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Nutraceutical UPDATE

Melatonin

New Research Shows Impressive Health Benefits

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New research indicates that melatonin does much more than help some people sleep better. Exciting studies show that melatonin's multifaceted effects may improve treatment outcomes in cancer patients and extend their lives. Additional applications of melatonin include guarding the nervous system against degenerative diseases—such as Alzheimer's disease and stroke—and preventing debilitating migraines.

Melatonin is secreted from the pineal gland deep inside the brain. For more than a quarter-century, scientists have been intrigued by melatonin's ability to coordinate the body's physiological rhythms that help set the brain's biological clock.

The principal factor affecting melatonin is light, which inhibits the secretion of this hormone.

Darkness has the opposite effect from light, resulting in signaling to the pineal gland to increase melatonin secretion. The normal cycles of melatonin production are altered due to factors including aging, medications, and light exposure at night. While the long-term health effects of disrupted melatonin secretion are not yet fully known, some scientists have suggested that years of working nights could lead to adverse effects—even cancer.

Fortunately, melatonin supplements can safely and effectively restore balance to the body's circadian rhythm of this important hormone—helping achieve a restful night's sleep and keeping your biological clock ticking throughout a long, healthy life span.

NEUROPROTECTIVE BENEFITS

Melatonin is a powerful and versatile antioxidant produced within the body. Melatonin protects both lipids and proteins against damage, and can scavenge some of the most dangerous free radicals in the body—including hydroxyl radicals and hydrogen peroxide. Unlike other antioxidants, melatonin easily diffuses into all cells, and even crosses the blood-brain barrier to protect the delicate brain.¹

Unfortunately, levels of naturally produced melatonin decline with advancing age, leaving older adults with limited antioxidant protection against conditions associated with oxidative stress, particularly neurodegenerative diseases.¹ Supplementing with melatonin may thus help older adults enhance their antioxidant protection against some of the most ravaging diseases of aging, such as Alzheimer's disease, Parkinson's disease, and stroke.

Melatonin levels are particularly low in patients with Alzheimer's disease. Nearly half of affected individuals suffer from sleep disturbances and "sundowning"—increased confusion, agitation, and other symptoms in the afternoon and evening.² Not surprisingly, melatonin supplementation benefits patients with Alzheimer's disease by improving sleep and reducing late-day aggravation of symptoms. Melatonin has also been found to decrease cognitive deterioration in individuals with Alzheimer's disease, possibly by protecting brain cells from the toxic protein, beta-amyloid.²

Melatonin may likewise play an important role in assisting patients suffering from Parkinson's disease. Parkinson's disease is associated with disrupted melatonin secretion in the brain, and supplemental melatonin may help improve sleep efficiency in affected adults.³

The brain can suffer dramatic, irreparable damage when an individual suffers a stroke. Utilizing animal models of stroke, scientists have found that melatonin may offer important protection against stroke-related damage and deterioration. When administered at the time of stroke, melatonin limited the area of brain tissue damage, decreased brain cell death, lessened behavioral deficits, and reduced the rate of stroke-related death. These investigators believe that melatonin's protective actions stem from its free-radical-scavenging and antioxidant activities, and suggest that melatonin may hold promise in improving stroke outcomes in humans.⁴



Melatonin may help manage one of the leading risk factors for stroke—elevated blood pressure. While an earlier study reported that hypertensive men taking melatonin experienced reduced nighttime blood pressure, a newer study confirms the same benefit for women.⁵ In a randomized, double-blind study, 18 women

(aged 47 to 63) with either normal blood pressure or treated high blood pressure received a three-week course of slow-release melatonin (3 mg) or placebo, one hour before bedtime. Researchers recorded blood pressure readings for 41 hours at the end of the trial. While the daytime blood pressure readings remained unchanged compared to placebo, the melatonin treatment significantly decreased nighttime blood pressure, without modifying heart rate.⁶

FIGHTING CANCER

One of melatonin's most important applications is in fighting a wide array of cancers, including breast and liver cancers, non-small-cell lung cancer, and brain metastases from solid tumors.⁷

When women with metastatic breast cancer who had failed to respond to tamoxifen received melatonin supplements (20 mg every evening), they demonstrated an improved response to the chemotherapy drug. More than one quarter of the subjects—whose disease otherwise was expected to progress rapidly—began responding to the chemotherapy treatment. Most of the women also experienced anxiety relief from the melatonin supplementation.⁸ Laboratory studies suggest that melatonin may help fight hormone-responsive breast cancers by inhibiting the aromatase enzyme, which is responsible for the local synthesis of estrogens.^{9,10}

Emerging research suggests that melatonin may help fight one of the most common malignancies in aging men—prostate cancer. In the laboratory, scientists treated androgen-sensitive and androgen-insensitive prostate cancer cells with pharmacological concentrations of melatonin. Treatment with melatonin dramatically reduced the number of prostate cancer cells, while the remaining cells displayed signs of slowed replication and increased differentiation—characteristics of healthy, non-cancerous cells. Melatonin may thus hold promise against prostate cancers, whether they are hormone-sensitive or hormone-insensitive.¹¹

Scientists conducted a meta-analysis of 10 randomized, controlled trials examining melatonin's effects (alone or as an adjuvant treatment) on patients with various types of cancer. Supplementation with melatonin reduced the relative risk of death at one year by an impressive 34%—regardless of the type of cancer or the melatonin dosage. Importantly, no adverse effects were reported.¹²

In addition to its benefits for cancer survival, melatonin may also help counteract the toxicity of chemotherapy treatment. Two-hundred-fifty individuals undergoing chemotherapy for advanced cancers of the lung, breast, gastrointestinal tract, or head and neck received chemotherapy, either alone or in combination with melatonin (20 mg/day). After one year, the melatonin-supplemented individuals demonstrated a higher rate of survival, and were significantly protected against many of the side effects associated with chemotherapy, including decreased platelet count, neurotoxicity, heart damage, mouth sores, and fatigue.¹³



MIGRAINE PREVENTION

A promising study suggests that migraine sufferers may be able to reduce the frequency and severity of their headaches by using melatonin. Researchers gave 34 migraine sufferers (29 women and 5 men) a 3-mg dose of melatonin, 30 minutes before bedtime, for three months. Of the 32 patients who finished the study, more than two thirds experienced at least a 50% reduction in number of headaches per month. Additionally, the intensity and duration of headaches decreased. The scientists believe that melatonin's anti-inflammatory effect and free-radical-scavenging effects contribute to its headache-relieving benefits.¹⁴

PROMOTING HEALTHY SLEEP

Obtaining sufficient amounts of quality sleep is an absolute necessity for good health, yet many of us experience sleep difficulties on occasion. Insomnia occurs due to a variety of factors—ranging from long hours of work or travel to sleep-disruptive

conditions, such as urinary frequency and stressful events. Elderly adults may be particularly susceptible to difficulty sleeping and nighttime awakenings, due to the decline in melatonin levels associated with aging.¹⁵ Melatonin can help promote healthy sleep patterns in some people, regardless of the cause of insomnia.

A large analysis revealed several of melatonin's sleep-enhancing benefits. Reviewing 15 studies of sleep in healthy adults, scientists noted that melatonin administration significantly reduced sleep latency (the amount of time needed to fall asleep), while boosting sleep efficiency (the percentage of time in bed spent asleep) and increasing total sleep duration.¹⁶

Men with benign prostatic enlargement often experience poor sleep due to nighttime urinary frequency. Scientists from the United Kingdom found that melatonin may offer an effective solution. When 20 older men were treated with 2 mg of melatonin each day for one month, they experienced a significant decrease in nighttime urination, and reported that their condition was less bothersome than before treatment.¹⁵



Individuals who work the night shift are often chronically tired due to difficulty falling asleep during the daytime. Supplementing with melatonin has helped improve the length and quality of daytime sleep in these individuals. These findings demonstrate an important characteristic of melatonin: the hormone exerts its hypnotic (sleep-inducing) and sedative (anxiety-relieving) effects, regardless of dosage time.⁷

Traveling to different time zones often leads to the fatigue and insomnia known as jet lag. Supplementing with melatonin can help prevent or reduce jet lag, particularly when traveling across several time zones. Melatonin works by helping re-synchronize the body's circadian rhythms, helping the traveler adapt to the local time.⁷

DOSAGE AND INTERACTIONS

Melatonin is used in doses ranging from 0.3-5.0 mg to promote sleep, with doses of 1-3 mg most common.¹⁷ Studies examining melatonin's effects on cancer have utilized doses of 3-50 mg/day.⁷

Melatonin has a sedating effect, which may be magnified by the use of benzodiazepines or other sedating drugs such as antihistamines or antidepressants. Similarly, the use of melatonin with valerian, 5-hydroxytryptophan, or alcohol may increase sedation.¹⁷

The bioavailability of oral melatonin is increased by co-administration of the antidepressant drug fluvoxamine (Luvox®).¹⁷ Beta blockers, as well as aspirin and other non-steroidal anti-inflammatory drugs, may decrease melatonin production in the body.¹⁷

CONCLUSION

A factor in restorative sleep, melatonin's benefits extend to neuroprotection and fighting cancer. Its powerful antioxidant effect offers important enhancements to the brain and nervous system, helping protect against age-related damage. Most exciting are melatonin's benefits for cancer patients—relieving anxiety and improving survival from an array of cancers. Finally, migraine sufferers using melatonin may enjoy a vast decline in the frequency and severity of their headaches—leading to a tremendously improved quality of life.



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