
Melatonin

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General Feature

Melatonin is a molecule that has been found in every animal and plant studied to date, from human beings to the most primitive one-celled algae that evolved more than three billion years ago. In each organism, Melatonin's molecular structure is identical. This sameness is a rare occurrence in biology.

In all the life forms studied, Melatonin has been produced in the same circadian (daily secretion pattern) rhythm, with higher levels produced at night than during the daytime.

In humans, Melatonin is produced and secreted by the pineal gland in the brain. It is synthesized from serotonin, which itself is synthesized from 5-hydroxytryptophan and tryptophan. In the human body Melatonin acts as a hormone, neurotransmitter, antioxidant and immune system modulator.

It is best known for its ability to induce sleep and elevate mood. Humans produce five to ten times more Melatonin at night than during the day, a circadian rhythm found in animals as well. Peak amounts occur around two or three o'clock in the morning.

After puberty the body's production of Melatonin declines. By age 40 humans produce approximately 60 percent less Melatonin than a 10 year old and by age 70 or 80 Melatonin levels may be undetectable.¹

With respect to its antioxidant properties, Melatonin is unique in that it is both a water-soluble antioxidant and a fat-soluble antioxidant. Some studies suggest that as an antioxidant it is twice as effective as Vitamin E, five times as efficient as glutathione, and five hundred times more effective than the synthetic DMSO. However, Melatonin is produced in picograms (a trillionth of a gram – the smallest amount of any hormone), whereas Vitamin E, and other antioxidants, are present in much higher concentrations.²

Supplementation Studies and Clinical Applications

1. Insomnia

Low Melatonin secretion at night which commonly accompanies aging, can be a cause of insomnia. Several double-blind trials show that Melatonin supplementation can be useful in the treatment of insomnia. Taken within one hour of bedtime, Melatonin has been shown to shorten the time needed to fall asleep, reduce the number of night awakenings, and improve sleep quality. Low Melatonin levels are an extremely common cause of insomnia in the elderly, who manufacture 90-99 percent less Melatonin than a ten-year old.³⁻¹⁰

2. Jet Lag

Several double-blind studies demonstrate that Melatonin is very effective in relieving jet lag. The best approach appears to be taking Melatonin in the first evening after arriving at the new destination (where there is a time zone change). Shift workers may also take advantage of this strategy to reset the body internal wake-sleep cycle.¹¹⁻¹⁶

3. Other Considerations

As Melatonin is also an antioxidant, an immune system modulator and a core temperature regulator it is being tested for various other health applications:

- a. Tension and cluster headaches - Some preliminary, double-blind studies suggest that Melatonin supplementation may help in certain cases (1-3 mg at night).^{17,18} This effect has been attributed to Melatonin's ability to prevent a rise in core temperature, which is linked to cluster headaches.^{35,36}
- b. Sarcoidosis - Preliminary evidence has shown improvement in patients with sarcoidosis (20 mg at night).¹⁹
- c. Adjunctive Cancer Treatment - Early trials indicate that Melatonin supplementation, as an adjunct to cancer treatment may help inhibit the progression of breast cancer, reduce the PSA levels in prostate cancer patients and improve disease-free survival in melanoma patients, as well as patients with brain and lung cancer (20 mg at night). Of course, more research is required before any conclusive statements can be made about this application.²⁰⁻²⁷ In a study of cancer patients with solid tumors in various organs the intake of Melatonin (40 mg per day) enhanced the effectiveness of interleukin-2 therapy by enhancing its anti-tumor immune effect or by increasing susceptibility of cancer cells to the cytotoxicity by cytotoxic lymphocytes.³⁷
- d. Immune System and AIDS - Maestroni and Conti demonstrated in 1995 that T-helper-2 lymphocytes possess Melatonin receptors. When Melatonin docks with its receptor on the T-helper cell, a cascade of events is set in motion releasing important signalling agents (cytokines) that strengthen immune function in various ways. For example, natural killer cell production rose by 240 percent in healthy young men taking 20 mg of Melatonin each night for a period of two months.

Melatonin may also inhibit viral replication and has been shown to increase T-helper cell numbers and natural killer cell numbers in HIV-infected individuals. Further research is underway to substantiate these findings (20 mg at night).^{28,29}
- e. Birth Control/Contraceptive - Very high doses of Melatonin inhibits ovulation in animals and women. A new birth control is now being tested known as B-Oval. It contains no estrogen, but rather high dose Melatonin (75 mg) and 0.3 mg of progestin.³⁰

Dosage Ranges

Insomnia and Jet Lag (Shift Workers) - 0.1 mg to 3.0 mg (note 0.1 mg equals 100 mcg), one to two hours before bedtime. It is best to start with a small dose and work up, based upon improved sleep with no awakening and morning drowsiness.

N.B. Taking a high dosage of Melatonin (5 – 75 mg) should only be undertaken with knowledge of a physician, who is able to monitor blood work and other parameters, as these dosages are still experimental and long-term safety is unknown at this time.³⁸

Adverse Side Effects and Toxicity

Taking doses that are too high can result in morning grogginess, headaches and/or abdominal cramps.^{31,32}

Melatonin testing in humans and animals indicate that it is very non-toxic.^{1,33}

Contraindications and Drug-Nutrient Interactions

Some cases of depression can be aggravated by Melatonin supplementation.³⁴ Some antidepressant drugs stimulate the production of Melatonin and others, such as fluoxetine (Prozac), may lower Melatonin levels. It is probably best at this time not to combine Melatonin with any other drug that targets brain chemistry or neurotransmitter levels.^{35,36}

A number of drugs have been shown to deplete Melatonin levels. Some of these include aspirin, ibuprofen, beta-blockers, calcium channel blockers, sleeping pills, tranquilizers, fluoxetine (Prozac), caffeine, steroids and tobacco.¹

The clinical significance of this is yet to be determined, in regards to whether or not patients on these substances require Melatonin supplementation to compensate for the depletion of Melatonin (author's note).

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