

Chronic Pain Due to Mitochondrial Dysfunction, Niacinamide Can Treat It

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STORY AT-A-GLANCE

- › Chronic pain may not be a disorder of its own but a symptom of underlying mitochondrial dysfunction
- › Nicotinamide riboside (NR) – a form of vitamin B3 and precursor to nicotinamide adenine dinucleotide (NAD+) – helps relieve chronic pain in mice by improving mitochondrial function
- › Niacinamide, another form of vitamin B3 involved in similar cellular processes as NR, may also be useful for relieving chronic pain
- › Linoleic acid (LA) in vegetable and seed oils causes mitochondrial dysfunction
- › Lowering your intake of LA, which is common in ultraprocessed foods, is one of the most straightforward ways to improve mitochondrial health and, thus, potentially relieve chronic pain

About 21% of U.S. adults suffer from chronic pain, with new cases occurring more often than new cases of other common conditions like diabetes, depression and high blood pressure.¹ Pain is considered chronic if it occurs every day or most days over a period of three months or more.

For about 8%, the chronic pain is considered high-impact,² meaning it limits life or work activities, demonstrating the heavy burden this condition places on those affected.

Many reach for dangerous opioid drugs for relief, which suppress mitochondria³ – the last thing you want if you’re struggling with chronic pain.

Chronic Pain Is a Symptom of Mitochondrial Dysfunction

Researchers with Utrecht University in the Netherlands revealed that nicotinamide riboside (NR) – a form of vitamin B3 and precursor to nicotinamide adenine dinucleotide (NAD+), a molecule involved in DNA repair and healthy aging – helps relieve chronic pain in mice⁴ by improving mitochondrial function.

“Previous research has linked chronic pain to dysfunctional mitochondria, particularly those in specialized nerve cells, called sensory neurons, which detect changes in the environment,” New Scientist reported.⁵

For the study, an inflammatory substance was injected into the paws of 15 mice, which led to changes in mitochondrial function, even a week later after the inflammation had resolved. The mitochondrial changes were associated with greater pain in the mice, which also had lower levels of NR in the mitochondria of their sensory neurons compared to mice that didn’t experience inflammation.⁶

NR plays an important role in mitochondrial function, so researchers gave the mice a high dose, which alleviated pain.

“Together these findings indicate two things: first, that inflammation can impair mitochondrial function in sensory neurons and that these impairments increase the risk of chronic pain, even after inflammation has resolved. Second, that taking nicotinamide riboside supplements may help treat this chronic pain by restoring mitochondrial function,” according to New Scientist.⁷

The study may help shed some light on why some people continue to experience pain even after inflammation has healed, which remains a largely unanswered question. The researchers noticed that even after the initial pain from inflammation goes away, the nerve cells involved in sensing pain still show changes in their mitochondria that disrupt the balance of certain chemicals in the cells.

However, adding the NAD⁺ precursor NR helped mice recover from pain, even when it was chronic. This suggests that managing mitochondria function in these nerve cells is crucial for overcoming persistent pain after inflammation.

Vitamin B3 for Chronic Pain

As noted in the blog [To Extract Knowledge From Matter](#), which is inspired by the work of the late Ray Peat, niacinamide, another form of vitamin B3 involved in similar cellular processes as NR, may be useful for relieving chronic pain:⁸

“The study ... is one of the first to demonstrate that chronic pain is not an organic disorder of its own, but a symptom of an underlying mitochondrial dysfunction. This not only explain why the intervention with niacinamide worked in alleviating the pain (by improving mitochondrial function), but also why treating chronic pain with opioids is about the worst intervention one could choose.

Why? Because opioids are among the most potent suppressors of mitochondria, which means that as soon as one stops taking them the chronic pain will be much worse, leading to more opioid use and so on – a vicious cycle with usually lethal outcome (overdose).”

In fact, one study found that people who use opioids tend to have fewer mitochondria in their blood. Further, being exposed to the synthetic opioid fentanyl before birth was found to change the number of mitochondria in the blood and the activity of genes related to mitochondria in the nucleus accumbens, a brain area important for feeling pleasure, in young offspring.⁹

[To Extract Knowledge From Matter](#) continued explaining why the featured study’s use of vitamin B3 is superior to opioids for chronic pain:¹⁰

“The niacinamide dose used in this study was on the high-side (HED [human equivalent dose] ~35mg/kg daily), but considering it was administrated only

once and the pain was completely resolved, it is a low-risk intervention in such doses for humans, especially compared to opioids.

Also, there are prior animal studies showing that lower doses (HED 3mg/kg daily) taken for a few weeks can also relieve chronic pain, which lowers the risk of such intervention even more.”

Your Mitochondria Need Niacinamide

Niacinamide, also known as nicotinamide, is a form of niacin (vitamin B3) that plays a vital role in energy metabolism. 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.

Niacinamide at a dose of 50 milligrams (mg) three times per day will provide the fuel for the rate limiting enzyme for NAD+, NAMPT. Niacinamide also has potent antiobesity effects, can help prevent neurodegeneration and heart failure, and reverse leaky gut.

Niacinamide may also 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,” writes Peat’s student Georgi Dinkov, a bioenergetic researcher.¹¹

I recommend getting niacinamide in powder form because the lowest available dose in most supplements is 500 mg, and that will decrease NAD+ due to negative feedback on NAMPT, which is the opposite of what you're looking for. Niacinamide will only cost you about 25 cents a month if you get it as a powder. Typically, 1/64 of a teaspoon of niacinamide powder is about 50 mg.

I also recommend taking one aspirin tablet daily. Aspirin plays a role in mitochondria function¹² and also has other health benefits. Importantly, it helps increase the oxidation of glucose as fuel for your body while inhibiting the oxidation of fatty acids, specifically **linoleic acid** (LA). Dinkov adds:¹³

“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.”

Why Avoiding LA in Ultraprocessed Foods Is Important for Pain Relief

Lowering your LA is the single most important strategy you can take to not only lower reductive stress in your mitochondria but improve your overall health, including relief of chronic pain. LA is an omega-6 fat found in the vegetable oils and seed oils common in most ultraprocessed foods.

The main reason why excess LA causes disease is that it prevents your mitochondria from working well. Mitochondria produce most of your cellular energy in the form of ATP, and without ATP, your cells cannot function and repair themselves normally.

Polyunsaturated fats (PUFAs) such as LA are easily damaged by oxygen in a process called oxidation,¹⁴ which triggers the creation of damaging free radicals.¹⁵ These, in turn, give rise to advanced lipoxidation end products (ALEs)¹⁶ and in the case of omega-6 fats, oxidized LA metabolites (OXLAMs).^{17,18}

These ALEs and OXLAMs then go on to cause mitochondrial dysfunction, which is a hallmark of most chronic disease. In addition to oxidation, inflammation and mitochondrial dysfunction, processed seed oils can also inhibit cardiolipin, an important fat in the inner membrane of your mitochondria.

Cardiolipin is important because it influences the structure of the cristae inside your mitochondria, which is the area where energy production occurs. If cardiolipin is damaged, then the complexes will not be close enough together to form supercomplexes, and thus the mitochondrial energy production will be impaired.

Cardiolipin also works like a cellular alarm system that triggers apoptosis (cell death) by signaling caspase-3 when something goes wrong with the cell. If the cardiolipin is damaged from oxidative stress due to having too much LA, it cannot signal caspase-3, which means apoptosis does not occur.

As a result, dysfunctional cells are allowed to continue to grow, which can turn into a cancerous cell. The type of dietary fat that promotes healthy cardiolipin is omega-3 fat, and the type that destroys it is omega-6, especially LA.

The good news is that dietary changes can improve the composition of fats in your cardiolipin in a matter of weeks, or even days. So, even though it will take years to lower your total body burden of LA, you will likely notice improvements well before then.

How to Optimize Your Mitochondrial Function

To optimize your mitochondrial function, you want to avoid LA as much as possible and increase your intake of omega-3s. Primary sources of LA include seed oils used in cooking, ultraprocessed foods and restaurant foods made with seed oils, condiments, seeds and nuts, most olive oils and avocado oils (due to the high prevalence of adulteration with cheaper seed oils).

Animal foods raised on grains, such as conventional chicken and pork, are also high in LA. Another major culprit that destroys mitochondrial function is excess iron – and almost everyone has too much iron. You can learn more about the [health risks of excess iron](#) in my interview with Christy Sutton, D.C. The most effective way to lower your iron is to donate blood two to four times a year.

As mentioned, I also recommend taking 50 mg of niacinamide three times per day. It's also 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 – and felt – within two to three weeks.

Sources and References

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