

Product Overview

- Convenient single capsule sleep support
- Melatonin to initiate feelings of sleepiness & support overall wellness
- Magnesium to quiet excitatory pathways and support inhibitory pathways within the brain which promotes sleep
- Superior form of Magnesium (Magnesium glycinate) for enhanced absorption
- L-theanine to reduce feelings of anxiety and promote calmness
- All-natural excipients

Product Summary

Sleep is one of the most critical elements of human existence. Failure to obtain optimal levels of sleep affects everything from cardiovascular and immune system to cognition, metabolic health and social interactions. However, despite the need for sleep, many individuals struggle to fall and stay asleep on a nightly basis. To assist with this issue, Evolve Wellness has created Evolve Sleep.

Evolve Sleep is a convenient capsular product designed to support feelings of sleepiness as well as enhance sleep quality and promote overall wellness. Evolve Sleep can easily be titrated up depending on the patient/client needs. Each capsule of Evolve Sleep contains 3 mg of melatonin, 100 mg of magnesium & 150 mg of L-theanine.

Target Market/Population

A wide range of individuals may benefit from consumption of Evolve Sleep including those having trouble falling and staying asleep at night as well as those experiencing jet lag while flying across multiple time zones.

Suggested Use

Evolve Wellness recommends consuming 1 capsule of Evolve Sleep approximately 30-60 minutes prior to desired sleep time. One may increase to 2 or 3 at the discretion of a health care professional. Do not exceed 3 capsules per 24 day.

The Science

Melatonin

Secreted within the brain by the pineal gland, melatonin is a neurohormone which promotes feelings of sleepiness and helps to establish one's natural circadian (i.e 24 hour) rhythm. Multiple research studies have shown supplemental melatonin to not only decrease the time required to fall asleep but also, improve overall sleep quality.¹⁻⁴

With advancing age, it appears that the body's ability to naturally produce melatonin decreases.^{5,6} One particular study noted almost a 40-50% reduction in peak nocturnal melatonin production as well as total melatonin secretion over 24 hours (melatonin index), when comparing young (mean age ~ 37 yo) and elderly (mean age ~82) individuals.⁵ In a cross section study of Chinese, it was found drop-offs were most significant after age 60.⁶

This age-related decline in melatonin production may contribute to various chronic disease processes as melatonin is a powerful antioxidant. Human based research studies have shown supplemental melatonin to reduce blood pressure and improve lipid profiles in individuals with metabolic syndrome, improve aspects of cognition in those with mild cognitive impairment as well as improve bone density in post-menopausal women.⁷⁻⁹ It's also been noted to assist with reducing migraine pain in one small study.¹⁰

Weight management is another area where supplemental melatonin has shown promise in human based trials.^{11,12} When studied in postmenopausal women, one research group found that supplementing

1-3g of melatonin over the course of a year led to a ~7% loss in fat mass while trending towards an ~ 3.5% improvements in lean mass; these changes were brought about in the absence of any exercise or nutrition intervention.¹¹

To the best of the Evolve Wellness Science Team's knowledge there has not been any published research demonstrating melatonin supplementation will interfere with one's ability to naturally produce melatonin once they are no longer consuming it. Additionally, withdrawal symptoms following continuous melatonin use for 6-12 months appear minimal; although some individuals sleep patterns may return to their baseline levels.^{13,14}

Magnesium

Magnesium plays a key role in assisting a healthy sleep cycle through multiple mechanisms which promote a calm state and promote sleep. Within the brain, magnesium acts as an antagonist to excitatory NMDA receptors within the brain, which, when fully activated prevent one from falling and maintaining a normal, healthy sleep cycle.¹⁵

When giving to individuals experiencing insomnia, magnesium has been shown to improve one's sleep time, sleep efficiency, sleep onset latency and melatonin production.¹⁶ Additionally, magnesium appears effective in combating the effects of restless leg syndrome which can interfere with sleep.¹⁷

Not all forms of magnesium are equal; when chelated with an amino acid, magnesium is absorbed more efficiently.¹⁸ For this reason Evolve Sleep uses magnesium in the magnesium glycinate form as opposed to magnesium oxide.

L-Theanine

Present in tea leaves, L-theanine is a naturally occurring amino acid which has been shown to promote a state of 'calmness'/reduce anxiety; likely through its effects on alpha wave production within the brain.¹⁹ Although it doesn't cause feelings of 'sleepiness', by reducing feelings of anxiety, one may find it easier to fall asleep.

Currently there is not an extensive amount of research which has directly examined the effects of L-theanine on sleep. However, preliminary evidence has shown that L-theanine administration to improve various

parameters of sleep quality in both patients with major depressive disorder as well as boys with ADHD.^{20,21}

References

1. Kamoun A, Hammouda O, Yahia A, Dhari O, Ksentini H, Driss T, Souissi N, Elleuch MH Effects of Melatonin Ingestion Before Nocturnal Sleep on Postural Balance and Subjective Sleep Quality in Older Adults. *J Aging Phys Act.* 2018 Aug 30:1-27.
2. Costello RB, Lentino CV, Boyd CC, O'Connell ML, Crawford CC, Sprengel ML, Deuster PA. The effectiveness of melatonin for promoting healthy sleep: a rapid evidence assessment of the literature. *Nutr J.* 2014 Nov 7;13:106.
3. Sletten TL, Magee M, Murray JM, Gordon CJ, Lovato N, Kennaway DJ, Gwini SM, Bartlett DJ, Lockley SW, Lack LC, Grunstein RR, Rajaratnam SMW; Delayed Sleep on Melatonin (DelSoM) Study Group. Efficacy of melatonin with behavioural sleep-wake scheduling for delayed sleep-wake phase disorder: A double-blind, randomised clinical trial. *PLoS Med.* 2018 Jun 18;15(6):e1002587.
4. Andrade C, Srihari BS, Reddy KP, Chandramma L. Melatonin in medically ill patients with insomnia: a double-blind, placebo-controlled study. *J Clin Psychiatry.* 2001 Jan;62(1):41-5.
5. Magri F, Sarra S, Cinchetti W, Guazzoni V, Fioravanti M, Cravello L, Ferrari E. Qualitative and quantitative changes of melatonin levels in physiological and pathological aging and in centenarians. *J Pineal Res.* 2004 May;36(4):256-61.
6. Zhao ZY, Xie Y, Fu YR, Bogdan A, Touitou Y. Aging and the circadian rhythm of melatonin: a cross-sectional study of Chinese subjects 30-110 yr of age. *Chronobiol Int.* 2002 Nov;19(6):1171-82.
7. Koziróg M1, Poliwczyk AR, Duchnowicz P, Koter-Michalak M, Sikora J, Broncel M. Melatonin treatment improves blood pressure, lipid profile, and parameters of oxidative stress in patients with metabolic syndrome. *J Pineal Res.* 2011 Apr;50(3):261-6.
8. Cardinali DP1, Vigo DE, Olivar N, Vidal MF, Furio AM, Brusco LI. Therapeutic application of melatonin in mild cognitive impairment. *Am J Neurodegener Dis.* 2012;1(3):280-91.
9. Amstrup AK, Sikjaer T, Heickendorff L, Mosekilde L, Rejnmark L. Melatonin improves bone mineral density at the femoral neck in postmenopausal women with osteopenia: a randomized controlled trial. *J Pineal Res.* 2015 Sep;59(2):221-9.
10. Peres MF, Zukerman E, da Cunha Tanuri F, Moreira FR, Cipolla-Neto J. Melatonin, 3 mg, is effective for migraine prevention. *Neurology.* 2004 Aug 24;63(4):757.
11. Amstrup AK, Sikjaer T, Pedersen SB, Heickendorff L, Mosekilde L, Rejnmark L. Reduced fat mass and increased lean mass in response to 1 year of melatonin treatment in postmenopausal women: A randomized placebo-controlled trial. *Clin Endocrinol (Oxf).* 2016 Mar;84(3):342-7.
12. Szewczyk-Golec K, Rajewski P, Gackowski M, Miła-Kierzenkowska C, Wesołowski R, Sutkowy P, Pawłowska M, Woźniak A. Melatonin Supplementation Lowers Oxidative Stress and Regulates Adipokines in Obese Patients on a Calorie-Restricted Diet. *Oxid Med Cell Longev.* 2017;2017:8494107.

13. Wade AG, Ford I, Crawford G, McConnachie A, Nir T, Laudon M, Zisapel N. Nightly treatment of primary insomnia with prolonged release melatonin for 6 months: a randomized placebo controlled trial on age and endogenous melatonin as predictors of efficacy and safety. *BMC Med.* 2010 Aug 16;8:51.
14. Lemoine P1, Garfinkel D, Laudon M, Nir T, Zisapel N. Prolonged-release melatonin for insomnia - an open-label long-term study of efficacy, safety, and withdrawal. *Ther Clin Risk Manag.* 2011;7:301-11.
15. Johnson JW, Ascher P. Voltage-dependent block by intracellular Mg²⁺ of N-methyl-D-aspartate-activated channels. *Biophys J.* 1990 May;57(5):1085-90.
16. Abbasi B, Kimiagar M, Sadeghniaat K, Shirazi MM, Hedayati M, Rashidkhani B. The effect of magnesium supplementation on primary insomnia in elderly: A double-blind placebo-controlled clinical trial. *J Res Med Sci.* 2012 Dec;17(12):1161-9.
17. Hornyak M1, Voderholzer U, Hohagen F, Berger M, Riemann D. Magnesium therapy for periodic leg movements-related insomnia and restless legs syndrome: an open pilot study. *Sleep.* 1998 Aug 1;21(5):501-5.
18. Schuette SA, Lashner BA, Janghorbani M. Bioavailability of magnesium diglycinate vs magnesium oxide in patients with ileal resection. *JPEN J Parenter Enteral Nutr.* 1994 Sep-Oct;18(5):430-5.
19. Song CH, Jung JH, Oh JS, Kim KS. Effects of Theanine on the Release of Brain Alpha Wave in Adult Males. *Korean J Nutr.* 2003 Nov;36(9):918-923.
20. Hidese S, Ota M, Wakabayashi C, Noda T, Ozawa H, Okubo T, Kunugi H. Effects of chronic l-theanine administration in patients with major depressive disorder: an open-label study. *Acta Neuropsychiatr.* 2017 Apr;29(2):72-79.
21. Lyon MR1, Kapoor MP, Juneja LR. The effects of L-theanine (Suntheanine®) on objective sleep quality in boys with attention deficit hyperactivity disorder (ADHD): a randomized, double-blind, placebo-controlled clinical trial. *Altern Med Rev.* 2011 Dec;16(4):348-54.