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CLASS 3* DIETARY SUPPLEMENTS



HPRC DIETARY SUPPLEMENTS CLASSIFICATION SYSTEM:

MELATONIN

Background

Melatonin is a light-sensitive hormone and a potent antioxidant synthesized from tryptophan. Concentrations of melatonin in the plasma (i.e., within the circulatory system) exhibit a 10- to 50-fold increase during the night due to synthesis and secretion by the pineal gland. Plasma melatonin levels peak at nighttime (~50-200 pg/ml) with low to non-detectable levels during the day. However, there are significant individual differences in peak melatonin levels. Dietary sources of melatonin include numerous fruits and seeds, and it is also available as a supplement. Melatonin has FDA orphan drug status (i.e., approved for use in treating rare medical conditions) for the treatment of both non-24-hour sleep-wake disorder and circadian rhythm sleep disorders in blind people with no light perception.

Some studies have shown that supplemental melatonin administration can increase sleep propensity, although it is not as effective as prescription sleep medications.² Overall, melatonin is not a panacea for all sleep problems, but it appears to be effective for people with disturbed sleep/wake cycles such as those traveling across time zones, elderly with low melatonin levels, and others with disrupted cycles.³

Dose Range and Upper Limit

Food and Nutrition Board DRI:

RDA/AI: Not relevant for this substance. However, for insomnia, typical dosage is .3 to 5 mg at or before bedtime.³ Dosage varies when melatonin is used for other purposes.³

Upper Limit: Not relevant for this substance.

Doses Used In Randomized Clinical Trials: Melatonin doses used in human studies range from 0.1 to 1000 mg. Studies vary from one-time ingestion to six months of daily ingestion.⁴

Toxicology Data: There is limited overdose data. Doses in the pharmacologic range (1-36 mg) showed side effects that include confusion, optic neuropathy, headache, a psychotic episode, seizure, autoimmune hepatitis, and skin eruptions. There were individual side effects with no consistent pattern seen.⁵

Evaluation of Potential Benefits

Melatonin helps increase total sleep time in individuals suffering from sleep restriction or altered sleep schedule, relieve daytime fatigue associated with jet lag, reduce the time it takes to fall asleep in people with delayed sleep phase syndrome, and re-set the body's sleep-wake cycle.³

Potential Detrimental Effects on...

Military Performance: In healthy subjects, daytime doses of oral melatonin 0.1 to 1 milligram produced significant drowsiness, fatigue, and performance decrements, which peaked approximately three to four hours after ingestion.³ Melatonin also can reduce oral and body temperature.^{3,6} Use of melatonin could also result in central nervous system effects (e.g., somnolence, headaches, increased frequency of seizures, nightmares), cardiovascular effects (e.g., hypotension or hypertension), gastrointestinal effects (e.g., diarrhea, abdominal pain), and dermatological effects.⁴ If melatonin is used for daytime sleep promotion, unwanted circadian phase shifts can occur; and if used to accelerate circadian phase shifts, potential unwanted sleep promotion can occur.⁶

^{*}Except for flight personnel.

There are special considerations related to use by pilots, however. The Navy includes melatonin among its "Class C supplements," which are described as "not authorized for use by any aviation personnel," by default of not otherwise being listed as either class A or class B.⁷ Anyone who has taken melatonin is removed from aviation duty for at least 24 hours after it was last taken, in keeping with the recommendations of a study by the FAA.⁸

Military Survivability: No data found.

Other Health Risks

Given that melatonin is a "timing hormone," oral supplementation of melatonin should occur near bedtime to avoid potential side effects. There are no known serious adverse effects or health risks from melatonin use by healthy individuals.

Interactions with Medications or Other Bioactive Substances

Fluvoxamine in combination with melatonin can increase central nervous system depression.3

When taken with nifedipine, melatonin has increased blood pressure and heart rate (clinical trials).3

Taking melatonin with verapamil (Calan, etc.) can increase melatonin excretion.³

Taking melatonin with warfarin may increase the risk of bleeding (case reports).3

Theoretically, melatonin could be problematic if used in combination with caffeine (interferes with effectiveness of melatonin), central-nervous-system depressants (i.e., sedatives and tranquilizers, as well as alcohol; increases sedative effects), anticoagulants (including aspirin, non-steroidal anti-inflammatory drugs; could promote bleeding), immunosupressants (melatonin stimulates immune function), anti-diabetes drugs (decreases effectiveness), contraceptives (could increase melatonin's effects), verapamil (could increase melatonin's effects), or benzodiazepines (also could increase melatonin's effects).

For details of these and other potential interactions, visit the Natural Medicines Comprehensive Database.3

Withdrawal Effects

No data found.

Concern Level (see Dietary Supplement Risk Matrix)

Benefit potential: Moderate

Risk (safety concern): Minimal (exception: High for flight personnel)

Classification score: **3** (**10** for flight personnel)

Evidence suggests that melatonin enhances various measures of sleep quality and helps shift circadian rhythms due to jet lag, night shift work, etc. However, it is best to seek the guidance of a physician before using melatonin. For flight personnel, it should not be used under any circumstances.

References

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