

Melatonin 3 mg

TECHNICAL SUMMARY

Melatonin is a potent free radical scavenger naturally produced in the pineal gland.* It is involved in many of the body's regulatory processes, including regulation of glandular secretory functions related to the maintenance of normal sleep/wake cycles and aspects of immune system function.* Supplemental melatonin has been shown to support healthy sleep patterns especially when travelling across time zones or for shift workers.*

Structure Formulas:

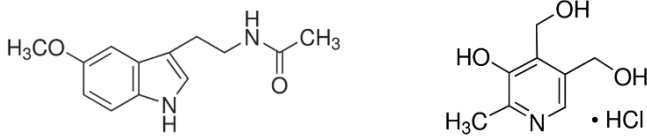


Fig. 1: Chemical structure of melatonin (left) and vitamin B6 (right).

Chemical Names:

Melatonin: *N*-acetyl-5-methoxytryptamine

Vitamin B₆: 4,5-bis(hydroxymethyl)-2-methylpyridin-3-ol hydrochloride

Allergen and Additive Disclosure: Not manufactured with wheat, gluten, soy, milk, egg, fish, shellfish, or tree nut ingredients. Produced in a GMP facility that processes other ingredients containing these allergens.

Delivery Form: Lozenge

ROLE AS NUTRIENT/FUNCTION

Melatonin acts as a potent free radical scavenger of reactive oxygen species and a neuroprotectant.* It influences a variety of biological processes, including circadian rhythm, neuroendocrine, immune and cardiovascular functions.* Taken at bedtime, melatonin contributes to the ease of falling asleep and alleviates manifestations of poorly coupled circadian rhythms. * In addition to being produced by the pineal gland, melatonin has been shown to be generated locally by neuroendocrine cells in many tissues including in the GI tract.* In the gastric and intestinal mucosa, melatonin acts via specific membrane receptors and also as a free radical scavenger.* It exerts protective, immune supporting, and free radical scavenging effects on the gastric lining, and helps support healthy pH levels as well as normal pepsin and gastrin production.*

B vitamins are required as co-enzymes for numerous complex reactions that are essential to cellular functions.* Vitamin B₆ acts as a coenzyme in the endogenous biosynthesis of melatonin, and its deficiency has been implicated in sleep disturbances.*

NATUROKINETICS®

Liberation: This product is in chewable mint form to deliver a delicious tasting melatonin supplement.

Supplement Facts

Serving Size 1 Lozenge

	Amount Per Serving	% Daily Value
Vitamin B ₆ (from Pyridoxine HCl)	3 mg	176%
Melatonin	3 mg	†

† Daily Value not established.

Other ingredients: Fructose, Cellulose, Stearic Acid (vegetable source), Mannitol, Natural Peppermint Flavor, Sorbitol and Magnesium Stearate (vegetable source).

- **Healthy Sleep Cycle***
- **Chewable, Fast Absorption***

SUGGESTED USAGE: Take 1 lozenge prior to bedtime, or as directed by your healthcare practitioner.

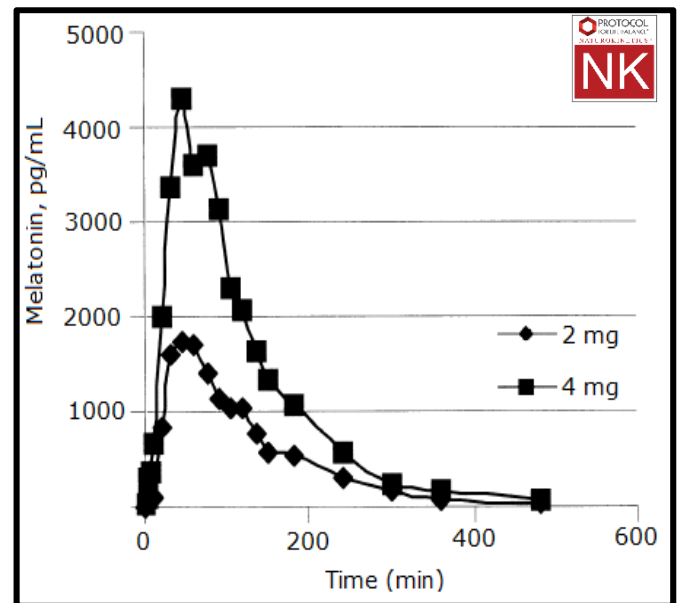


Fig. 2. Mean serum concentration versus time profile following single oral administration of 2 and 4 mg of melatonin tablets in healthy volunteers. Adapted from DeMuro et al. 2000.

Absorption: After ingestion of 1 to 5 mg melatonin, peak plasma levels for melatonin are 10-100 times the usual nighttime plasma levels within 1 hour of administration. In healthy volunteers with normal sleep-wake cycles, single administration of 2 or 4 mg melatonin tablets results in maximum plasma concentrations in approximately 1 hour (T_{max}) with absolute bioavailability of about 15% due to significant first-pass hepatic metabolism (Figure 2).

Vitamin B₆ is absorbed in the jejunum via passive diffusion and some evidence suggest this transport is pH dependent.

Distribution: Melatonin is subject to systemic distribution with levels detected in saliva. Melatonin is lipid-soluble and easily crosses the blood-brain barrier.

Upon absorption, vitamin B₆ enters the portal circulation where it binds to albumin in the plasma and hemoglobin for transport throughout the body. Vitamin B₆ is mainly stored in muscle tissue and the liver.

Metabolism: Endogenous melatonin is metabolized in the liver into 6-sulfatoxymelatonin which then undergoes conjugation and excretion as a sulfate or glucuronide. In the pineal gland and retina, melatonin is metabolized via deacetylation to 5-methoxytryptamine. Tissue uptake requires removal of the phosphate group by plasma membrane tissue nonspecific phosphatase.

Vitamin B₆ is metabolized in the liver and undergoes phosphorylation via pyridoxal kinase. It is converted to pyridoxal-5'-phosphate which is catalyzed by flavin-mononucleotide-dependent pyridoxamine 5'-phosphate for circulation throughout the body.

Elimination: Melatonin and its metabolite 6-sulfatoxymelatonin are primarily eliminated in the urine. Vitamin B₆ is eliminated only in the urine.

CLINICAL VALIDATION

- **Free Radical Scavenger.*** In a double blind, placebo-controlled clinical trial, 20 physically trained healthy volunteers received 3 mg melatonin or placebo supplementation followed by a physical test which involved a 50 km run and 2800 m climb. The supplementation protocol included: one 3 mg capsule 2 days before the test, one 3 mg capsule per meal 1 day before, and one 3 mg capsule the morning of and again 1 hour before. Markers of oxidative stress such as lipid peroxidation were significantly lower in the melatonin receiving group vs. placebo.*
- **Support of Healthy Sleep Cycle.*** In a randomized, controlled, crossover clinical trial, 17 healthy volunteers typically working 12--hour shifts for 2 weeks (week 1, the night shift and week 2, the day shift) received melatonin (3 mg, 1 hour before bedtime), a placebo, or bright light (30-minute exposure) during the first 4 days of the night shift and the first 4 days of the day shift. In the melatonin group, volunteers described less sleepiness at work during the day shift and increased sleep time by 15-20 minutes per day.*

SAFETY INFORMATION

Tolerability: Oral melatonin is well tolerated. Doses of melatonin as high as 50 mg/kg of body weight have been used in humans without reported adverse effects.

B vitamin supplementation could unmask the symptoms of polycythemia vera (a rare blood condition affecting 22 of every 100,000 individuals in the United States).

Contraindications: Do not drive or use machinery for 4 to 5 hours after taking melatonin.

INTERACTIONS

Drug Interactions: Concomitant use of melatonin with alcohol, benzodiazepines, or other similar drugs might cause increased sedation.

Melatonin may exhibit interaction with anti-coagulant/anti-platelet, antidepressant, anti-hypertensive, anticonvulsant, and anti-diabetic drugs.

Supplement Interactions: Melatonin may potentiate the effects of supplements with sedative components (e.g. 5-HTP, kava kava, valerian root). Melatonin may increase the effects of herbal supplements that have antiplatelet/anticoagulant properties, such as angelica, clove, garlic, ginger, ginkgo, *Panax ginseng*, and others.

Interaction with Lab Tests: Melatonin supplementation may increase human growth hormone serum levels and decrease serum luteinizing hormone levels.

STORAGE

Store in a cool, dry place in original sealed container.