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The Wide-Ranging Health Benefits of Niacinamide

Analysis by Dr. Joseph Mercola ✔ Fact Checked | June 22, 2023

STORY AT-A-GLANCE

- Niacinamide (aka nicotinamide) is a form of niacin (vitamin B3) that plays an important role in energy metabolism. Without it, your mitochondria cannot make energy
- Niacinamide is also a precursor to NAD+, which is essential in the conversion of food to energy, maintaining DNA integrity and ensuring proper cell function. NAD+ is also a primary fuel for longevity proteins that become depleted with age
- According to recent research, a century-long decline in our basic metabolic rate (BMR) can by itself account for the obesity epidemic. For some reason, we're spending less energy (burning fewer calories) now, when resting, than people did in decades past
- Consumption of polyunsaturated fats may be to blame for this BMR decline. Niacinamide has potent antiobesity effects and also helps inhibit release of inflammatory PUFAs from fat cells
- Niacinamide can also help prevent neurodegeneration, kidney disease and heart failure, and reverse leaky gut

In a series of articles, biohacker Georgi Dinkov highlights a variety of benefits of niacinamide (aka nicotinamide), a form of niacin (vitamin B3) that plays a vital role in energy metabolism, as it's essential for the mitochondrial electron transport chain to function. Without it, your mitochondria cannot make energy.

Niacinamide is so important because it is a precursor for NAD+, which is involved in the conversion of food to energy, maintaining DNA integrity and ensuring proper cell

function. NAD+ is also a primary fuel for sirtuins, longevity proteins that become depleted with age.

As such, niacinamide can be an important longevity hack. As I've explained in previous articles, niacinamide at a dose of 50 milligrams per day will provide the fuel for NAMPT, the rate limiting enzyme for NAD+. Niacinamide also has potent antiobesity effects, can help prevent neurodegeneration and heart failure, and reverse leaky gut.

Obesity Epidemic Linked to Decline in Basic Metabolic Rate

In a May 2023 article,[1] Dinkov reviewed evidence showing that lack of exercise and increased calorie intake are not the cause of the obesity epidemic. Interestingly, there has been a century-long decline in our basic metabolic rate (BMR), or basal energy expenditure. BMR refers to the number of calories your body burns when you're at rest, which accounts for 60% to 75% of your total daily energy expenditure.

According to research published in the April 2023 issue of Nature Metabolism,[2] the adjusted basal metabolic rates (BMR) in the U.S. and Europe have declined by 14.7% in men and 2% in women since the 1990s. While the decline in women was not considered significant, when they looked at a larger data set that stretched back 100 years, a significant drop was confirmed for both sexes.

This, the authors believe, is "a previously unrecognized factor" in the obesity epidemic. In plain English, what this means is that, for some reason, we're burning fewer calories now when resting or even sleeping than people did in decades past.

> *"It does not take much acumen to realize that with double digit declines over a 3-decade period, by now our BMR is probably only half of the BMR of people who lived at the turn of the 20th century,"* Dinkov writes.[3]
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> *"What makes the situation worse is that if BMR has declined so much, the current guidelines for 'optimal' health — reduced caloric intake and plenty of exercise — are virtually guaranteed to make the situation even worse since they will invariably further lower the BMR ...*

What could be causing these declines in BMR? Well, chronic stress aside, that decline in BMR mirrors almost perfectly the curves of PUFA [polyunsaturated fat] consumption rates in the general population.

Namely, as the BMR curve has steadily declined over the last 100 years the PUFA consumption rate curve has steadily moved upwards over time. Unless this trend of ever-increasing PUFA consumption is interrupted, I don't see the decline of BMR flattening (let alone reversing) any time soon."

Niacinamide's Antiobesity Effects

In another article, Dinkov cites recent research[4,5] showing that niacinamide reprograms cellular metabolism in adipose (fat) tissue and increases mitochondrial biogenesis, which in turn results in fat loss. Basically, it ameliorates obesity-related metabolic dysfunction by increasing fatty acid catabolism.

> **"Obese mice given a daily dose of 2.5 mg of niacinamide per kilo of bodyweight for three weeks lost 47% of their body fat. They also saw increases in lean muscle mass."**

Obese mice that were given a daily dose of 2.5 mg of niacinamide per kilo of bodyweight for three weeks lost 47% of their body fat, and this was true whether they ate a regular diet or a high-fat one. They also saw increases in lean muscle mass, mitochondrial biogenesis and energy production, CO2 levels, and physical activity. Insulin sensitivity was also improved.

Niacinamide Is Helpful When Clearing PUFAs

Where does niacinamide fit into this? Primarily, it has to do with the fact that it raises NAD+, and NAD+ inhibits the release of inflammatory polyunsaturated fats (PUFAs) such

as linoleic acid (LA) from your fat cells. Another term for this is anti-lipolytic.

This is a good thing, because when LA is released from your fat cells it is metabolized into highly inflammatory molecules, so you want to release it from your cells very gradually.

PUFAs such as LA are not typically burned as fuel like saturated fats. Instead, they're stored,[6] and the half-life of PUFAs, which get embedded and integrated into your cell membranes, is about 680 days. This means that to rid your body of LA will take approximately seven years, provided you don't load more in.

It is fascinating to note that most of the body fat in obese individuals is composed of PUFAs. Saturated dietary fat is mostly burned (oxidized) and used up. So, most people have large stores of LA, and these stores need to be lowered to safe levels of 1% to 2% LA.

If your cells are loaded with these inflammatory fats (which they will be if you've been eating processed foods), rapid release of LA from your fat cells will precipitate or increase inflammation, so you really want to limit that. Aside from niacinamide, aspirin is also an anti-lipolytic and also slows down the release of LA from your fat cells.

Taking a high-quality vitamin E supplement once a day can also be helpful. In addition to impairing the release of LA from fat cells, just like NAD+ and aspirin, vitamin E also helps prevent the LA from converting into dangerous oxidative linoleic acid metabolites (OXLAMs) once released, so it does double-duty.

Most vitamin E supplements are garbage. To ensure you're getting a high-quality vitamin E, you want most of the vitamin E isomer as alpha tocopherol, typically about 150 units. It should also have the other tocopherol isomers, alpha, beta and gamma, but at far lower doses.

Additionally, it should have alpha, beta and gamma tocotrienols. Finally, it should only have the "D" isomer. Avoid all vitamin E supplements that are "DL," as half of it is the wrong isomer and not biologically useful and may even be harmful.

Niacinamide May Protect Against Neurodegeneration

In another May 2023 article,[7] Dinkov reviews evidence showing niacinamide may help prevent neurodegeneration by allowing for higher energy levels through energy metabolism in the mitochondria. "There are many studies, going back decades, demonstrating that a drop in NAD+ levels, and thus of NAD/NADH, is a common feature of virtually all neurodegenerative diseases," he writes.

Studies have also demonstrated that raising NAD+ levels can help prevent and treat many neurological conditions, including Alzheimer's and ischemic stroke. Dinkov goes on to cite a recent study[8,9] that suggests the primary purpose of autophagy, particularly autophagy in your brain, is to maintain optimal NAD+ levels.

When autophagy is low, the resulting NAD depletion causes cytotoxicity in the brain cells and degeneration of brain tissue. Since declining NAD+ levels appear to be what's behind the neurodegenerative processes, the authors suggest the remedy is to raise NAD+ using precursors such as nicotinamide, nicotinamide mononucleotide (NMN), nicotinamide riboside (NR) or niacin (vitamin B3).

Of these, I'm convinced niacinamide is the best. I'll review why in the next section. The reason so few promote it is because it's incredibly inexpensive, so there's no financial incentive at play.

Another inexpensive solution to increasing or modulating autophagy is aspirin,[10] which may activate autophagy without the downside of fasting's increasing cortisol levels. Also, as Georgi states below:

> *"Since aspirin is known to modulate autophagy (raise it when it is abnormally low and lower it when it is abnormally high) and niacinamide is a very effective NAD precursor, it is reasonable to try them in combination that should be synergistic when it comes to protecting the brain (and the entire organism) from diseases and even aging."*

Dinkov continues by mentioning some surprising tidbits that I was previously unaware of:

> *"Last but not least, the study is one of the few to pour cold water on everybody's favorite anti-aging target — the sirtuins (SIRT). I mentioned SIRT years ago in a post demonstrating that its activity is greatly increased in cancer and that SIRT promotes fatty acid oxidation (FAO), which drives cancer growth and metastases.*
>
> *Now, [this study] demonstrates that the sirtuin genes are also heavy consumers of NAD and also mentions that their activity actually increases in aging and pathological states. Conversely, inhibiting the sirtuins (SIRT) would be beneficial, as the study itself demonstrates ...*
>
> *The really good news here is that niacinamide is not only a precursor to NAD+, but is also an inhibitor (in higher doses) of both NAD-consuming enzymes mentioned in the study (PARP-1 and SIRT). None of the other NAD precursors have been shown (so far) to inhibit the NAD-consuming enzymes."*

Why Choose Niacinamide?

The reason I'm convinced niacinamide is the best NAD+ precursor is because the immediate breakdown product of NAD+ is niacinamide. As you can see in the illustration below, when NAD is used up, it gets broken down into niacinamide.

This niacinamide is then recycled. First, it's converted into NMN, and then into NAD+. This is likely why some researchers promote NMN. However, the enzyme NMNAT1-3 that converts NMN to NAD+ is not the rate limiting enzyme. NAMPT is what controls how much NAD+ you make. So, flooding your body with NMN is not going to be as useful as using small amounts of niacinamide and activating NAMPT.

The ideal dosing of niacinamide is from 50 mg three times a day. It is the rare person that will not respond favorably to this simple intervention for increasing NAD+.

Niacinamide Prevents Kidney Disease

Speaking of NAD+, NAD+ deficiency has been linked to kidney disease, and niacinamide can help prevent that too.[11] As Dinkov explains in a May 18, 2023, article:[12]

> *"Many studies have ... shown that elevated lipolysis (delivering inflammatory PUFA to the kidneys) and, consequently, elevated fatty acid oxidation (FAO) as per the Randle Cycle are the ... likely culprits. It is well-known that one of the effects of elevated FAO is a decline in the mitochondrial NAD/NADH ratio — i.e. relative deficiency of NAD+.*
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> *This is actually the primary mechanism through which elevated FAO inhibits glucose oxidation since lower NAD/NADH ratio inhibits the activity of the enzyme pyruvate dehydrogenase.*
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> *In any event, the study ... demonstrates that relative deficiency in NAD+ (i.e. lower NAD/NADH ratio) is the direct cause of kidney damage due to the resulting OXPHOS dysfunction. Conversely, elevating NAD+ (and thus NAD/NADH) levels with precursors such as nicotinamide mononucleotide (NMN) or nicotinamide riboside (NR) was effective in completely preventing kidney damage and CKD.*
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> *Since NMN is no longer available over the counter and NR is rather expensive, niacinamide remains as the most viable option for replicating the study in humans with CKD, especially considering the fact that niacinamide is just as effective as an NAD+ precursor as NMN/NR while also having potential additional benefits the other two precursor do not.*
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> *Namely, niacinamide is an inhibitor of the NAD-consuming enzymes PARP-1 and CD38, so taking niacinamide not only directly increases NAD+ levels but also inhibits its excessive consumption/decline. I can't find the actual published study that article is based on, but other studies have demonstrated benefits for*

CKD in animals from human-equivalent (HED) doses in the 250mg-500mg daily range."

Niacinamide for Leaky Gut

Niacinamide also holds out the promise of healing for all those who struggle with increased gut permeability, so-called "leaky gut," and related problems. When lipopolysaccharide (LPS), an endotoxin, leaks from your gut into your bloodstream, it causes low-grade systemic inflammation that fuels a wide range of chronic diseases and conditions.

While certain toxins such as glyphosate and gluten have been implicated in leaky gut, recent research[13,14] suggests it may be rooted in an energy deficiency which, again, niacinamide can help fix. Dinkov explains:[15]

"Since apparently intestinal epithelial cells (forming the bulk of the gut barrier) consume at least 20% of the ATP we synthesize daily, any sizable drop in ATP levels results in massive dysfunction in both the structure and function of these cells ...

Endotoxin (LPS), produced by the gram-negative members of our microbiome, is known to deplete ATP levels in the epithelial cells. The study used another known ATP depleting agent — ethanol — to cause the energetic deficiency in the epithelial cells and, unsurprisingly, found that endotoxin levels in the blood massively increased.

However ... administering niacinamide at a human-equivalent dose of 30mg/kg daily, for 10 days, fully prevented the endotoxemia caused by ethanol, and reversed all the energetic (ATP, NAD, Krebs cycle function) deficits as well, thereby restoring the gut barrier function.

In fact, niacinamide supplementation reversed the energetic deficits to a level surpassing the healthy control group! As I mentioned above, the study is relevant even for people who do not drink alcohol since endotoxin naturally

formed in our intestines in response to feeding can also cause similar energetic depletion in the intestinal cells and thus cause the same state of 'leaky gut' as ethanol.

While 30mg/kg of niacinamide daily is not a small dose, it is below the daily dose even mainstream medicine considers toxic, and the duration of usage was just 10 days. Furthermore, the treatment lasted 10 days since ethanol was also administered for 10 days. If a person is not drinking daily, then the niacinamide treatment would also likely not be needed daily.

In the absence of daily drinking, I think a reasonable protocol would be to take 30mg/kg on weekends (2 days), maybe twice a month, as a general prophylactic and/or gut-repair regimen.

A daily dose of 200 mg-300 mg would probably have similar beneficial effects as the larger doses taken sporadically. Several human studies already demonstrated that a daily dose of 300 mg niacinamide raises NAD levels to the same degree as 1,000 mg daily."

Niacinamide for Heart Failure Prevention

Finally, niacinamide may also act as a preventive against heart failure — again because heart failure is a localized symptom of energy deficiency and mitochondrial dysfunction. As explained by Dinkov,[16] when your NAD+ level drops, your ATP level also drops, and this puts stress on the cardiomyocytes in your heart. Cardiomyocytes are specialized cells in your heart that generate contractive force.

Thusly stressed, the cardiomyocytes release pro-fibrotic mediators that further suppress mitochondrial function. Over time, this leads to cell death, collagen deposition and fibrosis, which are hallmarks of heart failure.

Research[17] published in February 2023 found that replenishing NAD+ prevented this energetic dysfunction, and therefore the subsequent development of heart failure. Here, the human-equivalent of 3.5 mg per kilo of bodyweight was administered via daily

injection for two months, but Dinkov and I both believe that oral niacinamide might be just as effective, although you might have to use it for a longer period of time.

General Niacinamide Recommendations

As a blanket recommendation for optimal health, I recommend taking 50 mg of niacinamide three times per day. Niacinamide will only cost you about 25 cents a month if you get it as a powder. Typically, one-sixty-fourth of a teaspoon of niacinamide powder is about 50 mg. You can easily find a set of measuring spoons on Amazon that have a 1/64 teaspoon.

The reason I recommend getting it in powder form is because in most supplement brands, the lowest available dose is 500 mg, and that will decrease NAD+ due to negative feedback on NAMPT, which is the opposite of what you're looking for.

Also, please note that although niacinamide and niacin are both called vitamin B3, niacin will not activate NAMPT like niacinamide, so it is best to use niacinamide. Additionally, niacinamide, unlike niacin, will not cause flushing which is due to a large release of histamine.

It would also be helpful to make sure you're getting all the other B vitamins, as they too are crucial for mitochondrial function, especially regular niacin, riboflavin, and folate. Oftentimes, decreased mitochondrial function is due to a deficiency in B vitamins, and that's easy to fix with a low dose high quality B complex. Usually, when this is the case, improvement can be seen within two to three weeks.