

## Even More Health Benefits of Niacinamide

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### STORY AT-A-GLANCE

- › Niacinamide, also known as nicotinamide (a form of vitamin B3), is important for healthy mitochondrial function and cellular energy production
- › Patients with established glaucoma scored significantly higher on visual field tests after taking niacinamide and calcium pyruvate daily for about two months
- › Niacinamide can be used to treat declining testosterone levels in men and women, and protects against stress by lowering cortisol
- › Niacinamide has anticancer and antiaging effects, and can be useful in the treatment of Alzheimer's disease and COVID-19
- › It may also be valuable in the treatment of both alcoholic liver disease and nonalcoholic liver disease (NAFLD), as low NAD is involved in the disease process

I recently posted [an article detailing the importance of niacinamide](#) (aka, nicotinamide, a form of vitamin B3 or niacin) for healthy mitochondrial function and cellular energy production, and how it can help reverse obesity and leaky gut, and prevent neurodegeneration, kidney disease and heart failure. Here, I'll review several additional conditions that can be prevented and/or treated with this inexpensive and readily available supplement.

**More Niacinamide Is NOT Better, There's a Goldilocks' Dose**

Keep in mind that the dosages used in the research studies discussed below do vary widely, but as a rule, I only recommend taking small doses of 50 milligrams of niacinamide three times a day.

This dosage has been shown to optimize energy metabolism and boost NAD<sup>+</sup> levels, which are foundational for everything else to work. It can be taken four times a day if you space them out. Take a dose as soon as you get up, before going to bed, and twice evenly spaced between those times.

The problem with taking too much vitamin B3, whether in the form of niacin or niacinamide, is that it might backfire and contribute to cardiovascular disease as documented by the Cleveland Clinic. ZeroHedge reports:<sup>1</sup>

*“The new study out of the Cleveland Clinic, published in Nature Medicine,<sup>2</sup> determined there is a delicate balance between too much niacin and just enough – a sort of Goldilocks effect ... [As] observed by the Cleveland Clinic team, too much niacin creates a byproduct known as 4PY.*

*This product circulates within the bloodstream and is associated with a higher risk of heart attack, stroke, and other cardiac events. Additionally, 4PY was shown in preclinical studies to trigger vascular inflammation, damaging blood vessels and eventually leading to atherosclerosis.*

*The researchers discovered this by examining data from 1,162 patients who had experienced major cardiovascular events. Just under half of the patients (442) were female. Initially, the team sought common markers that could lead to cardiovascular events. The most common factor within the pool of patients was excess levels of niacin.*

*The findings led to additional studies to validate the initial research. Both cohort studies, conducted in the United States and Europe, confirmed that niacin breakdown predicted an individual's future risk of heart attack, stroke, and death from cardiovascular disease.”*

## Niacinamide Limits Damage From PUFA Peroxidation

With that caveat out of the way, let's take a look at some of the health benefits associated with niacinamide supplementation, starting with its ability to ameliorate damage caused by linoleic acid (LA) consumption.

One of the most toxic metabolic byproducts of LA is 4 HNE, a toxic aldehyde that appears to play a causative role in heart failure.<sup>3</sup> Fortunately, there is an enzyme system called aldehyde dehydrogenases that deactivates 4 HNE. The best way to increase the activity of this enzyme system is to make sure you have sufficient NAD<sup>+</sup>, and the most efficient way to optimize your NAD<sup>+</sup> level is to make sure you're getting 50 mg of niacinamide three times a day.

## Raise Your Testosterone Naturally With Niacinamide

Niacinamide can be used to treat problems associated with declining testosterone levels due to aging, as demonstrated in a February 2022 Nature Aging study.<sup>4</sup> This study also involved eye health, specifically evaporative dry eye disease, but with a focus on the effects of androgens.

They found that by raising NAD<sup>+</sup>, local testosterone distribution in the meibomian gland in the eyelids, which produces oil to prevent the evaporation of tears, was improved. As a result, age-related atrophy of the gland was reduced, which alleviated the dry eye condition. In this case, they used a 5% solution of the NAD<sup>+</sup> precursors nicotinamide mononucleotide (NMN) or nicotinamide riboside (NR). The two regimens assessed were as follows:

- **Chronic** — 2 mg NAD<sup>+</sup> precursor four times a day in each eye for 90 days.
- **Acute** — 5 mg NAD<sup>+</sup> precursor six times a day in each eye for 14 days.

However, as noted by biohacker Georgi Dinkov,<sup>5</sup> plain niacinamide has been shown to be just as effective as NMN and NR for raising NAD<sup>+</sup>, so there's no reason why it wouldn't

work as well. Moreover, these findings are also applicable for other tissues and organs affected by declining testosterone, not just your eyes.

It confirms that niacinamide is a necessary cofactor to address the nearly universal decline in testosterone in both males and females, so this is yet another reason that most people need it. Dinkov writes:<sup>6</sup>

*“... the findings that androgen (in this case, testosterone) deficiency seen almost universally with advancing age is apparently due primarily to deficiency of the co-factor NAD+, which can apparently be remediated by supplementing NAD+ precursors such as niacinamide.*

*It appears that the rate-limiting step for androgen (testosterone) synthesis is the enzyme 3b-HSD, for which NAD+ is the main cofactor. Thus, a decline in NAD+ seen in aging (and disease) leads to decline in 3b-HSD activity and thus reduced androgen (testosterone) levels.*

*Conversely, the study found that restoring NAD+ levels almost fully remediated the reduced function of 3b-HSD, the androgen (testosterone deficiency), and thus was basically curative for the specific condition (dry-eye) the study investigated ...*

*As far as the systemic steroidogenic deficiency seen with aging that I mentioned earlier, oral dosing of an NAD+ precursor such as niacinamide would likely be needed, and human studies have demonstrated that daily doses in the 300 mg-500 mg daily range optimally stimulate NAD+ synthesis. (It would be better to start with 50 mg three times a day (150 mg) and increase if necessary.)*

*While most studies found that higher daily oral doses are unable to further raise NAD+ levels through the precursor pathway, higher doses of niacinamide specifically have been shown to inhibit the enzyme PARP-1, which is a ‘consumer’ of NAD+ and inhibiting it also raises NAD+ levels.*

*So, experimenting with the niacinamide with doses in the 500mg-1,500mg daily range would probably identify an optimal daily dose regimen for most people looking to increase steroidogenesis, especially if precursors such as pregnenolone and/or DHEA are taken as well."*

To address declining testosterone, I recommend taking:

- 50 mg of niacinamide three times a day
- 5 mg to 10 mg of DHEA orally once a day
- 50 mg of oral pregnenolone once a day

Ideally, take the hormone supplements DHEA and pregnenolone with a saturated fat, like a teaspoon of butter, to make sure they bypass metabolism in the liver, which will radically decrease their effectiveness.

## **Niacinamide Protects Against Stress**

Another phenomenally important human study<sup>7,8,9</sup> confirms that niacinamide lowers cortisol by increasing NAD<sup>+</sup>. NAD<sup>+</sup> is the cofactor for an enzyme called 11b-HSD2, which deactivates cortisol by turning it into cortisone. So, increasing NAD<sup>+</sup> with niacinamide will help lower cortisol, and this can benefit just about everyone, seeing how most people are plagued by stress and have elevated cortisol, which in turn drives inflammation and inhibits fat loss.

Raising NAD<sup>+</sup> with niacinamide supplementation was also shown to improve glucose metabolism and insulin sensitivity. It also increased ATP levels, which is your cellular energy currency. As such, niacinamide may be one of the most important supplements you can take.

Importantly, this study used plain niacinamide rather than the more expensive NMN or NR, so we don't have to infer these benefits. They took place using plain niacinamide and D-ribose. The dosages used were 240 mg of niacinamide twice a day, and 1,280 mg of D-ribose twice a day, for one week.

## Anticancer Effects

Niacinamide can also help prevent and treat cancer. As noted in one 2022 study in *Nature Metabolism*,<sup>10,11</sup> limiting fat availability to cancer cells may be one of the keys to curing cancer. NAD<sup>+</sup> also plays an important role, and niacinamide raises NAD<sup>+</sup>:

*“Production of oxidized biomass, which requires regeneration of the cofactor NAD<sup>+</sup>, can be a proliferation bottleneck that is influenced by environmental conditions ... Here, we show that de novo lipid biosynthesis can impose a substantial NAD<sup>+</sup> consumption cost in proliferating cancer cells.*

*When electron acceptors are limited, environmental lipids become crucial for proliferation because NAD<sup>+</sup> is required to generate precursors for fatty acid biosynthesis. We find that both oxidative and even net reductive pathways for lipogenic citrate synthesis are gated by reactions that depend on NAD<sup>+</sup> availability.”*

An earlier study,<sup>12</sup> published in 2020, found that niacin (vitamin B3) could control the growth of brain tumors by reactivating myeloid cells (a type of bone marrow cell). As explained by the authors:

*“Although innate immune cells are typically present inside tumors, they often have an inactive phenotype such that they are ineffective at killing the cancer cells or even promote tumor growth. Sarkar et. al. discovered that it may be possible to reprogram these cells to a more active type using niacin (vitamin B3).*

*The authors showed that niacin-exposed monocytes can inhibit the growth of brain tumor-initiating cells. Moreover, niacin treatment of intracranial mouse models of glioblastoma increased monocyte and macrophage infiltration into the tumors, stimulated antitumor immune responses, and extended the animals' survival ...”*

Here, a mere 7 mg of niacin per kilo of bodyweight per day halted the growth of brain tumors and nearly doubled survival times. The niacin group also survived longer than those receiving chemotherapy alone. While this study used niacin, niacinamide would work just as well. Tying the results back to the study above, Dinkov notes:<sup>13</sup>

*“The proposed mechanism of action was immune system activation. I, personally, do not buy this explanation as a main mechanism of action. IMHO vitamin B3’s known effects on inhibiting lipolysis ... and promoting the oxidation of glucose are probably more important for inhibiting the tumor growth and prolonging survival.”*

## **Antiaging Effects**

Niacinamide and other B vitamins also have important antiaging effects. In a December 2021 article, Dinkov reviewed a 2011 study<sup>14</sup> that suggests fasting can speed up aging by depleting your energy reserves, and that vitamin B2 has the opposite effect and slows the aging process. Commenting on this finding, Dinkov wrote:<sup>15</sup>

*“[This is] a great study that not only suggests a dirt cheap and widely available option for retarding aging, but once again demonstrates that stress (e.g. fasting) directly causes aging by depleting/blocking OXPHOS [oxidative phosphorylation, the metabolic pathway cells use to oxidize nutrients, thereby releasing chemical energy to produce ATP], and the key mechanism for stopping/reversing aging is by restoring energy production.*

*The proposed ‘senolytic’ in this study is the humble vitamin B2, also known as riboflavin. Vitamin B2 is the precursor for FAD [flavin adenine dinucleotide] – a key coenzyme, responsible for about 20% of the energy produced in the OXPHOS process. Btw, the other 80% are controlled by NAD – a molecule synthesized endogenously from the precursor niacinamide.*

*There has been an explosion in publications over the last decade touting NAD as the cure to virtually every disease out there, and many of those claims are*

*well-backed by evidence. While there are ... proprietary NAD precursors such as nicotinamide riboside and nicotinamide mononucleotide, plain old niacinamide works just as well and is drastically cheaper.*

*Niacin is another NAD precursor but [it] increases histamine and serotonin, and still has to be converted into niacinamide before it can end up as NAD. So, no reason to take anything else but niacinamide.*

*Doing so, raises the NAD/NADH ratio, shifts the cell redox state towards oxidation (as opposed to reduction), and the ample energy produced by the cell can be used for all types of maintenance 'work' the cells need to perform in order to stay healthy, prevent aging, etc ...*

*[V]itamin B2 has a similar metabolic role as well. It is a precursor to the co-factor FAD and taking B2 raises FAD and thus the FAD/FADH ratio, which facilitates electron flow through the electron chain complexes I&II. Conversely, having insufficient levels of FAD (and/or low FAD/FADH ratio) can effectively block the ETC [electron transport chain].*

*This crucial role of FAD in the ETC demonstrates why excessive fatty acid oxidation (FAO) is harmful. Namely, FAD is consumed in the process of beta-oxidation of fatty acids and as such excessive FAO can consume too much FAD, drop the FAD/FADH ratio, and thus block electron flow through ETC.*

*This reduction/blockade of ETC is exactly what is seen in most chronic, degenerative diseases, but especially in conditions such as cancer, diabetes, Alzheimer's disease, autoimmune conditions, etc.*

*Well, the [Physiology] study ... found that this reduction of mitochondrial activity (ETC) is exactly what triggers the senescence process, and activating mitochondria (specifically ETC II) by supplementing vitamin B2 prevented cellular aging. Here is the actual explanation from the study authors:*



*'... Cells under stress produce SLC52A1, and increase their absorption of vitamin B2 from outside the cell. Once inside the cell, the vitamin B2 is converted into FAD and increases mitochondrial energy production by becoming a coenzyme of mitochondrial respiratory chain complex II. As a result of the AMPK and p53 (which induce cellular senescence) are inactive, therefore stress-mediated cellular senescence is suppressed.'*

## **Niacinamide for Liver Disease**

Niacinamide may also be valuable in the treatment of both alcoholic liver disease and nonalcoholic liver disease (NAFLD). By now, you can probably guess why. It's because low NAD is involved in the disease process.

A study<sup>16,17</sup> published in 2016 showed that chronic alcohol bingeing injures your liver and other organs by reducing NAD<sup>+</sup>, which is a required cofactor for important enzymes and mitochondrial renewal.

In short, a decline in the NAD/NADH ratio (your redox status) is a main driver of alcohol-related pathologies, and not just in your liver but in all organs. The answer is to increase NAD<sup>+</sup>, which is effectively done using niacinamide. According to Dinkov, niacinamide also works synergistically with **methylene blue**:<sup>18</sup>

*"Both [niacinamide and methylene blue] can raise the NAD/NADH ratio quite robustly on their own, but in combination are synergistic and may allow for much lower doses to achieve the same effects.*

*People have sent me emails showing their blood tests demonstrated the same increase in NAD/NADH from a combination of 1mg MB [methylene blue] and 250 mg niacinamide as using 5mg+ MB or 750mg-1,000mg niacinamide separately."*

Related to this is the importance of eating the correct fats. You want to increase your saturated fat and avoid PUFAs, especially linoleic acid (LA), as PUFAS are stored and accumulated whereas saturated fats are burned for energy.<sup>19,20</sup> It can take up to seven

years to clear LA from your body due to its long half-life. In the meantime, you need to be careful about not pushing the LA out too rapidly through fasting, low-carb diets or vigorous exercise.

**“Niacinamide can help while you’re clearing stored PUFAs from your cells, as it’s an anti-lipolytic agent.”**

The accumulation of PUFAs in your cells are, I believe, one of the greatest contributors to chronic and degenerative diseases of all kinds, as they wreak havoc with your cellular machinery and impair mitochondrial function (and hence reduce energy production). Niacinamide can be helpful while you’re clearing stored PUFAs from your cells, as it’s an anti-lipolytic agent.

## **Niacinamide for Alzheimer’s Disease**

Niacinamide is required for healthy metabolism and, as such, it can also be useful in early Alzheimer’s treatment.<sup>21</sup> Combining it with methylene blue may boost benefits even further, as they work synergistically, and methylene blue alone has been shown to stop the progression of Alzheimer’s.<sup>22</sup>

Increasing the carbs only seems to work when your fat intake is below 35% of your total daily carbs. If it is higher, the Randle cycle will prevent the extra carbs from being metabolized in the mitochondria and will shuttle them to glycolysis which increases lactic acid and will likely worsen one’s health.

Thiamine, the B1 mentioned in the study, is a cofactor for the enzyme that converts the glucose metabolite pyruvate into acetyl-CoA, which is what is pushed into the mitochondria to be burned as fuel. Taking niacinamide (vitamin B3) will help three of the complexes in the mitochondria work and vitamin B2, riboflavin, will help one complex to produce the ATP, so using all three would be ideal.

Niacinamide is the only one that appears to benefit from lowering the dosing to 50 mg three times a day. As reported by Dinkov:<sup>23</sup>

*“[A 2019] study<sup>24</sup> demonstrated that increasing levels of acetyl-CoA (the starting intermediate of the Krebs cycle), even at a stage of very advanced aging/AD [Alzheimer’s disease], can reverse aspects of both pathologies.*

*While the study used patented compounds, the same effects can be achieved by ensuring a steady supply of dietary carbs combined with increasing the function of pyruvate dehydrogenase (PDH). Increasing the activity of PDH can be achieved by supplementing with vitamin B1 (a cofactor of PDH), keeping the NAD/NADH ratio as high as possible and keeping fatty acid oxidation (FAO) down ...*

*[T]hese approaches have been successfully tested in many animal models and one of the molecules that works through the latter two mechanisms is niacinamide. In fact, there is a human clinical trial<sup>25</sup> [completed in August 2022] with 3 grams of niacinamide daily for treating AD, and though the results have not been published yet the leaked information suggests highly positive results. Methylene blue (MB) can do the same ...”*

## **Niacinamide and COVID-19**

As it turns out, raising NAD<sup>+</sup> appears to be therapeutic for COVID infection as well.<sup>26</sup> The reason for this is because SARS-CoV-2 infection dysregulates NAD synthesis and the NAD metabolome, which is a component of your innate immunity.

As noted by Dinkov, this study again demonstrates “the crucial role energy plays even in ‘non-metabolic’ diseases such as viral infections.” Indeed, without energy your body cannot defend itself against infection and disease, and since NAD<sup>+</sup> is such a crucial component of energy production, it makes perfect sense that having higher NAD levels will make you more resilient against viral infections. The answer again, then, is niacinamide, with or without methylene blue.

By now, you should have a good idea about how important niacinamide is for your health, and why I think it's one of the most important supplements you can take on a daily basis.

## **Niacinamide Helps Treat Glaucoma**

Research<sup>27,28</sup> published in November 2021 reported that patients with established glaucoma scored significantly higher on visual field tests after taking 3 grams of niacinamide in combination with 3 grams of (calcium) pyruvate daily for about two months. As reported by the authors:

*“Given the decrease in NAD with aging, which may render retinal neurons more vulnerable to disease-related insults, the investigators hypothesized that increasing NAD may support the mitochondrial activity of RGCs and decrease their susceptibility to glaucoma.*

*In a rat model of ocular hypertension, retinal and optic nerve NAD declined as a function of IOP, while nicotinamide was neuroprotective at a range of doses. In addition, nicotinamide has been shown to be low in the sera of patients with primary open-angle glaucoma. These data further support a role for NAD in glaucoma.*

*Furthermore, Harder et al reported that an IOP-mediated decrease in retinal pyruvate levels was associated with dysregulated glucose metabolism prior to detectable optic nerve degeneration in metabolic studies of DBA/2J mice.*

*They also found that oral supplementation with pyruvate protected both rat and mouse models of glaucoma from neurodegeneration, with a combination of nicotinamide and pyruvate being the most protective in the chronic mouse model ...*

*Given the significant neuroprotective effects observed in recent studies, the similarities in cellular biology of NAD<sup>+</sup> and pyruvate pathways between mice and humans, as well as the safety profile of these supplements, we investigated*

*the effect of nicotinamide and pyruvate on the visual function of patients with treated manifest glaucoma ...*

*[R]esults suggest that treatment with nicotinamide and pyruvate tripled the likelihood of improvement of test locations relative to placebo.”*

If you have glaucoma and want to give niacinamide a try, I recommend limiting your dose to 50 mg three times a day, before increasing to 3 grams a day, which I believe is excessive.

## Sources and References

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- <sup>1</sup> [ZeroHedge February 21, 2024](#)
- <sup>2</sup> [Nature Medicine February 19, 2024; 30: 424-434](#)
- <sup>3</sup> [Haidut.me February 21, 2024 \(Archived\)](#)
- <sup>4</sup> [Nature Aging 2022; 2: 105-114](#)
- <sup>5, 6</sup> [Haidut.me March 31, 2022 \(Archived\)](#)
- <sup>7</sup> [Nutrients June 2022; 14\(11\): 2219](#)
- <sup>8</sup> [Nutritional Outlook July 11, 2022](#)
- <sup>9</sup> [Haidut.me July 12, 2022 \(Archived\)](#)
- <sup>10</sup> [Nature Metabolism 2022; 4: 711-723](#)
- <sup>11, 13</sup> [Haidut.me July 14, 2022 \(Archived\)](#)
- <sup>12</sup> [Science Translational Medicine April 1, 2020; 12\(537\)](#)
- <sup>14</sup> [Physiology August 2011; 26\(4\): 214-224](#)
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- <sup>21, 25</sup> [Clinical Trials Nicotinamide as an Early Alzheimer's Treatment NCT03061474](#)
- <sup>22</sup> [Haidut.me December 2, 2019 \(Archived\)](#)
- <sup>23</sup> [Haidut.me December 13, 2019 \(Archived\)](#)
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