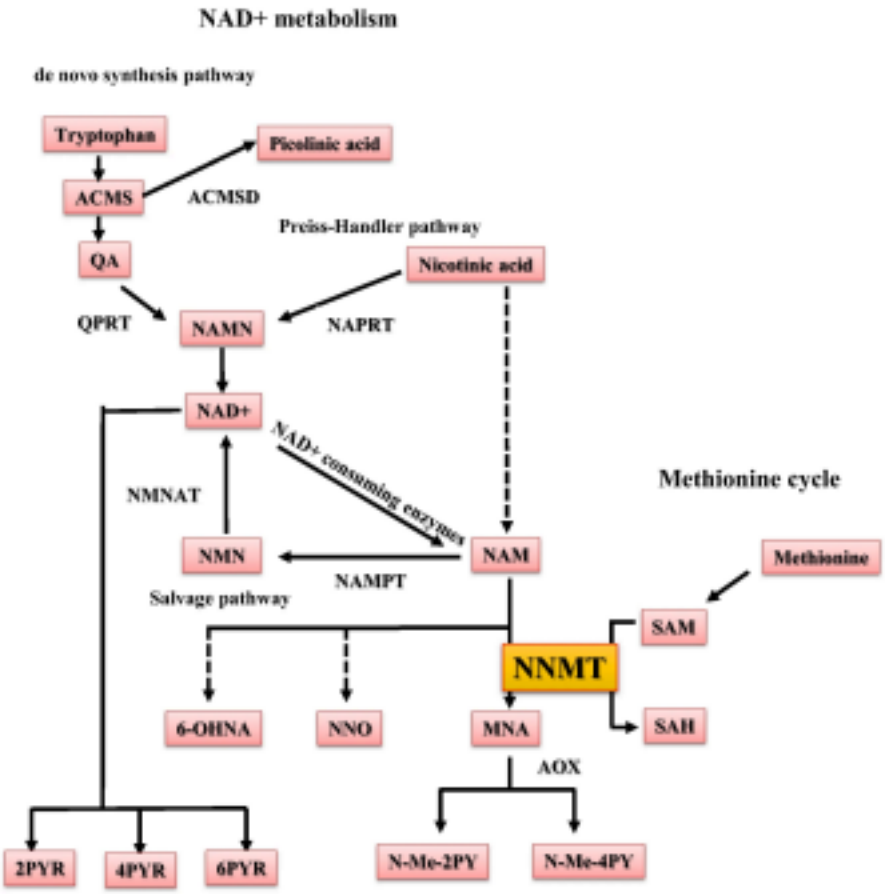
Blazejczyk, A., Switalska, M., Chlopicki, S. *et al.* 1-methylnicotinamide and its structural analog 1,4-dimethylpyridine for the prevention of cancer metastasis. *J Exp Clin Cancer Res* 35, 110 (2016)

Abstract

Full Text

Inflammation :
Karolina Sidor, Aldona Jeznach, Grażyna Hoser, Tomasz Skirecki,
1-Methylnicotinamide (1-MNA) inhibits the activation of the NLRP3 inflammasome in human macrophages, International Immunopharmacology, Volume 121, **2023**, 110445
Abstract
Full Text

Full NAD+ Metabolism Pathway Illustrated for Reference:



https://www.nature.com/articles/s41598-022-10476-6/figures/1