

Melatonin and its Effects: The Truth Behind this Popular Supplement

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Abstract

Melatonin is a significant hormone secreted in the pineal gland of the brain that is primarily known for regulating the sleep-wake cycle. This sleep-wake cycle is affected by two processes known as process C for circadian and process S for sleep. Process C work as an endogenous clock driving the cycle's rhythm, and process S functions through a homeostatic sleep behavior that keeps up with the sleep and wakefulness acquired. The short-term consumption of melatonin as a supplement has been successful in treating sleep-related disorders of many kinds such as jet lag and delayed sleep phase syndrome. It is worth noting, there are many after-effects that can occur with melatonin consumption, such as short-term depression, dizziness, headaches, and irritability. Easy accessibility to melatonin supplementation can lead to *habit-forming side effects*, resulting in dependency. While there is a lack of information and studies on dependency, it can be underestimated, leading to complications in the side effects correlating with substance abuse. There is a lack of knowledge in users who do not have a general understanding on the exact duration of treatment. This can be uncertainty on whether supplements should be taken once for minor cases such as jet lag, or consistently for a period of time for major sleeping disorders. The goal of this study is to inform users of the possible effects that can come with taking melatonin supplements, because although already a naturally produced hormone, melatonin can alter users' body cycles in the long run.

Keywords: sleep-wake cycle, short-term consumption, lack of information

Methods

The initial interest for this study came from the constant misinterpretation of melatonin constantly being considered a drug, and not a hormone. As a hormone, melatonin is in charge of sending chemical messengers throughout the body in order to regulate the sleep-wake cycle. The sleep-wake cycle is a daily pattern responsible for determining the appropriate sleep and wake times, affected by physical, mental, and behavioral changes known as the circadian rhythms.

For this research, my information was found through a systematic review. This method allowed me to select and evaluate evidence in order to assess the results and derive conclusions. Specific keywords that were used included the following: "melatonin FDA banned," "melatonin supplementation dependency," "melatonin overdose case," among others. Regardless of searching through primary, secondary, academic, and medical sources, there was not enough research on melatonin supplementation as whole to find many results on these searches. "Melatonin FDA banned" was possibly one of the easier searches within Google Scholar, with a few switches in wording to "melatonin legality" or "melatonin illegal" and a few article searches. "Melatonin supplementation dependency" on the other hand, was quite difficult to

come across. Medical sources such as *BioMed Central* and *PubMed Central* hardly offered, if any, information on the specific correlation between melatonin and dependency. It rather cited about the relationship of melatonin to other sources such as tobacco, insomnia, and therapy, with information citing centralized around 2010 for *BioMed Central* and around 2015 for *PubMed Central*. "Melatonin overdose case" was also among the easier searches to find, with many records showing cases of users overdosing on melatonin supplements. *EBSCOhost* was among one of the sources used, but with only three databases, my information was retrieved from *PubMed*, which offered more articles on this topic. On both sites, information was cited back to 1997. This was something interesting to note due to the lack of released information on melatonin supplements.

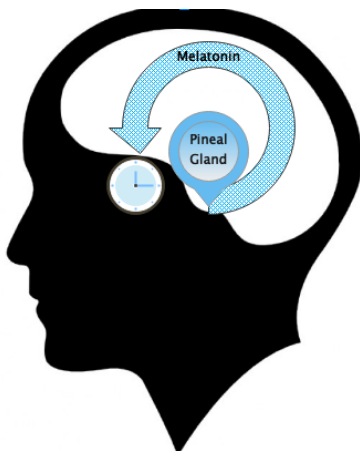
Looking for specific data, it could be said that 150 databases could have been looked through, but only about 20 were kept for potential information on the findings of melatonin and its effects. 150 databases were looked through for keywords, but not many actually contained information specific to melatonin, but rather the mention of the hormone.

Introduction

[Melatonin's anatomy and physiology] To understand the effects of melatonin, it is necessary to first understand what melatonin is and its significance. Melatonin is a naturally produced hormone in the body, which is responsible for sending chemical messengers throughout the body to coordinate specific functions. In melatonin's case, specific functions would be regulating the sleep-wake cycle. Melatonin is produced right above the center of the brain, in an area called the pineal gland, which is about the size of a pea. In order for melatonin to be able to carry out its functions, there is a process to the way it works. Melatonin works through the influence of light and dark detection with the eye retina. Light detection helps regulate the body's energy levels produced by serotonin—a neurotransmitter produced in the intestines and the brain that contributes to feelings of well-being and happiness. The circadian rhythm works as an internal clock scheduling the release of melatonin, releasing higher levels during dark detection and lower levels during light detection.

[The sleep-wake cycle] While melatonin has many functions, one of its most important contributions is helping regulate the sleep-wake cycle. This sleep-wake cycle is affected by two processes known as process C for circadian, working as an endogenous clock driving the cycle's rhythm, and process S for sleep, functioning through a homeostatic sleep behavior that keeps up with the sleep and wakefulness acquired. The sleep-wake cycle is responsible for producing and releasing melatonin at different rates throughout the day. Melatonin production tends to increase during the dark, but it is known to decrease when it is light.

Melatonin and the Sleep-Wake Cycle



[Supplementation] Melatonin has been studied since the 1950's, but it did not become a nutritional supplement until the 1990's. In 1958, Aaron B. Learner and his colleagues from Yale University first isolated this hormone. Melatonin obtained its name due to their studies in which the substance had the ability to lighten a frog's color. With easier accessibility to melatonin supplements within the United States than other countries, this supplement became popularized due to its effects on sleep, cancer, and other hormones. Melatonin's availability in supplement form allows users to treat short-term disorders. These short-term disorders can include jetlag and delayed sleep phase syndrome—a condition where delayed sleep causes difficulty in being able to wake up at the desired time. Consuming excessive melatonin can impact the natural circadian rhythm over time. One should keep in mind that dependency can arise not from consuming melatonin supplements itself, but from the side-effects of melatonin supplements that can be habit-forming. Dependency varies in definition and is often misinterpreted with addiction. The difference between them is that dependency is characterized by symptoms of tolerance and withdrawal, addiction is the change in behavior caused by brain biochemical changes due to substance abuse.

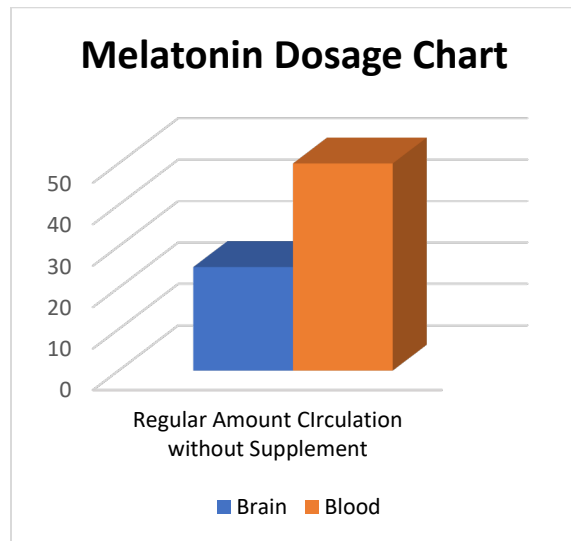
By researching the relationship of melatonin to its effects, impactful results were found both mentally and physically. Studies demonstrated that there is not more than two years' worth of collected innovative research. Not finding long-term research made it harder to identify melatonin's long-term impact on users, whether it be beneficial or detrimental.

Results

Melatonin Availability Chart

United States	United Kingdom	Germany
<ul style="list-style-type: none">•accessibility: over-the-counter•legality: legal•form: liquid, spray, chewables and tablets	<ul style="list-style-type: none">•accessibility: prescription needed•legality: known as <i>Circadin</i>, legal but with age and health requirements•form: tablets	<ul style="list-style-type: none">•accessibility: prescription needed•legality: known as <i>Circadin</i>, legal but must be over 55 years old•form: typically tablet, but form can change

Melatonin supplements are available in different forms including liquid, spray, chewable and tablets. Supplementation availability does vary, and while there is easy access to melatonin supplements in the United States such as an over-the-counter option found at local drug stores, there are other countries that limit it (as seen on the Melatonin Availability Chart above). Melatonin supplements are classified as dietary and therefore not FDA approved under the Dietary Supplementation Health and Education Act of 1994. As mentioned, because of the easy access to melatonin in some countries, it is necessary to keep in mind the recommended dosages versus actual dosages.



While studies show that recommended dosages vary from 0.1 to 5 milligrams, recorded dosages have shown to greatly exceed this amount. A case recorded a 66-year old man consuming melatonin supplements the night before his prostate surgery in hopes of aiding him in relaxation and a proper night's sleep. This case is significant because the user ran the possibility of affecting or postponing his surgery the following day due to upping the average dosage of 5mg, to 24mg for relaxation. Another case indicated that a 4-year old girl accidentally swallowed 39 milligrams of melatonin in liquid form, greatly surpassing the recommended amount. Sleep routines are recommended for children as melatonin supplements are not exactly sleeping pills, but children with neurodevelopmental disorders among other children are often found consuming melatonin supplements. If melatonin supplementation is used, it is recommended to be taken at extremely low dosages with the consultation of a pediatrician, for a very short period of time. While this case resulted in no symptoms shown on the patient, there are a variety of

factors that may have affected these results, such as age and lack of brain development.

There were notable differences in both the brain and blood before melatonin supplementation consumption. According to "Melatonin the "light of night" in human biology," the average melatonin in the brain varies from 10 to 60 pg/ml. It is shown that melatonin peaks in early childhood but decreases in older people producing a negligible amount of melatonin. Due to these statistics, the average melatonin in the brain for childhood to older people was considered at 25 pg/ml (as seen on the Melatonin Dosage Chart above). While studies show that different tissues or body fluids contain a range of melatonin concentrations, according to "Significance of High Levels of Endogenous Melatonin," the average melatonin in the blood is about 50pg/ml.

Because of a lack of studies, and an unknown amount of melatonin supplementation users, there was an inability in calculating the exact amount of melatonin circulating in the brain and blood once the supplement was consumed. Results did show that serum melatonin concentrations in the body were 10 to 100 times higher than the usual nighttime peak.

Melatonin Side Effects Table

Short-term side effects	Long-term side effects
<input type="checkbox"/> dizziness	<input type="checkbox"/> depression
<input type="checkbox"/> headaches	<input type="checkbox"/> nightmares
<input type="checkbox"/> nausea	<input type="checkbox"/> low blood pressure

While melatonin is a natural compound that circulates in the body, like a drug, studies show that it is dependent. Dependency does not arise from the consumption of melatonin but rather from the habit-forming side effects of melatonin consumption, which are viewed as addictive. Melatonin is often considered a drug, and this is related to the constant misunderstanding of the differences between dependency and addiction. Dependency is characterized by symptoms of tolerance and withdrawal, but addiction is characterized by changes in behavior caused by biochemical changes in the brain due to constant substance abuse. Because dependency is underestimated, it can result in complications correlating to melatonin supplementation due to over-dosage or inability to correctly measure the body-to-supplement dosage ratio. It is difficult to calculate the necessary dosage according to each body type, and it is especially difficult to self-change the dosage increments throughout time as the user's body becomes familiar

with the supplement. This often leads to dependency due to the easy accessibility of melatonin supplements, at least all over the United States, and in other countries. It is recommended that melatonin dosages start out small, and as the body becomes more familiar with it, one can slowly increase the supplement intake. This will help the body familiarize with the supplement and help a user rest without obtaining full side effects. The recommended melatonin dose lasts about 5 hours in the body, but overuse of this supplement can cause a disruption in the circadian rhythm. By disrupting the circadian rhythm, this can lead to daytime sleeping.

Dose-dependent effects have not been completely evaluated in users consuming large doses of melatonin supplementation over long periods of time, therefore, they cannot be accounted for due to lack of research. Hypotheses are based on short-term side effects, which include dizziness, headaches, and nausea. There is a higher possibility of experiencing less common side effects if more melatonin supplementation than recommended is consumed during a longer period of time. While there is no specific time frame to define long term, there are only up to two years' worth of research in this topic, displaying the differences between short term and long-term side effects during this time gap (as seen on the Melatonin Side Effects chart). The more intense side effects that can occur during a long-term consumption include nightmares, depression, and low blood pressure.

Discussion

When considering taking melatonin as a supplement, it is important to keep in mind both the positive and negative effects that could arise. Doctors are so quick to recommend or prescribe melatonin supplements for mild uses, compared to other aids. Other prescribed sleeping aids can be more dependent and even harmful. Temazepam, for example, is a sedative treating insomnia, but the user does run the risk of suffering paranoid or suicidal ideation, and impaired memory, judgement and coordination, all effects far more harmful than melatonin supplementation.

Melatonin supplementation has the possibility of helping with cell protection. This includes the involvement of modifying the immune response and blood cell formation. Melatonin also has a lot of therapeutic potential. While there are not many studies to confirm this and it is just a mere possibility, melatonin supplements are being reinforced into cancer therapies for therapeutic effects to reduce the side effects of chemotherapy especially or radiation. Melatonin supplements are not just used for sleeping, but also for migraines, attention deficit hyperactivity

disorder known as (ADHD), and irritable bowel syndrome (IBS).

The lack of long-term research with melatonin supplementation limits not only researchers' advances but also users' knowledge. Less research leading to unknown effects in the long run makes it more difficult to identify on whether effects will be beneficial or detrimental, among other factors. Supplementation can also lead to habit forming side effects that result in dependency. Considering the short-term effects of melatonin, it leads to consider the detrimental effects of using melatonin supplements long-term wise.

Concentration from natural foods and varying dosages are important factors when considering melatonin supplements. This uneven concentration leads to an uneven distribution and a difference in the biophysical dynamic features of the foods. Because melatonin concentration varies in plants and animal foods, this leads to unknown amounts circulating in the body after melatonin consumption. There is not easy access or enough proven data calculating how much melatonin is appropriate to take when considering all health factors. It is necessary to calculate self-changing dosages as the body becomes familiar with the supplement.

The main purpose of learning about the uses of melatonin along with the possible side effects that can be either beneficial or detrimental in the long run is for the reader or user to gain awareness when it comes to consuming melatonin supplementation. There is very little information and studies, with so many possible unknown risks that can come with melatonin consumption if consumed long-term. While there is not a lot of long-term research to consider, it is necessary to keep in mind both the positive and negative side effects that can be found affecting users both physically and mentally.

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