

## Melatonin and Melatonin-Rich Foods

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**ABSTRACT:** Vegetables and fruits are found in the most popular diets. And they are considered as rich sources of vitamins and minerals. Vitamin and mineral deficiency are one of the major causes of various diseases that are common nowadays. Especially vitamins which are known to affect directly on various hormones in our body. Melatonin (N-acetyl-5-methoxytryptamine), one of these hormones, is synthesized in various peripheral organs and tissues, especially the pineal gland and retina. Endogenous melatonin secretion rhythm is regulated by the suprachiasmatic nucleus and maintained with a bright dark cycle. Melatonin hormone is responsible for many activities in the human body. In addition to, especially is found in various foods (milk and milk product, nuts, olive oil, and various fruits). In this review, the recent studies that focused on the biosynthesis and metabolism of melatonin in addition to those investigated food content of melatonin and their effects on physiological and biological human health.

**Keywords:** Melatonin, Melatonin hormone, Vegetables, fruits.

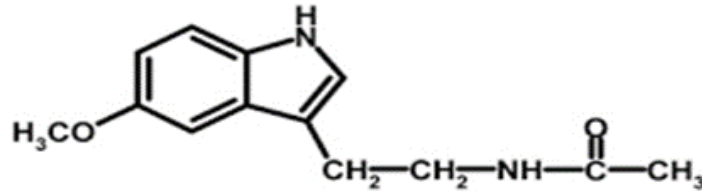
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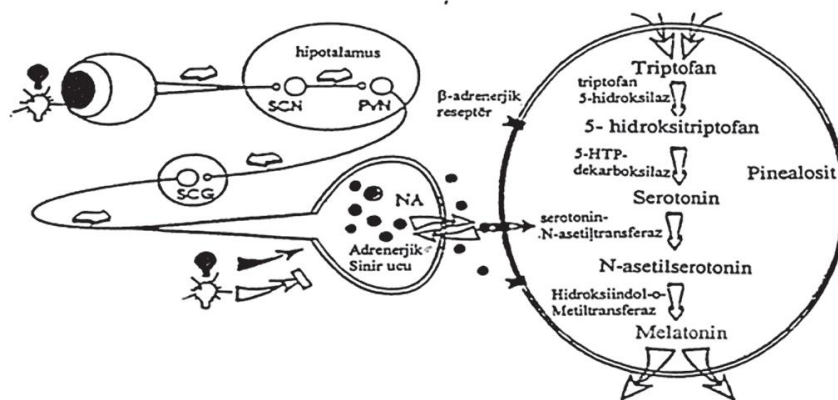
## INTRODUCTION

N-acetyl-5-methoxytryptamine (Figure 1), also known as the hormone melatonin, is a natural neurotransmitter secreted by the pineal gland. This hormone, which is known to increase secretion in the dark, has important functions in the regeneration of cells, strengthening of the immune system, regulation of sleep rhythm and body temperature, as well as being a powerful antioxidant (Claustrat et al., 2005; Ozçelik et al., 2013; Atasoy, 2019).



**Figure 1.** Melatonin (Atasoy, 2019)

The secretion of the melatonin hormone is due to the sensitivity of the pinealocyte cells to light. Thanks to this sensitivity, the obstruction caused by light disappears in the dark and the melatonin secretion of melanocytes increases. Especially between 23:00 and 05:00, melatonin secretion peaks and its concentration in the blood increases 3-10 times. Melatonin release has a special circadian rhythm and begins to increase at 21.00-22.00 hours, reaching a peak at 02.00-04.00 hours. It starts to decrease at 05.00-07.00 in the morning and decreases to basal levels after 07.00. While the blood concentration of melatonin is around 0-20 pg dl<sup>-1</sup> during daytime hours, it increases to 50-200 pg dl<sup>-1</sup> during night hours. An average of 30 mg of melatonin is synthesized during the night (Cam and Erdogan, 2003; Claustrat et al., 2005; Mollaoglu and Ozguner, 2005; Ozcelik et al., 2013).



**Figure 2.** Regulation of melatonin synthesis in dark / light stimulation. (Beyer et al., 1998; Sener, 2010).

As with biochemical, physiological, and behavioural variables, melatonin levels in plasma show regular fluctuations in a 24-hour period. This circadian rhythm is controlled by central pacemakers in the SCN (Suprachiasmatic nucleus) in the hypothalamus, and the main regulator of the rhythm is the light / dark cycle in the external environment (Figure 2). Pineal functions are acutely suppressed when exposed to night light (Liebmann, 1997; Sener, 2010).

The relationship between melatonin and cortisol is important for both hormones in terms of their effects on the immune system. Melatonin and cortisol levels move in the opposite direction. Cortisol is low during sleep hours, whereas melatonin peaks within a few hours after cortisol reaches its lowest level. Interruption of this normal secretion is important in terms of health deterioration or cancer risk. Researchers have reported that various diseases can occur with low melatonin and high cortisol levels.

So the balance between these two hormones is important for good health. In determining this, the melatonin-cortisol index has been used as a marker in determining the conditions related to depression, heart diseases, osteoporosis and weight gain, in addition to information about immune functions (Millet et al., 1999; Guardiola-Lemaitre, 2007; Sener, 2010). Some findings regarding the relationship between melatonin and cortisol are summarized below:

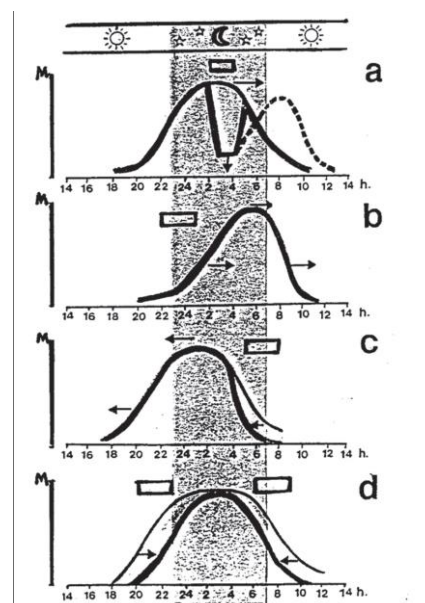
- Increase in weight gain has been reported to correlate with low melatonin and high cortisol levels (Guardiola-Lemaitre, 2007; Sener, 2010).

- Melatonin levels are lower in patients with depression compared to patients without depression, and cortisol levels were found to be higher in patients with depression during sleep times.

- High cortisol and low melatonin leads to bone loss. Estradiol levels must also be sufficient for melatonin to show its positive effects on the bone.

- Melatonin levels are low in people exposed to light at night and increases the risk of breast cancer. The risk of breast cancer is also associated with cortisol; high cortisol during the day and in the evening increases the risk. Also, it has been reported that melatonin levels are low in the endometrium, prostate, lung, gastric, and colon cancers, and melatonin can be protective against cancer with its antioxidant effects (Reiter et al., 2009; Sener, 2010).

**Light applications (or appliances) and effects on Melatonin secretion:** While early studies reported that only bright light (daylight) suppresses melatonin level in humans, recent findings suggested that artificial light (lighting system in the dark period) has a similar effect. Melatonin secretion is freely distributed within 24 hours in the visually impaired, ie people with "0" light perception. (Reiter, 1991; Şener, 2010; Reiter, 2002). While the artificial light at night acutely suppresses the synthesis and secretion of melatonin (Figure 4), the light with the onset of dusk shifts the plasma melatonin concentration peak seen between 02.00-04.00 at night, whereas the application of light before sunrise (dawn) in the morning causes this concentration peak to appear early (Figure 4b, c). The light exposure in the morning and evening hours causes a contraction in the phase (Figure 4d) (Claustrat et al., 1998; Şener, 2010).



**Figure 4.** The effects of bright light (□) on melatonin release. a) Inhibition of secretion b) Phase shift. c) Early phase) Phase contraction (Claustrat et al., 1998; Sener, 2010).

Melatonin has been reported to be more beneficial than other antioxidants in eliminating hypoxia and damage-dependent reoxygenation. Also, it is thought that physiological deficiency of melatonin may

increase hypoxia and oxidative damage. Therefore, it is thought that the use of melatonin may be important in oxidative damage related to heart diseases (Reiter and Tan, 2003; Ozcelik et al., 2013). It is also reported to be more effective than ascorbic acid in preventing cardiac arrhythmias. (Tan et al., 1998; Ozcelik et al., 2013).

In an in-vivo study, it was found that intravenous melatonin administration prevented ventricular tachycardia, ventricular fibrillation, and premature ventricular contraction (Lee et al., 2002; Ozcelik et al., 2013). Moreover, it is thought that melatonin, which is released during the night, may play an important role in balancing high blood pressure, as it lowers blood pressure and heart rate (Yıldız and Akdemir, 2009; Ozcelik et al., 2013).

Melatonin has a direct effect on the bone. It has been found that serum calcium concentration decreases with suppression of melatonin secretion and increases with melatonin administration. Melatonin administration to ovariectomized rats reduced bone loss (Ostrowska et al., 2002; Şener, 2010). Melatonin is found in abundance in the bone marrow. The effects of melatonin on bone cells is thought to be through autocoid effects. Melatonin also increases bone matrix proteins in a dose-dependent manner. Osteoblastic protein, osteoprotegerin is increased by melatonin (Suzuki et al., 2008; Şener, 2010). It is thought that the use of melatonin, in addition to bisphosphonates in the treatment of osteoporosis, protects bones by both; reducing the side effects associated with the drug and the positive effects directly on the bone.

As a matter of fact, the protective effect of melatonin has been demonstrated against gastric damage caused by alendronate (Şener et al., 2005; Şener, 2010).

### **Foods Containing Melatonin**

Since, the pinealocyte cells (pineal gland, conarium, or epiphysis cerebri) are sensitive to light, secretion of melatonin occurs in dark environment, not in the light (Paredes et al., 2009; Huang and Mazza, 2011).

In a study that included 24 kinds of edible plants, the amount of melatonin found in edible plants, effects of plasma melatonin rate, and binding efficiency of melatonin receptors in vertebrates have been investigated. At the same time, it has been stated that these plants could be beneficial in terms of nutrition due to the antioxidant properties of melatonin. Melatonin levels of other plants are shown in Table 1.

In another study, melatonin levels in poppy, anise, coriander, celery, flax, green cardamom, clover, fennel, sunflower, almond, goji berry (*Lycium barbarum*), black and white mustard seeds has been investigated. The amount of melatonin in analyzed samples was found to vary between 2 to 190 ng g<sup>-1</sup> with black white mustard having the highest concentration of melatonin (189 ng g<sup>-1</sup>) and black mustard (129 ng g<sup>-1</sup>) (Manchester et al., 2000).

The effect of walnut consumption on the serum melatonin level in the blood of rats has been examined in another study. The study found that the melatonin level in walnuts was  $3.5 \pm 1.0$  ng g<sup>-1</sup> and it was observed that the serum melatonin level of rats fed with walnuts increased compared to those fed with normal diet. Furthermore, the fiber present in walnuts also play an important role in digestive system (Reiter et al., 2005; Binici et al., 2021).

In a study examining the amount of melatonin in extra virgin olive oil, sunflower oil, and refined olive oil, it was observed that the amount of melatonin in extra virgin olive oil samples was higher than in sunflower and refined olive oil samples (de la Puerta et al., 2007). A group of researchers has reported the amount of melatonin that there was no significant difference in melatonin between the samples, but a remarkable difference between the amounts of trans-resveratrol (Mercolini et al., 2008). Stürtz et al. (2011) investigating the melatonin levels found in various tomato (*Lycopersicon esculentum*) varieties

(Bond, Borsalina, Catalina, Gordal, Lucinda, Marbone, Myriade, Pitenza, Santonio, Perlino, Platero, and RAF) and various strawberry (*Fragaria ananassa*) varieties (*Camarosa, Candonga, Festival, and Primoris*) in different years (2009-10), the amount of melatonin in tomato samples was found between 4.11 ng g<sup>-1</sup> and 114.52 ng g<sup>-1</sup>, while in strawberry samples it was found between 1.38–11.26 ng g<sup>-1</sup>. While the amount of melatonin in tomato samples varied according to harvest years, it has been reported that parallel values were obtained in strawberry samples. In other studies investigating the amount of melatonin in various fruits such as grape, banana, orange, pineapple, mango, and papaya, the amount of melatonin in various fruits as reported by the researchers (Mercolini et al., 2012; Johns et al., 2013). In a study by Sang et al. (2020) melatonin contents of fourteen different grains and mulberry leaves had been analyzed. using HPLC- FD. Among the analyzed samples, highest melatonin contents according to the study were: white sesame (75.24), sunflower (67.45), soybeans (56.49), fresh mulberry leaves (51.57). Kocadağlı et al. (2014) study which included the samples of beer, walnut, tomato, cocoa powder, sour cherry, black and green tea, cherry, cherry concentrate, kefir, breadcrumbs and red wine, melatonin and its isomer were present in beer, hazelnut, tomato and cherry samples, but only melatonin isomer was detected in black and green tea, cherry, cherry concentrate and red wine. It was also reported that the highest melatonin isomer values were in red wine (170.7 ± 29.90 ng g<sup>-1</sup>) and the highest melatonin value was in breadcrumbs (341.7 ± 29.30 ng g<sup>-1</sup>) among the analyzed samples.

**Table 1.** Average amount of melatonin in various plants (Hattori et al., 1995).

Plant	Amount (pg g <sup>-1</sup> )	Plant	Amount (pg g <sup>-1</sup> )
Spinach	38.7±5.5	Strawberry	12.4±3.1
Cucumber	24.6±3.5	Apple	47.6±3.1
Kiwi	24.4±1.7	Daisy varieties	416.8±54.6
Cabbage	107.4±7.3	Japanese butterbur	49.5±5.6
Japanese Raddish	657.2±29.0	Tomato	32.2±2.4
Chinese Cabbage	112.5±10.3	Rice	1006.0±58.5
Japanese ashitaba	623.9±63.1	Barley	378.1±25.8
Carrot	55.3±11.9	Sweet Corn	1366.1±465.1
Oat	1796.1±43.3	Kentucky blue grass	5288.1±368.3
Taro	54.6±23.0	Zinger	583.7±50.3
Pineapple	36.2±8.4	Asparagus	9.5±3.2
Onion	31.5±4.8	Green Onion	85.7±8.0

## CONCLUSION

Today, the roles of free radicals in various diseases especially cancer, cardiovascular and neurodegenerative diseases, and aging, have been established. And it has brought the use of antioxidants to the agenda and studies on this issue have gradually gained momentum. Compared to many other antioxidants, melatonin continues to be relevant with both its powerful radical scavenging property and its ability to increase antioxidant enzyme activities.

Although there are many studies investigated the melatonin profiles of foods such as various vegetables, fruits, legume seeds, milk and dairy products, coffee and cocoa beans, there are only a limited number of studies examining the melatonin profiles in the human body, especially the effect of consumption of such foods on melatonin profiles in the human body. Moreover, those studies have included oral supplementation of melatonin rather than as a food supplement. From those studies, it is also established that oral supplementation supports the increase of melatonin hormone in the body. But, it is unclear that whether food or external supplements are more effective, due to limited studies, environmental and living conditions, regular sports activities, dietary habits and quality, and factors



affecting these components. Although, it has been found in many research studies that consuming foods rich in melatonin, regular sports activities, and exposure to sunlight generally increases its concentration in the body, more scientific studies on the effect of melatonin rich diet on human health could provide accurate and systematic results on this subject.

### Conflict of Interest

The article authors declare that there is no conflict of interest between them.

### Author's Contributions

Halil İbrahim Binici wrote the original draft. İhsan Güngör Şat reviewed and edited the manuscript.

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