



Melatonin (5-Methoxy-N-Acetyltryptamine) is a hormone produced in the brain by the pineal gland from the amino acid tryptophan, that helps regulate sleep and wake cycle. The production and release of melatonin are stimulated by darkness and decreased by light, suggesting that melatonin is involved in circadian rhythm (the internal body clock) and regulation of diverse body functions. Levels of melatonin

in the blood are highest prior to bedtime. Most commonly, Melatonin supplements are used for people suffering from insomnia, delayed sleep phase syndrome (DSPS), insomnia associated with ADHD, insomnia due to certain high blood pressure medications called beta-blockers, and sleep problems in children with developmental disorders including autism, cerebral palsy, and intellectual disabilities. It is also used as a sleep aid after discontinuing the use of benzodiazepine drugs, to reduce the side effects of stopping smoking or long-term use of anti-anxiety medicine (Valium). It is also used to help regulate sleep/wake cycles in people who are blind. Melatonin has also been used in alternative medicine as an aid to treat insomnia caused by Alzheimer's disease or depression. No other hormone is available in the United States without a prescription. Because melatonin is contained naturally in some foods, the U.S. Dietary Supplement Health and Education Act of 1994 allow it to be sold as a dietary supplement. These do not need to be approved by the Food and Drug Administration (FDA) or controlled in the same way as drugs. Because it is not categorized as a drug, synthetic melatonin is made in factories that are not regulated by the FDA. Listed doses may not be controlled or accurate, meaning the amount of melatonin in a pill you take may not be the amount listed on the package. Most commercial products are offered at dosages that cause melatonin levels in the blood to rise to much higher levels than are naturally produced in the body.

When you walk down the dietary supplement aisle at CVS it is beyond overwhelming. Just to find where the melatonin was located was difficult. Once we found it, we realized there were at least ten different brands – Nature's Bounty, Sundown, Solgar, Radiance, Nature's Way, etc. If you decide to go with one brand, then you have to choose what dose and means of ingestion. The doses available range anywhere from 1 to 10 mg. They are available as tablets, lozenges, chewable gummies and liquid drops. In addition to all that, you must also decide if they want to take "quick dissolve, slow release, time-released, maximum, super, or triple strength" or a combination of any of these types. It seems dangerous to let the consumer decide how much and in what capacity to take this hormone. If a 120lb woman takes a 10mg dose because that is what her 200lb husband takes and has in the medicine cabinet, there could be extremely different effects for her than for him. There are a lot of drug interactions with Melatonin so it is risky to decide to take

something that has no approval from the FDA. Consumers can not be positive that the dose on the package is what they are actually receiving.

Melatonin oral supplementation should be taken near bedtime to avoid potential side effects. When taken with nifedipine, melatonin has increased blood pressure and heart rate. Also, taking melatonin with verapamil (Calan, etc.) can increase melatonin excretion. If you take warfarin, (which we learned in class is a drug that already has a narrow therapeutic range in of itself), with melatonin, there is an increased risk of bleeding. Even caffeine can interfere with this supplement because it counteracts the effectiveness. Alcohol and other central-nervous-system depressants (sedatives and tranquilizers) can increase the sedative effects. Anti-diabetes drugs (decreases effectiveness), contraceptives (could increase melatonin's effects), or benzodiazepines (also could increase melatonin's effects). Melatonin is metabolized in the liver by the cytochrome p450 enzyme CYP1A2. Fluvoxamine, cimetidine, ciprofloxacin, erythroymycin and tricyclic antidepressants, are drugs that inhibit CYP1A2 and can increase melatonin levels. NSAIDS, such as ibuprofen and naproxen, can decrease endogenous melatonin production, thereby requiring melatonin supplementation.

An interesting fact that we discovered when researching Melatonin was the restriction of its use for anyone on aviation duty. 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. 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 Federal Aviation Administration (FAA). At least the FAA is regulating its use even if the FDA is not!

Other brand names: Melatonin Olympian Labs®; Melatonin Tablets®; Melatonin Time Release®; Melatonin-BioDynamax®; Melatonin-Metabolic Response Modifier®; Melatonin-New Hope Health Products®; Melatonin-Optimum Nutrition®; Melaxen®; Nature's Bounty®; Puritan's Pride®; Rozerem®; Twinlab® Melatonin; Valdoxan®.

## References:

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