

LIGHTS OUT™

Formula 210108-02v1

VEGETARIAN • ALL NATURAL • NON-GMO • PLANT
DERIVED • BSE-FREE • CRUELTY FREE • SOY FREE •
DAIRY FREE • GLUTEN FREE • CGMP • NSF • FDA

L-Tryptophan: *The serotonin precursor amino acid, 250mg significantly reduced sleep latency and increased Stage IV (NREM, REM) sleep*

Mg/Serving: 300

[Höglund E, Överli Ø, Winberg S.](#) Tryptophan Metabolic Pathways and Brain Serotonergic Activity: A Comparative Review. *Front Endocrinol (Lausanne)*. 2019. 10:158.

[Hartmann E, Spinweber C.](#) Sleep induced by L-tryptophan. Effect of dosages within the normal dietary intake. *J Nerv Ment Dis*. 1979. 167(8):497-9.

[Gibson E.](#) Tryptophan supplementation and serotonin function: genetic variations in behavioural effects. *Proc Nutr Soc*. 2018. 77(2):174-188.

Valerian 0.8%: *200mg (as well as 187mg + 41.9mg hops extract) increased sleep quality and duration; a polyherbal extract (Valerian 300mg, Passiflora 80mg, Hops 30mg) significantly improved total sleep time, sleep latency, number of nightly awakenings and insomnia severity index scores similar to Ambien; 300mg alters functional brain connectivity in relation to anxiety, inducing relaxation.*

Mg/Serving: 300

[Oxman A, Flottorp S, Håvelsrud K et al.](#) A televised, web-based randomised trial of an herbal remedy (valerian) for insomnia. *PLoS One*. 2007. 2(10):e1040.

[Morin C, Koetter U, Bastien C et al.](#) Valerian-hops combination and diphenhydramine for treating insomnia: a randomized placebo-controlled clinical trial. *Sleep*. 2005. 28(11):1465-71.

[Maroo N, Hazra A, Das T.](#) Efficacy and safety of a polyherbal sedative-hypnotic formulation NSF-3 in primary insomnia in comparison to zolpidem: a randomized controlled trial. *Indian J Pharmacol*. 2013. 45(1):34-39.

[Roh D, Jung J, Yoon K et al.](#) Valerian extract alters functional brain connectivity: A randomized double-blind placebo-controlled trial. *Phytother Res*. 2019. 33(4):939-948.

[Donath F, Quispe S, Diefenbach K et al.](#) Critical evaluation of the effect of valerian extract on sleep structure and sleep quality. *Pharmacopsychiatry*. 2000. 33(2):47-53.

Passiflora 1.2%: *60mg significantly increases sleep time and efficiency; a polyherbal extract (Valerian 300mg, Passiflora 80mg, Hops 30mg) significantly improved total sleep time, sleep latency, number of nightly awakenings and insomnia severity index scores similar to Ambien.*

Mg/Serving: 80

[Lee J, Jung H, Lee S et al.](#) Effects of Passiflora incarnata Linnaeus on polysomnographic sleep parameters in subjects with insomnia disorder: a double-blind randomized placebo-controlled study. *Int Clin Psychopharmacol*. 2020. 35(1):29-35.

[Ngan A, Conduit R.](#) A double-blind, placebo-controlled investigation of the effects of Passiflora incarnata (passionflower) herbal tea on subjective sleep quality. *Phytother Res*. 2011. 25(8):1153-9.

[Elsas S, Rossi D, Raber J et al.](#) Passiflora incarnata L. (Passionflower) extracts elicit GABA currents in hippocampal neurons in vitro, and show anxiogenic and anticonvulsant effects in vivo, varying with extraction method. *Phytomedicine*. 2010. 17(12):940-949.

[Maroo N, Hazra A, Das T.](#) Efficacy and safety of a polyherbal sedative-hypnotic formulation NSF-3 in primary insomnia in comparison to zolpidem: a randomized controlled trial. *Indian J Pharmacol*. 2013. 45(1):34-39.

Hops 5:1: *41.9mg (+187mg Passiflora) increased sleep quality and duration; 30mg Hops (with 300mg valerian and 80mg Passiflora) significantly improved total sleep time, sleep latency, number of nightly awakenings and insomnia severity index scores similar to Ambien; and a hops/valerian combination was as effective as benzodiazepine (aka Valium, Xanax) for insomnia.*

Mg/Serving: 30

[Morin C, Koetter U, Bastien C et al.](#) Valerian-hops combination and diphenhydramine for treating insomnia: a randomized placebo-controlled clinical trial. *Sleep*. 2005. 28(11):1465-71.

[Maroo N, Hazra A, Das T.](#) Efficacy and safety of a polyherbal sedative-hypnotic formulation NSF-3 in primary insomnia in comparison to zolpidem: a randomized controlled trial. *Indian J Pharmacol*. 2013. 45(1):34-39.

[Schmitz M, Jäckel M.](#) [Comparative study for assessing quality of life of patients with exogenous sleep disorders (temporary sleep onset and sleep interruption disorders) treated with a hops-valerian preparation and a benzodiazepine drug]. *Wien Med Wochenschr*. 1998. 148(13):291-8.

Melatonin: 0.5mg decreased sleep onset time (by 34m); 2.5mg significantly improved sweep quality in hypertensive subjects; 3-5mg significantly increased REM sleep;
Mg/Serving: 12

[Stetten T, Magee M, Murray J et al.](#) 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. 15(6):e1002587.
[Scheer F, Morris C, Garcia J et al.](#) Repeated melatonin supplementation improves sleep in hypertensive patients treated with beta-blockers: a randomized controlled trial. *Sleep.* 2012. 35(10):1395-402.
[Kunz D, Mahlberg R, Müller C et al.](#) Melatonin in patients with reduced REM sleep duration: two randomized controlled trials. *J Clin Endocrinol Metab.* 2004. 89(1):128-34.
[Cajochen C, Kräuchi K, Möri D et al.](#) Melatonin and S-20098 increase REM sleep and wake-up propensity without modifying NREM sleep homeostasis. *Am J Physiol.* 1997. 272(4 Pt 2):R1189-96.
[Costello R, Lentino C, Boyd C et al.](#) The effectiveness of melatonin for promoting healthy sleep: a rapid evidence assessment of the literature. *Nutr J.* 2014;13:106.

Piperine: 10-20mg/day increases the bioavailability/absorption rates of vitamins (B1, B2, B3, B6, B9, B12, C), minerals (iodine, calcium, iron, zinc, copper, selenium, magnesium, potassium, manganese), amino acids (lysine, isoleucine, leucine, threonine, valine, tryptophan, phenylalanine, methionine), herbal compounds (curcumin, ginsenosides, quercetin, coenzyme Q10, resveratrol, EGCG, pine extract), and drugs (ibuprofen, diclofenac, rifampicin, ampicillin, tetracycline, pyrazinamide, fexofenadine). For example, it has been shown to increase curcumin levels by 2000%.

Mg/Serving: 10

[Ahmad, N, Fazal H, Abbasi B et al.](#) Khan, M.A. (2012) Biological Role of Piper nigrum L. (Black Pepper): A Review. *Asian Pac J Trop Biomed.* 2010, 5:1945-1953.
[Ajazuddin, Alexander A, Qureshi A et al.](#) Role of herbal bioactives as a potential bioavailability enhancer for Active Pharmaceutical Ingredients. *Fitoterapia.* 2014 Sep;97C:1-14.
[Allameh A, Saxena M, Biswas G et al.](#) Piperine, a plant alkaloid of the piper species, enhances the bioavailability of aflatoxin B1 in rat tissues. *Cancer Lett.* 1992 Jan 31;61(3):195-9.
[Alodeani E, Arshad M, Izhari M.](#) Drug likeness and physicochemical properties evaluation of the alkaloids found in black pepper: piperine, piperidine, piperettine and piperanine. *Eur J Pharm Med Res.* 2015, 2(6), 296-301.
[Alvarez-Berdugo D, Jiménez M, Clavé P et al.](#) Pharmacodynamics of TRPV1 Agonists in a Bioassay Using Human PC-3 Cells, *Sci World J.* 2014, ID 184526, 6 pages.
[Atal N, Bedi K:](#) Bioenhancers: Revolutionary concept to market. *J Ayur Integ Med* 2010. 1:96–9.
[Atal K, Zutshi U, Rao P:](#) Scientific evidence on the role of Ayurvedic herbs on bioavailability of drugs. *J Ethnopharm* 1981. 4(2): 229-32.
[Badmaev V, Majeed M, Norkus E:](#) Piperine, an alkaloid derived from black pepper increases serum response of beta-carotene during 14-days of oral beta-carotene supplementation. *Nutri Res.* 1999, 19(3): 381–388.
[Badmaev V, Majeed M, Prakash L:](#) Piperine derived from black pepper increases the plasma levels of coenzyme Q10 following oral supplementation. *J Nutri Biochem* 2000; 11(2):109–113.
[Bhardwaj K, Glaeser H, Becquemont L et al.](#) Piperine, a major constituent of black pepper, inhibits human P-glycoprotein and CYP3A4. *J Pharm Exp Ther.* 2002, 302(2):645-650.
[Chopra B, Dhingra A, Kapoor R et al.](#) Piperine and Its Various Physicochemical and Biological Aspects: A Review. *Open Chem J.* 2016, 3, 75-96.
[Dubey R, Leeners B, Imthurn B et al.](#) Piperine Decreases Binding of Drugs to Human Plasma and Increases Uptake by Brain Microvascular Endothelial Cells. *Phytother Res.* 2017, 31(12):1868-1874.
[Dudhatra G, Mody S, Awale M et al.](#) A Comprehensive Review on Pharmacotherapeutics of Herbal Bioenhancers. *Sci World J.* 2012, Sept: 637953.
[Gopal V, Prakash G, Velvizhi T:](#) Bio-Enhancer: A Pharmacognostic Perspective. *Eur J Mol Biol Biochem.* 2016;3(1):33-38.
[Jhanwar J, Gupta S:](#) Biopotentiality using Herbs: Novel Technique for Poor Bioavailable Drugs. *Int J PharmT Res* 2014. 6(2): 443-454.
[Johnson J, Nihal M, Siddiqui I et al.](#) Enhancing the bioavailability of resveratrol by combining it with piperine. *Mol Nutri Food Res.* 2011, 55(8): 1169–1176.
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[Kesarwani K, Gupta R, Mukerjee A:](#) Bioavailability enhancers of herbal origin: an overview. *Asian Pac J Trop Biomed.* 2013 Apr; 3(4):253-66.
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[Majeed M, Badmaev V, Rajendran R, Inventors:](#) Sabinsa Corporation, assignee. Use of piperine as a bioavailability enhancer. US patent 5,744,161. April 28, 1998.
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[Mujumdar A, Dhuley J, Deshmukh V et al.](#) Effect of piperine on pentobarbitone induced hypnosis in rats. *Indian J Exp Biol.* 1990a, 28:486-487.
[Muneer C, Pandey V:](#) Effect of Piperine on Oral Bioavailability of Diltiazem HCl in Rabbits. *Int J Pharm App.* 2012, 3(4):406-413.
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[Panahi Y, Ghanei M, Hajhashemi A et al.](#) Effects of Curcuminoids-Piperine Combination on Systemic Oxidative Stress, Clinical Symptoms and Quality of Life in Subjects with Chronic Pulmonary Complications Due to Sulfur Mustard: A Randomized Controlled Trial. *J Diet Suppl.* 2016;13(1):93-105.
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[Rahimnia A, Panahi Y, Alishiri G et al.](#) Impact of Supplementation with Curcuminoids on Systemic Inflammation in Patients with Knee Osteoarthritis: Findings from a Randomized Double-Blind Placebo-Controlled Trial. *Drug Res (Stuttg).* 2014 Jul 22. [Epub ahead of print]
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