



## The relationship between melatonin and sleep quality and its weight loss benefits

Alexandre Carli Pinto <sup>1</sup>, Danilo Everton Cunha Cavalcante <sup>2</sup>, Etianne Andrade Araújo <sup>3</sup>, Francione Moreira Cabral <sup>4</sup>, Jhonatas Mota Santos <sup>5</sup>, Kaline Viana Costa <sup>6</sup>

<sup>1</sup> University of Pernambuco, Recife, Brazil.

<sup>2</sup> Federal University of Maranhão, General Surgery and Medical Clinic, São Luis, Maranhão, Brazil.

<sup>3</sup> Etianne Bartz Institute, Fortaleza, Ceará, Brazil.

<sup>4</sup> Porto Velho Hospital, Rondônia, Brazil.

<sup>5</sup> State University of Pará, Brazil.

<sup>6</sup> Medical Diagnostics Center, São Luís, Maranhão, Brazil.

Corresponding Author: Dra Etianne Andrade Araújo. Etianne Bartz Institute, Fortaleza, Ceará, Brazil.

Email address: etianneandrade@hotmail.com

DOI: <https://doi.org/10.54448/ijn2137>

Received: 10-16-2021; Accepted: 10-21-2021; Published: 10-25-2021.

### Abstract

Melatonin is an endogenous substance easily found in the body. It is conceptualized as a hormone, derived from serotonin, synthesized by the pineal gland during the night period. As a hormone, melatonin has several functions, such as immunomodulation, antioxidant, anti-inflammatory, and antitumor, however its most compliant function is the control of the circadian rhythm, in addition to regularizing seasonality. Sleep is one of the primordial needs of the human being, after a period of physical and mental activities, it has a fundamental role to relax and re-establish the organism for a new cycle of activities. Thus, melatonin acts as a metabolism regulator influencing the quality of life, and its effectiveness in inducing sleep has led pharmaceutical companies to launch its synthetic version, widely sold as a supplement in some countries such as the United States and Europe. To analyze the importance of melatonin in the regulation of sleep, as well as to characterize its functions in the body that contribute to weight control. The work methodology consisted of a literature review, carried out through previously published research studies. Based on the literary subsidies that supported this research, it is concluded that the benefits achieved with the use of melatonin encompass the alignment of the sleep cycle and contribute to weight control, which may influence weight loss, as well as in other areas of the body.

**Keywords:** Melatonin. Sleep disorders. Weight loss.

Biological rhythm.

### Introduction

Melatonin is a hormone naturally produced by the pineal gland, and one of its basic functions is to induce sleep, also, it is linked to the circadian cycle, that is, the way the body organizes its functions during the sleep-wake cycle [1,2]. By regulating sleep functions throughout the body, most organs have receptors for melatonin [3]. With a mechanism of action not yet fully elucidated, the most accepted theory is that melatonin is capable of inducing sleep by reducing body temperature, by acting on receptors in peripheral blood vessels, determining vasodilation. In addition to acting on receptors in the hypothalamic sleep center. Unlike benzodiazepines, it does not lead to a hangover effect [4,5].

The synthesis of melatonin in the body occurs from serotonin followed by a sequence of reactions "conversion of tryptophan into serotonin; conversion of serotonin to N-acetylserotonin (mediated by aryl-alkyl-amine-N-acetyltransferase); conversion of N-acetylserotonin to melatonin (mediated by hydroxy-indole-O-methyltransferase)" [6]. Sleeping is something natural and essential to human beings, as necessary as food and that is why we should reflect on the importance of sleep in the routine we establish daily. Some studies show that people who accumulate the habit of not getting enough sleep and not sleeping well, increase the risk of developing diseases such as hypertension, dyslipidemia, acute myocardial infarc-

tion, panic syndrome, low immunity with frequent colds, among others [7].

Thus, it is possible to see that the practices of healthy habits in relation to sleep, as well as the diagnosis of sleep disorders and adequate treatment, can improve the quality of life, bringing benefits to the individual's health and well-being. Among the benefits related to sleep quality, weight loss is included, which becomes more efficient when the regulation of the circadian cycle is balanced, with melatonin being a great ally in this process [8].

The main objective of this study was to analyze the effects of melatonin on sleep quality and the benefits that this relationship can bring, highlighting its collaborative action in weight loss, weight control and quality of life, as well as addressing melatonin as a regulator of sleep and is justified by the importance of maintaining healthy habits so that this behavior is established naturally without the interference of therapeutic alternatives and, finally, so that it can trigger balance in the body's functions.

## Methods

This study was carried out from an integrative non-systematic bibliographic review in the PubMed, Scielo, and books database including articles from 2000 to 2021, to relate the effects of melatonin on sleep and the benefits that this relationship can bring to the body, collaborating with slimming and weight control. The following descriptors were used as search terms individually or in association: Melatonin, sleep disorders, circadian rhythm, weight loss, biological rhythm.

## Results and Discussion

### The restoration of sleep quality through melatonin regulation

Among the several actions of melatonin already proven, the following stand out: immunomodulatory (acting on lymphocytes, cytokines, among others), antiinflammatory (inhibiting prostaglandins and regulating COX-2), antitumor (inhibiting mitosis and suppressing the reuptake of linoleic acid, thus regulating estrogen receptors), antioxidant (regulating pro-oxidants involved in the synthesis of nitric oxide and lipoxygenases), and chronobiological (regulating biological rhythms) [7,9-11].

Silva, Pereira, and Kashiwabara explain that as melatonin is secreted at night, it can act in the regulation of the circadian rhythm of sleep and decrease body temperature [12]. Its plasma concentration is so low that it may be undetectable in many patients. However, minimum daily exogenous doses of melatonin can induce

sleep in healthy individuals, in addition to acting to improve sleep quality, being a substance currently studied for the treatment of insomnia. However, it is important to note that melatonin is erroneously called the sleep hormone. It could be the "hormone of darkness", providing the organism with the information that it is night. As proposed by Arendt and Skene, melatonin is a chronobiotic, a substance that synchronizes intrinsic biological rhythms [13]. Although the central nervous system - CNS regulates most circadian rhythms in mammals, directly or indirectly, many organs/tissues in the body can generate circadian rhythms independently or not from the CNS [10,13]. These peripheral circadian oscillators are found in cells from other regions of the CNS, as well as of the blood, adipose tissue, liver, heart [12,14,15].

The circadian rhythm can be defined as how our organism adapts to the duration of the light period (day) and the dark period (night), to synchronize physiological functions with the duration of a day (approximately 24 hours). Melatonin, in turn, is a hormone linked to the circadian cycle, that is, the way the body organizes its functions when we are awake and during sleep. The substance begins to be produced in the pineal gland in the early evening to help the body prepare for sleep. It reaches its maximum level when we are sleeping. With the rising of the sun and the return of light, the gland reduces the production of melatonin, signaling that it is time to wake up [15].

As mentioned at the beginning of this research, sleep is fundamental to the body, in addition to playing a fundamental biological role in memory consolidation, binocular vision, thermoregulation, energy conservation and restoration [15], and restoration of brain energy metabolism [16]. Due to these important functions, sleep disturbances can cause significant changes in the individual's physical, occupational, cognitive, and social functioning, in addition to substantially compromising the quality of life. Normal sleep varies throughout human development in terms of duration, distribution of stages, and circadian rhythm [17,18]. Variations in the amount of sleep are greater during childhood, decreasing from 16 hours a day, on average, in the first days of life, for 12 hours in the sixth month of life. After that age, the child's sleep time decreases 30 minutes a year until the age of five.

In adult life, the quantity decreases and the sleep cycle varies depending on age and the interference of external factors [16]. With advancing age, there are losses in the duration, maintenance, and quality of sleep, as the production of melatonin also decreases with advancing years and influences the circadian rhythm [19]. Pain, the use of medications, and different clinical conditions are examples of factors that can affect the quantity and quality

of sleep, especially among the elderly, who are more prone to these conditions [20].

Given the importance of circadian rhythm and sleep quality for a healthier and more quality life, the specialized literature classifies sleep-related disorders including four organized groups, including sleep disorders related to circadian rhythm, which include seven disorders associated with daytime hypersomnolence, such as rapid time zone change syndrome (jet lag) and sleep disorder caused by shift work [21,22]. However, according to studies by Roth [23] the most prevalent disorders in the general population are insomnia and obstructive sleep apnea syndrome, which is closely related to overweight and obesity. Still, on sleep disorders related to the circadian cycle, the classification described below on a scale from the smallest to the largest can be mentioned [24].

#### ✓ Sleep phase delay

Several clinical situations are associated with delays, advances, or disturbances in the physiological sleep rhythm, and in these cases, melatonin has good therapeutic action. The delayed sleep phase is a condition that expresses itself more in adolescence as a tendency to sleep late and wake up late. In some cases, parents confuse these symptoms with insomnia or daytime sleepiness. Exposure to the sun in the morning and the use of melatonin a few hours before the desired sleep time can restore regular sleep schedules.

#### ✓ Sleep phase advancement

Phase advancement is the opposite of the previous syndrome and is often seen in the elderly. These individuals go to bed very early and wake up in the early morning hours, causing a family disturbance. Exposure to light in the late afternoon usually prolongs the onset of sleep to more desired times.

#### ✓ Jet lag

People who move within a time zone may resent hormonal and body temperature changes that do not accompany socially desired wakefulness and sleep. There is usually a physiological tendency to delay the sleep phase so the westward shift is much better tolerated. Jet Lag becomes worse with older age when adaptation mechanisms are reduced. Fatigue, body aches, headache, irritability, and cognitive changes can occur despite the individual feeling awake. Adjusting your body temperature may take a few days. Various measures such as light exposure are used to minimize these symptoms. The use

of melatonin one hour before bedtime facilitates adaptation to jet lag.

#### ✓ Shift work

Workers who need to use a shift system are potentially subject to reduced sleep hours, poor sleep quality, and its implications, that is, fatigue, irritability, and cognitive changes. Men are more exposed to this type of work and changing shifts with reduced hours of sleep is potentially associated with drowsiness and serious accidents. Stress as a chronic injury can play a role in the appearance of pathological conditions and this is still a subject that needs further studies. Several work situations such as transport control, telephony, and hospital work require the shift system. Controlling exposure to light and the use of melatonin are some of the therapies used in this situation. Some studies show benefits after the use of melatonin in workers who are exposed to the rhythm of shifts, but this evidence is still controversial. Measures such as wearing sunglasses when leaving work and identifying individual problems should be encouraged, given that different jobs use a system of varied shifts [25,26]. Given the above, it is understood that sleep interferes with the quality of life and, therefore, it is essential to maintain a balanced circadian rhythm, seeking to maintain a routine of daytime and nighttime habits that respect the body's conditions and ensure adequate hours of sleep.

### The physiological role of melatonin

Melatonin is conceptualized as a non-steroidal in the dopaminergic hormone, derived from serotonin, produced by the pineal gland, being a substrate of tryptophan. However, for its production to occur in the body, stimulation of dark environments is necessary, as the retinal ganglion cells assimilate information from the external environment and carry it through the retinohypothalamic pathway, distributing it within the suprachiasmatic (SQN) and paraventricular nuclei of the hypothalamus. Subsequently, the information goes to the spinal cord in the preganglionic sympathetic neurons that will lead their axons to the superior cervical ganglia, so that through their coronary nerves and carotid branches that appear massively in the pineal gland can carry the message and make it possible the body through this mechanism to regulate its circadian cycle and the synthesis of melatonin [24].

Thus, it is understood that melatonin is derived from the metabolism of tryptophan, it can be either lipophilic or hydrophilic, and can be transported in body fluids such as plasma and cerebrospinal fluid (CSF) or bound to proteins such as albumin. Melatonin is even capable of modulating the transmission of calcium-dependent signals as a result of

its fixation to calmodulin and is controlled by the adenylyl-cyclase and phosphodiesterase system [25,26].

### Melatonin as a pharmacological alternative

Considering the benefits that endogenous melatonin (N-acetyl-5-methoxytryptamine) promotes to the body, the pharmaceutical industry already offers an exogenous version that is widely used in insomnia treatments, among others. Exogenous melatonin is already widely considered a pharmacological option in sleep disorders such as changes in circadian rhythm (jet lag, sleep delay syndrome, or advance) as well as in several neurological pathologies (depression) in which there is a decrease of the endogenous hormone [3]. The difference between treatment with melatonin and other common hypnotics is that there are no substantial changes in sleep architecture, unlike benzodiazepines, melatonin produces effects in stages 3 and 4 of sleep [23,24], with no record of the "hangover" effect, common with the use of benzodiazepines [25].

Research on the use of melatonin in children with multiple neurological disorders, which include severe insomnia, showed a significant improvement in the pattern and increase in sleep duration. Furthermore, children with normal development and chronic insomnia also improved with treatment with melatonin, but its use in medical practice, especially in children, needs further studies [15]. Another pathology treated with exogenous melatonin was refractory epilepsy, which manifested an exogenous response to the use of the hormone, with considerable benefit in the patients' electroencephalographic pattern, in addition to migraine, Parkinson's, and other diseases [26].

The benefits of melatonin are diverse and contribute to the most varied spheres of the body, weight loss can also be related to the synthesis of this hormone since it activates the molecules responsible for appetite suppression, stimulates metabolism, and controls uncontrolled desire to eat before bed.

### Melatonin and weight loss: benefits beyond sleep

Melatonin, both in its endogenous and exogenous form, has numerous benefits to the body, bringing a better quality of life to patients. However, several factors make up the set of elements linked to the concept of quality of life. These elements are linked to the individual's social, educational, and cultural situation. According to Nahas, conceptualizing quality of life is complex, as it involves multiple factors, the perception of well-being varies from individual to individual, but in general, it can be said that quality of life would be linked to essential factors of human needs, among them a healthy sleep [8].

A good night's sleep is essential for a healthier life, and for those who want to lose weight or even control their weight. However, it is not possible to say that the use of melatonin itself helps to lose weight. What happens is that during quality sleep, the body regulates satiety-related hormones (ghrelin and leptin). When there is little sleep or poor quality sleep, these hormones act worse, causing the person to eat more until they can feel satisfied.

In a research carried out by Galano (2011) [14] the effects of melatonin on weight loss in rats were analyzed. The results suggest that melatonin supplementation provoked reactions such as increasing the conversion of white fat to brown fat in rats. Results obtained in studies like this one show that melatonin acts directly in the regulation of a series of physiological reactions, positively and directly impacting weight loss.

### Conclusion

Sleep is part of a healthy routine and can influence the metabolism as well as the diet of the individual. Maintaining habits of organization of the circadian cycle contributes to the regulation of the body in addition to helping to restore energy through the rest needed daily. The consequences of sleep disorders unfold at subsequent levels that affect the affected person's quality of life. At the first level are the proximal or biological variables, which bring immediate consequences to the body and include physiological changes such as tiredness, fatigue, memory failures, attention and concentration difficulties, and even mood swings. These symptoms trigger the symptoms of the functional level that are observed in the medium term, at that time the implications happen in daily activities. The studies observed to support this research prove that from the reorganization of sleep through melatonin, it is possible to rehabilitate the affected person, contemplating the different realities experienced, from fatigue to eating. Taken together, this evidence supports a possible efficacy in the exogenous use of melatonin for the treatment of sleep disorders. However, although there is evidence that MEL administration induces sleep similar to natural sleep, further studies are needed to clarify the individual factors that determine its effectiveness. It was proven in this research, several benefits are achieved with the use of melatonin and its real effect in regulating the sleep cycle, however, weight control and weight loss stand out as one of the most emphatic senses during quality sleep, The body regulates the hormones related to satiety (ghrelin and leptin), a fact that affects weight control. Another fact that is evident, given the above, is that despite the different properties of melatonin in favor of the regulation of the circadian cycle, consultation and indication are necessary so that the use



and prescription of melatonin are defined.

## References

1. Gandolfi JV, Di Bernardo APA, Chanes DAV, Martin DF, Joles VB, Amendola CP, Sanches LC, Ciorlia GL, Lobo SM. The Effects of Melatonin Supplementation on Sleep Quality and Assessment of the Serum Melatonin in ICU Patients: A Randomized Controlled Trial. *Crit Care Med.* 2020 Dec;48(12):e1286-e1293. doi: 10.1097/CCM.0000000000004690. PMID: 33048904.
2. Fatemeh G, Sajjad M, Niloufar R, Neda S, Leila S, Khadijeh M. Effect of melatonin supplementation on sleep quality: a systematic review and meta-analysis of randomized controlled trials. *J Neurol.* 2021 Jan 8. doi: 10.1007/s00415-020-10381-w. Epub ahead of print. PMID: 33417003.
3. Pacheco D, Izaola Jáuregui O, Primo Martín D, de Luis Román DA. A circadian rhythm-related MTNR1B genetic variant (rs10830963) modulates glucose metabolism and insulin resistance after body weight loss secondary to biliopancreatic diversion surgery. *Nutr Hosp.* 2020 Dec 16;37(6):1143-1149. English. doi: 10.20960/nh.03153. PMID: 33119394.
4. Genario R, Cipolla-Neto J, Bueno AA, Santos HO. Melatonin supplementation in the management of obesity and obesity-associated disorders: A review of physiological mechanisms and clinical applications. *Pharmacol Res.* 2021 Jan;163:105254. doi: 10.1016/j.phrs.2020.105254. Epub 2020 Oct 17. PMID: 33080320.
5. Behrendt D, Ganz P. Endothelial function: from biology to clinical applications. *Am J Cardiol.* 2002.
6. Claustrat B, Brun J, Chazot G. The basic physiology and pathophysiology of melatonin. *Sleep Med Rev.* 2005, 9:11-24.
7. Ozata M, Mergen M, Oktenli C, Aydin A, Yavuz Sanisoglu S, Bolu E, et al. Increased oxidative stress and hypozincemia in male obesity. 2002, *Clin Biochem.*
8. Nahas MV. Atividade física, saúde e qualidade de vida: conceitos e sugestões para um estilo de vida ativo. 2003. 3ª edição. Londrina: Midiograf.
9. Botella-Carretero JI, Alvarez-Blasco F, Villafruela JJ, Balsa JA, Vazquez C, Escobar-Morreale HF. Vitamin D deficiency is associated with the metabolic syndrome in morbid obesity. *Clin Nutr.* 2007.
10. Ribot J, Felipe F, Bonet ML, Palou A. Changes of adiposity in response to vitamin a status correlate with changes of PPAR [gamma] 2 expression. *Obesity.* 2001; 500-509.
11. Parkes E. Nutritional management of patients after bariatric surgery. *Am J Med Sci.* 2006; 4: 207-213.
12. Silva VYNE, Pereira AMO, Kashiwabara TGB. Qualidade do sono e melatonina: relato de caso. *Brazilian Journal of Surgery and Clinical Research,* 2013,4, 1:32-36.
13. Arendt J. Melatonin: characteristics, concerns, and prospects. *J Biol Rhythms.* 2005; v. 4, p. 291-303.
14. Galano A, Dun T, Russel J. Melatonin as a natural ally against oxidative stress: a physicochemical examination. *Journal of pineal research:* 2011, 1-16
15. Ferrara M, De Gennaro L. How much sleep do we need? *Sleep Medicine,* 2001, 5:155- 179.
16. Poyares D, Tufik S. I Consenso Brasileiro de Insônia. *Hypnos Journal of Clinical and Experimental Sleep Research,* 2002, 4:1-45.
17. Tribl G, Schmeiser-Rieder A, Rosenberger A, Saletu B, Bolitschek J, Kapfhammer G, Katschnig H, Holzinger B, Popovic R, Kunze M, Zeitlhofer J. Sleep habits in the Austrian population. *Sleep Medicine,* 2002, 3:21-28.
18. Brzezinski A, Vangel MG, Wurtman RJ, Norrie G, Zhdanova I, Ben-Shushan A, Ford I Effects of exogenous melatonin on sleep: a meta-analysis. *Sleep Med Rev.* 2005; 9:41-50.
19. Dahlke, Rudiger. O sono como caminho: dormir bem para viver bem. São Paulo: Cultrix, 2008.
20. Fujioka K. Follow-up of nutritional and metabolic problems after bariatric surgery. *Diabetes Care* 2005; 28:481-484.
21. Roth T, Stubbs C, Walsh JK. Ramelton (TAK-375), a selective MT1/MT2-receptor agonist, reduces latency to persistent sleep in a model of transient insomnia related to a novel sleep environment. *Sleep.* 2005, 28:303-307.
22. Souza RC. Melatonina. Estudo Técnico, Consultoria Legislativa da Câmara dos Deputados, 2016.
23. Pacheco, M. B. et al. Propriedades da melatonina como fator de neuroproteção em doenças neurodegenerativas. In: SAFETY, HEALTH AND ENVIRONMENT WORLD CONGRESS, 13. 2013, Porto. Anais. Porto, 2013.
24. Fusatto, E. L. Análise da influência da administração da melatonina no sistema cardiovascular e muscular de ratos desnervados. 2012. 60 f. Dissertação (Mestrado em Fisioterapia) - Faculdade de Ciências da Saúde, Universidade Metodista de Piracicaba, Piracicaba, 2012.
25. Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick

MF. Decreased bioavailability of vitamin D in obesity. Am J Clin Nutr. 2000; 72, 3:690-693.

26. Shikora SA, Kim JJ, Tarnoff ME. Nutrition and gastrointestinal complications of bariatric surgery. Nutr Clin Pract. 2007; 22, 1: 29-40.

#### **ACKNOWLEDGEMENT**

Nil

#### **FUNDING**

Not applicable

#### **DATA SHARING STATEMENT**

No additional data are available

#### **CONFLICT OF INTEREST**

The authors declare no conflict of interest.

#### **ABOUT THE LICENSE**

© The author(s) 2021. The text of this article is open access and licensed under a Creative Commons Attribution 4.0 International License.