

Melatonin as a Potential Treatment for SARS-CoV-2

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✓ Fact Checked

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STORY AT-A-GLANCE

- › More than 140 scientific studies suggest melatonin is a useful agent for treating SARS-CoV-2, according to research published in Cellular and Molecular Life Sciences
- › Melatonin was most often researched for its ability to suppress inflammation and the cytokine storm related to COVID-19
- › When people with COVID-19 were given melatonin, either alone or in combination with other treatments, severity of infection was reduced, death rate was lowered and hospitalizations were shortened
- › Early on during the pandemic, a number of physicians and researchers called for melatonin in the treatment of COVID-19, but it was largely ignored
- › Since melatonin is nonpatentable and inexpensive, there was little interest from the pharmaceutical industry or their government counterparts in promoting this compound

More than 140 scientific studies suggest melatonin is a useful agent for treating SARS-CoV-2, according to research published in Cellular and Molecular Life Sciences.¹ Despite this, and its known antiviral and anti-inflammatory effects, melatonin has received little attention as a countermeasure for COVID-19.

After reviewing the published literature related to melatonin and SARS-CoV-2/COVID-19 in November 2021, the research team found melatonin was most often researched for its ability to suppress inflammation and the cytokine storm related to COVID-19.² Use of

melatonin as a treatment for people infected with SARS-CoV-2 was another common theme.

Overall, the data provide the rationale that melatonin could be used as a prophylactic agent against COVID-19 as well as a tool for treatment. When people with COVID-19 were given melatonin, either alone or in combination with other treatments, severity of infection was reduced, death rate was lowered and hospitalizations were shortened.

“Melatonin’s ability to arrest SARS-CoV-2 infections may reduce health care exhaustion by limiting the need for hospitalization,” the researchers noted, adding that it’s also safe – “melatonin has a high safety profile over a wide range of doses and lacks significant toxicity.”³

Melatonin Shows Promise for Treating COVID-19

One reason why melatonin works as an anti-COVID-19 agent is due to its role against sepsis (blood poisoning). The researchers explained:⁴

“While SARS-CoV-2 infections are generally thought of as a pulmonary issue, the consequences of this infection transcend the respiratory system. Ultimately, this disease becomes systemic with the development of severe sepsis or septic shock leading to multiple organ failure which is the condition that commonly leads to death of SARS-CoV-2-infected patients.”

Sepsis is a life-threatening condition triggered by a systemic infection that causes your body to overreact and launch an excessive and highly damaging immune response. Melatonin has prevented death in newborns suffering from severe bacterial sepsis⁵ and also appears to reverse septic shock symptoms by:⁶

- Decreasing synthesis of pro-inflammatory cytokines
- Preventing lipopolysaccharide (LPS)-induced oxidative damage, endotoxemia and metabolic alterations

- Suppressing gene expression of the bad form of nitric oxide, inducible nitric oxide synthase (iNOS)
- Preventing apoptosis (cell death)

The Mitochondria Connection

Many people are not aware that only 5% of your body's melatonin — which is also a potent anticancer agent — is produced in your pineal gland. The other 95% is produced inside your mitochondria — provided you get sufficient near infrared exposure which is typically from sun on your bare skin. This is why vitamin D is more than likely a biomarker for sun exposure, which is intricately involved in melatonin production.⁷

As such, there's also a mitochondrial component as to why melatonin appears so crucial for fighting viral infections like SARS-CoV-2. In fact, COVID-19 could be classified as a mitochondria-related disease, the researchers noted. They explained:⁸

“Numerous inter-related factors conspire to enhance the cytokine storm and multiple organ failure associated with COVID-19 disease severity and mortality, including elevated sPLA2-IIA, development of pro-inflammatory M1 macrophages, activation of HIF-1 α , conversion to Warburg-type metabolism of immune cells, damage to mitochondria, massive release of cytokines, oxidative stress, etc. ... each of these actions have been shown to be counteracted by melatonin.

A center piece of this series of processes may be the alterations in mitochondrial physiology and the shift of glucose oxidation to the cytosol [one of the liquids found inside cells]. This change in glucose handling markedly alters the metabolism of the mitochondria, which is critical to limiting cellular dysfunction, resisting disease, and preventing organismal death.”

In healthy cells, melatonin synthesis in mitochondria occurs when the glucose metabolite pyruvate enters the mitochondria. Glucose is a six-carbon molecule and is

divided into two three-carbon molecules of pyruvate. Once the pyruvate is inside the mitochondria, it is subsequently metabolized into acetyl-coenzyme A (acetyl-CoA).

Acetyl-CoA is a required co-substrate for the intramitochondrial production of melatonin, which occurs in healthy cells but likely not cells that are highly inflamed. Further, the team reported, “when intracellular glucose metabolism is reprogrammed from the mitochondria into the cytosol, the mitochondria can no longer synthesize” acetyl-CoA, contributing to disease.⁹

“Thus, in the absence of local melatonin synthesis in infected cells, the loss of this locally produced potent endogenously generated anti-inflammatory and antioxidant agent, the mitochondria lose a major portion of their protection against reactive oxygen species, inflammatory cytokines, etc., leading to their dysfunction; this contributes to a weakening of the cells with an increased susceptibility to cellular destruction by SARS-CoV-2.

This would help explain the published data documenting the ability of melatonin to resist virus-related diseases, including that related to several different coronaviruses.”

Melatonin Is a Master Antioxidant

Melatonin is one of the most important antioxidant molecules. In the human body — aside from having direct antioxidant effects — it also stimulates the synthesis of glutathione and other important antioxidants like superoxide dismutase and catalase.

Melatonin increases glutathione through a genomic effect on the enzyme that regulates the synthesis of gamma glutamylcysteine synthase, the rate limiting enzyme in glutathione synthesis. Melatonin activates that enzyme.

Glutathione tends to be found in high concentrations in cells, although some is also found, to a lesser degree, in the extracellular space and the mitochondria. Melatonin's antioxidant effects are quite diverse but include preventing free radical generation by

enhancing the efficiency of the electron transport chain so fewer electrons leach onto oxygen molecules to generate super oxide antiradical.

Melatonin's antioxidant prowess may be one reason why it's a known suppressor of hypoxia-inducible factor-1 α (HIF-1 α), also known as oxygen sensing transcription factor. HIF-1 α is activated under conditions of systemic low oxygen, and patients with elevated HIF-1 α have increased risk of mortality and related severe cytokine release. Melatonin, as an HIF-1 α inhibitor, may further contribute to a reduction in lung damage and COVID-19 severity.¹⁰

Early Calls for Melatonin Largely Ignored

Early on during the pandemic, a number of physicians and researchers called for melatonin in the treatment of COVID-19. The Frontline COVID-19 Critical Care Alliance (FLCCC) recommends the use of melatonin in their I-Care early COVID treatment protocol.¹¹ In April 2020, a team from the U.S., Israel and Russia also suggested melatonin could reduce the severity of the pandemic, stating:¹²

"... by using the safe over-the-counter drug melatonin, we may be immediately able to prevent the development of severe disease symptoms in coronavirus patients, reduce the severity of their symptoms, and/or reduce the immunopathology of coronavirus infection on patients' health after the active phase of the infection is over."

In May 2020, a paper 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. At the time, they noted:¹³

"Melatonin's multiple actions as an anti-inflammatory, anti-oxidant, and anti-viral (against other viruses) make it a reasonable choice for use. Melatonin is readily available, can be easily synthesized in large quantities, is inexpensive, has a very high safety profile and can be easily self-administered."

Then, in October 2020, a group from Turkey proposed using melatonin as a treatment for COVID-19 in the elderly, as it influences circadian rhythm, cardiovascular function and the immune system.¹⁴ 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 part by preventing age-related oxidative stress.

In December 2020, a team of scientists from Buenos Aires and the University of Toronto, Canada, also collaborated on a paper suggesting there was significant therapeutic potential for melatonin to “counteract the consequences of COVID-19 infections.”¹⁵

The writers postulated that melatonin has unique and wide-ranging effects as an anti-inflammatory agent, antioxidant 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. They further noted:¹⁶

“[I]ndirect evidence points out to a possible antiviral action of melatonin by interfering with SARS-CoV-2/angiotensin-converting enzyme 2 association ... As a cytoprotector, melatonin serves to combat several comorbidities such as diabetes, metabolic syndrome, and ischemic and non-ischemic cardiovascular diseases, which aggravate COVID-19 disease.”

They even suggested melatonin has neuroprotective properties that can potentially reduce the neurological sequelae documented in patients infected with COVID-19.¹⁷

Later, in August 2021, researchers with Texas Tech University again called for melatonin as an early treatment option for COVID-19, explaining:¹⁸

“Although melatonin acts to fight early viral replication, the use of melatonin in patients with COVID-19 is not meant to be used as a cure but instead as an agent that equips the body to better fight viral infection.

This is demonstrated by the fact that in cases where the immune system is suppressed, melatonin has been found to stimulate the immune system, and in

cases where there is inflammation, it has been found to show an immunosuppressive effect.

In the case of COVID-19, reduction of the long-lasting inflammatory and oxidative effects of the virus by melatonin allows the patient's own immune system to properly respond to infection and recover more efficiently with a reduced recovery time."

Why Melatonin Was Overlooked for COVID

The authors of the featured study called melatonin's failure to attract widespread attention as a potential COVID-19 treatment "disappointing" and due, in part, to "lack of promotion of its therapeutic use for this disease by any influential group."¹⁹ Yet melatonin not only appears effective for COVID-19 but also costs up to 100 times less than prescription drugs indicated for the condition.

Specifically, they found that melatonin is at least twice as effective as remdesivir or tocilizumab for reducing COVID-19 inflammatory markers. While the drugs were approved by the FDA to treat COVID-19, melatonin was not. Why? It all boils down to money:²⁰

"Both drugs have notable side effects and are given intravenously. In contrast, melatonin has a high safety profile and can be taken orally or administered by any other route. Since melatonin is non-patentable and is inexpensive, the incentive of the pharmaceutical industry to support its use is lost. Finally, pharmaceutical drugs are sometimes enthusiastically advanced by individuals who stand to gain financially."

As for dosing, the trials involved in the featured study used total melatonin doses ranging between 2 milligrams (mg) daily and 500 mg daily, taken orally once per day or divided into multiple doses over a 24-hour period.

Other physicians have used a dose of 1 mg per kilogram of body weight. If you have symptoms of COVID-19, you could consider taking oral or sublingual melatonin 30 to 45

minutes before bedtime, first thing in the morning, at 10 a.m. and again at 4 p.m. Ideally, work with a holistic health care provider who can guide you on proper dosing.

Although it has a high safety profile, using high-dose melatonin long term could be risky, as doses over 5 mg to 10 mg are likely to draw out heavy metals like mercury from your body. Unless you're following a good detoxification program and using a sauna regularly, these heavy metals could cause biological damage.

While there are likely benefits to supplementing with oral melatonin, keep in mind that it also helps to optimize your body's own production. It's relatively simple and inexpensive, and at the same time you will help to optimize your vitamin D levels. Optimizing melatonin production begins with getting enough bright sunlight during the day since this helps to set your circadian clock.

As the evening approaches and the sun sets, you'll want to avoid artificial lighting. Blue light from electronic screens and LED lights is particularly problematic and inhibits the production of melatonin. If you do need lighting, use incandescent light bulbs, candles or salt lamps. The blue light from electronic screens can be counteracted by using blue blocking software or wearing blue blocking glasses.

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