

# Niacin + Melatonin Support Metabolic Health

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## STORY AT-A-GLANCE

- › Niacin and melatonin have a unique effect on adiponectin, a peptide secreted by fat cells that plays a role in obesity-related diseases and has a direct action on the liver, skeletal muscle and vasculature
- › Niacin helped reduce obesity in an animal model and in one pilot study reduced abdominal fat by an average of 27% in participants; melatonin deficiency also correlates with obesity, and supplementation has led to significant weight loss in treatment groups
- › Niacin can reduce pro-inflammatory cytokine expression and has an anti-inflammatory effect, properties which some experts believe may help reduce the severity of COVID-19
- › Melatonin influences circadian rhythm and the immune system; it also reduces inflammation and is an antioxidant; one group of scientists called it a "silver bullet" in treating COVID-19 patients

Niacin is also called vitamin B3. It's a water-soluble vitamin that's found naturally in some foods. It can also be purchased as a supplement. Recent studies have shown that niacin plays a role in an active metabolism and may help prevent severe COVID-19.

Niacin is a precursor to nicotinamide adenine dinucleotide (NAD<sup>+</sup>), which is used to catalyze more than 400 enzymatic reactions in the body.<sup>1</sup> NAD<sup>+</sup> is necessary for genome stability and the control of genetic expression.

Once NAD<sup>+</sup> has been formed, it can be altered to form other necessary compounds such as nicotinamide adenine dinucleotide phosphate (NADP) and nicotinamide

adenine dinucleotide (NADH). The vitamin also helps convert carbohydrates into glucose and is part of the process in making several steroid hormones.<sup>2</sup>

It's rare to develop an outright deficiency unless you suffer from an underlying medical condition that reduces your absorption in the gastrointestinal tract.<sup>3</sup> Although it's available as a supplement, when taken in large doses there are several side effects that can be uncomfortable. One of those side effects is commonly known as a niacin flush.<sup>4</sup>

The side effect is so uncomfortable that many people use the niacinamide form as it does not produce the flushing side effect. However, when taken to affect cholesterol levels, niacinamide is not effective.<sup>5</sup> Symptoms of the niacin flush include burning, itching or tingling sensation.

The reaction goes away as the body builds up a tolerance; however, drinking alcohol with niacin makes the flush reaction worse.<sup>6</sup> While it is irritating, and sometimes alarming if you don't expect the effect, a niacin flush is nonetheless harmless.

## **Niacin and Melatonin Combination Improve Metabolism**

Adiponectin is secreted by adipocytes (fat cells) and plays a role in obesity-related diseases such as Type 2 diabetes and cardiovascular disease.<sup>7</sup> The peptide has a direct action on vasculature, liver and skeletal muscle. Data show that it has anti-inflammatory, anti-atherogenic and insulin sensitizing effects, which can help reduce body weight.

Data also show that adiponectin levels in people with coronary artery disease are lower and the peptide modulates endothelial function and inflammation.<sup>8</sup> Data has also shown it helps ameliorate hyperglycemia and hyperinsulinemia without weight gain, which led to the peptide being tested in animal models for obesity.

One pilot study<sup>9</sup> in 2002 evaluated the effects of niacin against abdominal fat and found after one year, 81% of those taking 3,000 mg a day reduce their intra-abdominal fat by an average of 27%. Animal studies<sup>10</sup> demonstrated that the administration of niacin attenuates obesity by increasing adiponectin.

Animal models have also demonstrated that niacin can reduce proinflammatory cytokines expression and has an anti-inflammatory cytokines effect. A second animal study<sup>11</sup> published two years later found similar results that suggested niacin “exerts beneficial effect on adiposity, glucose tolerance and insulin sensitivity, and plasma lipids, and that it specifically modulates the level of serum adiponectin under obese condition.”<sup>12</sup>

One animal study published in The FASEB Journal<sup>13</sup> evaluated pathways niacin may use to maintain energy homeostasis. The researchers bred mice deficient in the niacin receptor GPR109A. A high-fat diet induced obesity, which they found did not occur in wild-type mice who were treated with niacin.

Additionally, they found that the niacin triggered thermogenic activity in brown and white fat tissue and the mice treated with niacin had a decrease in the absorption of fatty acids and sterols in their intestinal tract.

Data have also shown that melatonin deficiency appears to correlate with obesity<sup>14</sup> and in a human study melatonin supplementation appeared to regulate adiponectin activity leading to significant weight loss in the treatment group.

When melatonin supplementation was evaluated in 56 postmenopausal women,<sup>15</sup> the researchers found that melatonin supplementation contributed to a significant improvement in the quality of sleep and in body weight reduction. This led to a recent animal study<sup>16</sup> in which researchers evaluated the combination of niacin and melatonin on obesity.

The results of the animal study were encouraging as they found the effects of melatonin and niacin supplementation, in addition to treadmill exercise, resulted in weight loss after just 10 days. Weight loss was greater in the melatonin and niacin group than in the niacin only group and these two groups experienced greater weight loss than the control group.

## **Potential Effect Niacin May Have on COVID Infection**

The anti-inflammatory effects of niacin and the effects it has on cytokine have led to several papers postulating the role that niacin may play against COVID-19. Additionally, there are two more studies in clinical trials with anticipated completion dates of December 2021 and June 2022.

One study<sup>17</sup> is evaluating the potential use of nicotinamide riboside in patients who have COVID-19 to protect kidney function and the second<sup>18</sup> is using a form of vitamin B3 to determine if it reduces the severity of the disease. A third study is investigating niacin and COVID in the elderly.<sup>19</sup> Since the start of 2020, three papers have been published evaluating the potential effectiveness of niacin against COVID-19.

One paper published in *Maturitas* was a collaboration between scientists in Australia and the United Arab Emirates. The scientists postulated that the effect B vitamins have on the immune system and immune competence may make it a useful adjunct as a treatment strategy and possible prevention. They wrote:<sup>20</sup>

*“Vitamin B assists in proper activation of both the innate and adaptive immune responses, reduces pro-inflammatory cytokine levels, improves respiratory function, maintains endothelial integrity, prevents hypercoagulability and can reduce the length of stay in hospital.*

*Therefore, vitamin B status should be assessed in COVID-19 patients and vitamin B could be used as a non-pharmaceutical adjunct to current treatments.”*

The paper goes on to detail how each of the B vitamins may help manage some of the symptoms from COVID-19, including how niacin is a building block of NAD and NADP, which are vital to combating inflammation.<sup>21</sup> One lab study<sup>22</sup> published in late 2020 analyzed niacin as a potential treatment for patients with colorectal cancer who may have an increased susceptibility to COVID-19.

They demonstrated that niacin had molecular functions that could help treat patients with colorectal cancer who had COVID-19, but the results were not validated in humans, so the researchers recommended further investigation to confirm the potential use.

Recently a paper<sup>23</sup> written by Dmitry Kats, Ph.D., focuses specifically on niacin and has raised the question about whether it may be a crucial player in the disease process.

A marked elevation of proinflammatory cytokines has been blamed for a chain of events that lead to multiple organ failure and death. Potentially controlling these cytokines could reduce the downstream damage. NAD<sup>+</sup> plays an important role in controlling pro-inflammatory cytokines, and niacin is a building block of NAD. As Kats explains:<sup>24</sup>

*“NA [niacin] is in fact the only compound to readily produce NAADP if needed in acidic environments (as is characteristic to ensuing inflammatory disease pathology), which in turn provides a potential energy/H<sup>+</sup> pump-out action of its inverse, downstream kinetic (heat) energy inflammation to ultimately restore NAD<sup>+</sup> to normal, pre-inflammatory levels, as well as other inflammatorily-depleted cofactors and biochemical pathways towards a more thermodynamically homeostatic health status.”*

## **The Curious Case of Smokers Reduced Risk of COVID-19**

In early 2020, data showed that there were a low number of daily smokers who went on to be symptomatic with COVID-19.<sup>25</sup> This is curious, since COVID-19 begins primarily as a respiratory condition, and smoking is well-known for its harmful effects on the lungs.

However, if this is considered in light of niacin, an insufficiency of niacin may increase the risk of severe disease. Interestingly, nicotine and niacin are analogues – meaning they have similar means by which they work.<sup>26</sup> In fact, successful nicotine addiction detoxification uses niacin to help replace nicotine in the body.<sup>27</sup>

This relationship may also help explain how teenagers become addicted so quickly to smoking. One researcher postulated that if a teen’s diet is insufficient in niacin, it would increase the body’s craving for tobacco.<sup>28</sup> According to the National Institutes of Health Office of Dietary Supplements<sup>29</sup> the recommended daily allowance for niacin is 16 mg for men and 14 mg for women who are not pregnant or lactating.

One serving of beef liver contains 14.9 mg, which meets a woman's requirement. Otherwise, to meet the daily requirement, a person would need to eat two servings of chicken, or two servings of salmon, or 3 servings of ground beef or 3 cups of brown rice. One medium potato contains just 2.3 mg, and one slice of whole wheat bread contains just 1.4 mg.<sup>30</sup>

These may be sufficient amounts to avoid pellagra, which is a severe niacin deficiency that can cause neurological symptoms and progress to paranoid and suicidal behaviors with auditory and visual hallucinations.<sup>31</sup> Left untreated, pellagra can lead to death. However, it is easy to see how dietary intake may lead to chronic insufficiency.

According to Kats, the downstream effect of niacin is appropriate calcium signaling, which is responsible for inhibiting SARS-CoV-2 from infecting a cell and for driving it out of an already infected cell.<sup>32</sup> The process is regulated by nicotinic acid adenine dinucleotide phosphate (NAADP), which is generated from NADP.<sup>33</sup>

Niacin is a precursor to NAD, which can be altered to NADP. So, without enough niacin, your body cannot make enough NAADP that affects calcium signaling and may therefore increase the risk of severe COVID-19.

## **Melatonin Helps Protect Brain Cells During COVID Infection**

The combination of melatonin and niacin may also have added benefits if you're sick with COVID-19. The Frontline COVID-19 Critical Care Alliance (FLCCC) also recommends the use of melatonin in their outpatient<sup>34</sup> and inpatient<sup>35</sup> treatment protocols.

In May 2020, a paper<sup>36</sup> written by a group of scientists from the U.S. and Spain strongly suggested that melatonin be considered for prophylaxis or treatment of SARS-CoV-2. Dr. Paul Marik was one of those scientists.

Marik had developed a treatment protocol for sepsis with outstanding results,<sup>37</sup> and later was part of the team of critical care doctors who developed the IMASK and MATH+ protocols.<sup>38</sup> Other groups of doctors were also questioning whether melatonin may be useful in treating COVID-19.

More specifically a group from Turkey<sup>39</sup> proposed using melatonin in the elderly as it influences circadian rhythm, cardiovascular function and the immune system. Researchers know that melatonin levels decline with age, which is also associated with age-related diseases. They postulated that for this reason melatonin supplementation may be beneficial in treating older adults.

In December 2020, a team of scientists from Buenos Aires and the University of Toronto, Canada, collaborated on a paper<sup>40</sup> suggesting that there was a significant therapeutic potential for melatonin to “counteract the consequences of COVID-19 infections.”<sup>41</sup>

The writers postulated that melatonin has unique and wide-ranging effects as an anti-inflammatory agent, antioxidants and immunomodulatory compound and could be the “silver bullet” in treating COVID-19 patients. Given at night, it could effectively reverse sleep disorders and help control delirium in some patients.

Melatonin is a known cytoprotector and has served in the past to combat several of the comorbidities associated with severe disease, including cardiovascular disease, diabetes and metabolic syndrome. Additionally, melatonin has neuroprotective properties that can potentially reduce the neurological sequelae documented in patients infected with COVID-19.<sup>42</sup>

Another paper<sup>43</sup> published in February 2021 in the International Journal of Molecular Medicine also calls for melatonin to be used as an adjuvant treatment after they present a short review aimed at profiling melatonin from several recent clinical trials.

## **Can Melatonin Reduce a Niacin Flush?**

Many people find a niacin flush challenging and uncomfortable. Yet, compliance with taking the supplement is necessary for it to be used at home for treatment or prevention. Interestingly, Kats has anecdotal evidence that taking melatonin with niacin helps to reduce, and in some cases eliminate, the symptoms of a niacin flush.

In a Twitter<sup>44</sup> thread — which is now deleted as Twitter has suspended his account — he described the combination protocol he has been using, which he calls “niatonin.” In it he

said he finds a 50-to-1 ratio of niacin to melatonin the right amount for him.

However, he cautioned that if you are groggy in the morning then you have had too much melatonin and not enough niacin. Likewise, if you have a flush reaction, then you have had too much niacin and not enough melatonin to balance.

He also advises, from anecdotal evidence, that those with long-haul symptoms may find relief by supplementing with melatonin and those who have had an injury or reaction from the shot may find relief using the combination of niacin and melatonin.

## Word of Caution

Just be careful, though, as using high-dose melatonin long term could be a prescription for disaster. This is because doses of over 5 to 10 mg are likely to draw out heavy metals like mercury and unless you are on a good detoxification program and using sauna regularly these heavy metals could cause biological damage.

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