Melatonin is our sleep hormone, produced by the pineal gland deep within the brain. It is also produced in the GI tract and, to some extent, in the retina of the eyes.

**Physiology**

Melatonin production is dependent, of course, on adequate building blocks, cofactors (e.g., folate/SAMe and acetyl CoA donors such as pantethine) and enzyme availability. Its production in the pineal, however, is under another, powerful influence—our biological clock. Rising at nightfall or darkness, peaking between 2 and 4 a.m., dropping at dawn—melatonin’s circadian rhythm is controlled by a part of the hypothalamus known as the suprachiasmatic nuclei (SCN). The SCN are responsible for the timing of most circadian rhythms, including core body temperature, cortical secretion and sleep. The SCN itself is entrained by light exposure from the eyes and communicates directly with the pineal.

The pineal gland is innervated, not only by the hypothalamus, but also by the sympathetic nervous system (SNS). In normal function, the SNS’s norepinephrine (NE) provides tonic stimulation of the pineal (specifically, N-acetyltransferase activity) during the night, promoting melatonin synthesis. Glutamatergic neurons from the hypothalamus also stimulate nighttime production. GABA messages during the day inhibit pineal production, causing melatonin to fall in the morning and remain low during the day.¹ Acute elevations of NE have been shown to increase serum melatonin. In long-term stressful conditions, however, NE may contribute to insomnia by suppressing melatonin production.²

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² Acute elevations of NE have been shown to increase serum melatonin. In long-term stressful conditions, however, NE may contribute to insomnia by suppressing melatonin production.
Other Melatonin Functions

Central melatonin has other significant functions beyond its sleep-inducing ability. It is a potent antioxidant for the brain. Studies point to significant protective effects vs. Alzheimer’s Disease and Parkinson’s Disease. Melatonin also has well-studied anti-estrogenic potential. Not only does it interfere with estrogen (E2) signaling by modulating estrogen receptor pathways, it also, even in physiological concentrations, decreases aromatase activity. It is often used in efforts to reduce estrogen dependent cancer risk.

Melatonin also has a significant role in photoperiodic species. The duration of nocturnal melatonin secretion increases with the length of the winter nights, thereby providing an internal calendar that regulates seasonal cycles in reproduction and other functions in photoperiodic species. For example, during the long winter months, the increase in darkness increases melatonin, which in turn inhibits reproductive function until spring, when warmer weather is conducive to the survival of young. Although humans are not considered photoperiodic, the occurrence of seasonal affective disorder (SAD) and its successful treatment with light suggest that we have retained some photoperiodic responsiveness.

While melatonin inhibits the reproductive system, it has been shown to boost the immune system. In winter, when melatonin levels are at their highest, immunity is strengthened, whereas in summer, the immune system does not receive (and may not need) that same level of support. However, melatonin serves as part of the body’s inhibitory control on cortisol; melatonin suppresses cortisol production by the adrenal cortex. The gastrointestinal tract is a major source of extrapineal melatonin. GI tract melatonin periodicity seems to be related to food intake rather than circadian rhythm, and it has very distinct functions from central melatonin. It can protect GI mucosa from ulceration by its antioxidant action. It has been shown to be protective of the pancreas as it is a potent scavenger of radical oxygen species (ROS). It is involved in the regulation of gastrointestinal motility and sensation and has been shown to be efficacious in treating abdominal and rectal pain in IBS patients.

Melatonin and Depression

It is generally understood that patients suffering major depression have elevated melatonin levels. There is support in the literature for this. However, there are also reports of low melatonin associated with depression. Determining melatonin levels is recommended before using melatonin supplementation in depressed patients. Seasonal Affective Disorder (SAD) is a condition of regularly occurring depressions in winter with a remission the following spring or summer. In addition to depressed mood, patients tend to experience increased appetite, fatigue and an increased duration of sleep during the winter. For SAD patients, too much melatonin is produced, especially during the long nights of winter. This compromises serotonin levels, inducing or contributing to the sadness or depression associated with this condition. Bright light therapy to inhibit melatonin production has consistently shown efficacy in treating SAD.
Clinical Considerations

A large body of literature has accumulated from ongoing studies of melatonin's clinical usefulness. It is, of course, used before bedtime to induce sleep. Additionally, “Exogenous melatonin can synchronize some circadian rhythms, such as body core temperature. Current research is focusing on the properties of melatonin (and of light) as a resynchronizing agent in situations such as aging, blindness, shift work, night work, phase-advanced or phase-delayed sleep syndrome, and jet lag.” 17

It has been proven that the duration and organization of human sleep depends on its circadian phase, not on the duration of prior wakefulness. 18 Using exogenous melatonin to produce phase shifts in the melatonin rhythm has been successful in many clinical cases of circadian rhythm disorders. Melatonin affects phase change by modulating SCN neurons, causing a phase shift in the SCN’s circadian activity. When desiring to advance the sleep phase and produce sleep earlier than usual, melatonin is generally given from 1-2 hours to 3-4 hours before desired sleep time. For patients who get sleepy too early in the evening but awaken at 3 or 4 a.m., (common in the elderly), a phase delay is needed. Administering melatonin in the morning delays the circadian rhythm. 19

The literature describes only two successful approaches for adjusting desynchronized circadian rhythm. One, as described above, is using exogenous melatonin to advance or delay the desynchronized phase. The other is exposure to light, particularly blue spectrum light. 20 According to the time of exposure, light has two effects on melatonin secretion, either suppressing it or shifting it. Exposure to light in the evening delays the phase of the rhythm, promoting staying awake, while exposure to light in the morning is often used to drop melatonin production in Seasonal Affective Disorder.

Assessment of Melatonin

Measuring melatonin is one of the most useful assays available for patients with insomnia or circadian rhythm disorders. Without knowing levels, melatonin supplementation can be hit or miss. Watch for a melatonin assay from Sanesco in the near future.
One of the clinical “tools” available to practitioners considering the natural therapy options discussed by Dr Watkins is Sanesco’s Communication System Management (CSM) model. The CSM model is a clinical system designed to help you to assess, monitor, and correct key neurotransmitter imbalances that may be associated with your patients’ symptoms of anxiety and depression. The CSM model includes three integrated components.

- The CSM model utilizes a noninvasive lab assay measuring neurotransmitter and adrenal hormone levels to establish baseline levels of a patient’s biochemistry. Subsequent testing is used as an effective tool for monitoring treatment.

- As a model of individualized medicine, CSM includes patient-centered analysis of symptoms and lab results. With oversight by Sanesco’s Medical Board, highly trained clinical staff correlates 48 patient-reported symptoms, current dietary and lifestyle factors, supplement and medication intake, to the reported lab results; generating a comprehensive “Correlation Analysis” report. This Correlation Analysis report provides you with extensive patient specific information to help you open the window to your patient’s neuroendocrine system.

- The third component of the CSM model is using the nutraceutical supplements discussed in Dr Watkins’ monograph. Sanesco’s Targeted Nutritional Therapy products are safe and effective options for restoring some of the biochemical imbalances that may be associated with anxiety and depression, as well as other symptoms related to neuroendocrine system function.

Sanesco developed this “CSM” model in collaboration with a team of medical doctors, naturopathic doctors, nutritionists, and researchers. The goal was to provide a practical science-based individualized approach for looking at the key contributors to potential underlying causes of chronic symptoms.

Sanesco provides complimentary training to practitioners on the three components of this model through its CSM Certification Program. This exclusive program includes one-to-one interactive training sessions, live webinars, a self-tutorial library, and much more. Contact a Sanesco representative to enroll today - Call 866.670.5705 and Press “2”

The above statements have not been evaluated by the FDA. The products mentioned above are not intended to diagnose, treat, cure or prevent any disease.

Not all of the nutraceutical products mentioned in this monograph are distributed by or sold by Sanesco International. Contact a Sanesco representative for more information.