

Epigallocatechin gallate (EGCG: Green Tea Extract): 146-238mg EGCG significantly improved attention and psychomotor speeds in response to stimuli; 300mg EGCG significantly increased alpha, beta, theta cerebral activity, and increased self-rated calmness and reduced self-rated stress. Concomitant administration of piperine increases the oral bioavailability of EGCG by 130%.

Mg/Serving: 300

[Dietz C, Dekker M, Piqueras-Fiszman B et al.](#) An intervention study on the effect of matcha tea, in drink and snack bar formats, on mood and cognitive performance. *Food Res Int.* 2017. 99(Pt 1):72-83.

[Scholey A, Downey L, Ciorciari J et al.](#) Acute neurocognitive effects of epigallocatechin gallate (EGCG).

Appetite. 2012. 58(2):767-70. [Lambert J, Hong J, Kim D.](#) Piperine enhances the bioavailability of the tea

polyphenol (-)-epigallocatechin-3-gallate in mice. *J Nutr.* 2004. 134(8):1948-52.

L-Theanine: 100mg significantly reduced error rates; 200mg/day relaxes the mind without inducing drowsiness, reduced sleep latency/disturbances/medication, increasing verbal fluency and executive function; in combination with caffeine, it improved cognition, rapid visual information processing, reaction time, numeric working memory reaction time, ed sentence verification accuracy and reduced mind “wandering” and mental fatigue. Mg/Serving: 150

[Fuxe J, Morie K, Laud P et al.](#) Assessing the effects of caffeine and theanine on the maintenance of vigilance during a sustained attention task. *Neuropharmacology.* 2012. 62(7):2320-7.

[Nobre A, Rao A, Owen G.](#) L-theanine a natural constituent in tea, and its effect on mental state. *Asia Pac J Clin*

Nutr. 2008. 1:167-8. [Hidese S, Ogawa S, Ota M et al.](#) Effects of L-Theanine Administration on Stress-Related Symptoms and Cognitive Functions in Healthy Adults: A Randomized Controlled Trial. *Nutrients.* 2019. 11(10):2362.

[Kahathuduwa C, Dassanayake T, Amarakoon A et al.](#) Acute effects of theanine, caffeine and theanine-caffeine combination on attention. *Nutr Neurosci.* 2017. 20(6):369-377.

[Haskell C, Kennedy D, Milne A et al.](#) The effects of L-theanine, caffeine and their combination on cognition and mood. *Biol Psychol.* 2008. 77(2):113-22.

Caffeine: low-dose (40-100mg) caffeine significantly improved alertness & cognitive performance, increased concentration, arousal, focus, energy and alertness.

Mg/Serving: 150

[Durlach P.](#) The effects of a low dose of caffeine on cognitive performance. *Psychopharmacology (Berl).* 1998. 140(1):116-9.

[Smith A, Sturges W, Gallagher J.](#) Effects of a low dose of caffeine given in different drinks on mood and performance. *Human Psychopharmacology: Clinical and Experimental.* 1999. 14:473-482.

[Peeling P, Dawson B.](#) Influence of caffeine ingestion on perceived mood states, concentration, and arousal levels during a 75-min university lecture. *Adv Physiol Educ.* 2007. 31(4):332-5.

[Kahathuduwa C, Dassanayake T, Amarakoon A et al.](#) Acute effects of theanine, caffeine and theanine-caffeine combination on attention. *Nutr Neurosci.* 2017. 20(6):369-377.

Pine Bark Extract: 100-150mg maritime pine bark extract (Pycnogenol) significantly increased cognitive function, attention, working memory, episodic memory, and psychomotor performance while decreasing oxidative stress.

Mg/Serving: 150

[Belcaro G, Dugall M, Ippolito E et al.](#) The COFU3 Study. Improvement in cognitive function, attention, mental performance with Pycnogenol® in healthy subjects (55-70) with high oxidative stress. *J Neurosurg Sci.* 2015. 59(4):437-46.

[Ryan J, Croft K, Mori T et al.](#) An examination of the effects of the antioxidant Pycnogenol on cognitive performance, serum lipid profile, endocrinological and oxidative stress biomarkers in an elderly population. *J Psychopharmacol.* 2008. 22(5):553-62.

[Luzzi R, Belcaro G, Zulli C et al.](#) Pycnogenol® supplementation improves cognitive function, attention and mental performance in students. *Panminerva Med.* 2011. 53(3 Suppl 1):75-82.

[Pipingas A, Silberstein R, Vitetta L et al.](#) Improved cognitive performance after dietary supplementation with a Pinus radiata bark extract formulation. *Phytother Res.* 2008. 22(9):1168-74.

Ashwagandha: 120-300mg alleviated OCD similar to SSRIs; reduced stress/anxiety; increased cardiorespiratory function and improved QOL.

Mg/Serving: 200

[Jahanbakhsh S, Manteghi A, Emami S et al.](#): Evaluation of the efficacy of *Withania somnifera* (Ashwagandha) root extract in patients with obsessive-compulsive disorder: A randomized double-blind placebo-controlled trial. *Complement Ther Med*. 2016. 27:25-9.

[Chandrasekhar K, Kapoor J, Anishetty S.](#): A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full spectrum extract of Ashwagandha root in reducing stress and anxiety in adults. *Indian J Psych Med* 2012. 34(3), 255.

[Choudhary D, Bhattacharyya S, Bose S.](#): Efficacy and Safety of Ashwagandha (*Withania somnifera* (L.) Dunal) Root Extract in Improving Memory and Cognitive Functions. *Journal of Dietary Supplements*. 2017. 14(6):599-612.

[Langade D, Kanchi S, Salve J et al.](#): Efficacy and Safety of Ashwagandha (*Withania somnifera*) Root Extract in Insomnia and Anxiety: A Double-blind, Randomized, Placebo-controlled Study. *Cureus*. 2019. 11(9):e5797.

KSM-66® Ashwagandha: *Decreases cortisol levels by 27.9%, reduces perceived stress levels by 44%, aids in memory improvements, improves sleep quality, and enhances endurance and quality of life.*

Mg/Serving:

[Chandrasekhar K, Kapoor J, Anishetty S.](#): A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety in adults. *Indian J Psychol Med*. 2012;34(3):255-262.

[Choudhary D, Bhattacharyya S, Joshi K.](#): Body Weight Management in Adults Under Chronic Stress Through Treatment With Ashwagandha Root Extract: A Double-Blind, Randomized, Placebo-Controlled Trial. *J Evid Based Complementary Altern Med*. 2017;22(1):96-106.

[Choudhary D, Bhattacharyya S, Bose S.](#): Efficacy and Safety of Ashwagandha (*Withania somnifera* (L.) Dunal) Root Extract in Improving Memory and Cognitive Functions. *J Diet Suppl*. 2017;14(6):599-612.

[Langade D, Kanchi S, Salve J, et al.](#): Efficacy and Safety of Ashwagandha (*Withania somnifera*) Root Extract in Insomnia and Anxiety: A Double-blind, Randomized, Placebo-controlled Study. *Cureus*. 2019;11(9):e5797.

[Tiwaria, S., Gupta, S.K., Pathak, A.K.:](#) A double-blind, randomized, placebo-controlled trial on the effect of Ashwagandha (*Withania somnifera* dunal.) root extract in improving cardiorespiratory endurance and recovery in healthy athletic adults. *Journal of Ethnopharmacology*. 2021. 272.

L-Dopa: *100mg/day increased recall memory*

Mg/Serving: 150 (20%)

[Shellshear L, MacDonald A, Mahoney J et al.](#): Levodopa enhances explicit new-word learning in healthy adults: a preliminary study. *Hum Psychopharm*. 2015. 30(5):341-9.

[Lebedev A, Nilsson J, Lindström J et al.](#): Effects of daily L-dopa administration on learning and brain structure in older adults undergoing cognitive training: a randomised clinical trial. *Sci Rep*. 2020. 10(1):5227.

[Newman R, Weingartner H, Smallberg S et al.](#): Effortful and automatic memory: effects of dopamine. *Neurology*. 1984 Jun;34(6):805-7.

Resveratrol: *50-500mg/day significantly decreased fatigue, increased cerebral blood flow and memory performance. Concomitant administration of piperine increases the oral bioavailability of resveratrol by 229%.* Mg/Serving: 51

[Wightman E, Haskell-Ramsay C, Reay J et al.](#): The effects of chronic trans-resveratrol supplementation on aspects of cognitive function, mood, sleep, health and cerebral blood flow in healthy, young humans. *Br J Nutr* 2015. 14;114(9):1427-37.

[Köbe T, Witte A, Schnelle A et al.](#): Impact of Resveratrol on Glucose Control, Hippocampal Structure and Connectivity, and Memory Performance in Patients with Mild Cognitive Impairment. *Front Neurosci*. 2017. 11:105.

[Witte A, Kerti L, Margulies D et al.](#): Effects of resveratrol on memory performance, hippocampal functional connectivity, and glucose metabolism in healthy older adults. *J Neurosci*. 2014. 34(23):7862-70.

[Johnson J, Nihal M, Siddiqui I et al.](#): Enhancing the bioavailability of resveratrol by combining it with piperine. *Mol Nutr Food Res*. 2011. 5(8):1169-1176.

Curcumin: *90-180mg/day significantly improved cognitive function, memory improvement. Concomitant administration of piperine increases the oral bioavailability of curcumin by 2000%.*

Mg/Serving: 53

[Zhu L, Mei X, Zhang Z et al.](#): Curcumin intervention for cognitive function in different types of people: A systematic review and meta-analysis. *Phytother Res*. 2019. 33(3):524-533.

[Santos-Parker J, Strahler T, Bassett C et al](#): Curcumin supplementation improves vascular endothelial function in healthy middle-aged and older adults by increasing nitric oxide bioavailability and reducing oxidative stress. *Aging* 2017. 3;9(1):187-208.

[Panahi Y, Hosseini M, Khalili N et al](#): Effects of supplementation with curcumin on serum adipokine concentrations: A randomized controlled trial. *Nutrition*. 2016. 32(10):1116-22.

[Shoba G, Joy D, Joseph T et al](#): Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. *Planta Medica*, 1998. 64(4): 353–356.

Huperzine A: 100µg/day increased memory/learning performance
µg /Serving: 60

[Sun Q, Xu S, Pan J et al](#): Huperzine-A capsules enhance memory and learning performance in 34 pairs of matched adolescent students. *Zhongguo Yao Li Xue Bao*. 1999. 20(7):601-3.

[Tabira T, Kawamura N](#). A Study of a Supplement Containing Huperzine A and Curcumin in Dementia Patients and Individuals with Mild Cognitive Impairment. *J Alzheimers Dis*. 2018. 63(1):75-78..

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: 12

[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.

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[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 herbals 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](#): Biopotential 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. [Kang M, Cho J, Shim B et al](#): Bioavailability enhancing activities of natural compounds from medicinal plants. *J Med Plant Res*. 2009, 3(13): 1204–1211. [Kesarwani K, Gupta R, Mukerjee A](#): Bioavailability enhancers of herbal origin: an overview. *Asian Pac J Trop Biomed*. 2013 Apr; 3(4):253-66. [Khajuria A, Thusu N, Zutshi U](#): Piperine modulates permeability characteristics of intestine by inducing alterations in membrane dynamics: influence on brush border membrane fluidity, ultrastructure and enzyme kinetics. *Phytomedicine*. 2002 Apr;9(3):224-31.

[Khajuria A, Zutshi U, Bedi K](#): Permeability characteristics of piperine on oral absorption--an active alkaloid from

peppers and a bioavailability enhancer. *Indian J Exp Biol*. 1998 Jan;36(1):46-50.

[Kulkarni A, Dias R](#): Natural products as bioavailability enhancers. *Int J Inv Pharm Sci Res* 2017. 5(12):24-33.

[Lambert J, Hong J, Kim D et al](#): Piperine enhances the bioavailability of the tea polyphenol (-)-epigallocatechin-3-gallate in mice. *J Nutrition*. 2004. 134(8): 1948-52. [Majeed M, Badmaev V, Rajendran R, Inventors](#); Sabinsa Corporation, assignee. Use of piperine to increase the bioavailability of nutritional compounds. US patent 5,536,506, Jul. 16, 1996.

[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. [Meghwal M, Goswami T](#): Piper nigrum and Piperine: An Update. *Phyto Res* 2013. 27(8): 1121–1130.

[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. [Panahi Y, Badeli R, Karami G et al](#): Investigation of the Efficacy of Adjunctive Therapy with Bioavailability-Boosted Curcuminoids in Major Depressive Disorder. *Phytother Res*. 2015, 29(1):17-21.

[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. [Parmar V, Jain S, Bisht K et al](#): Phytochemistry of genus piper. *Phytochemistry* 1997. 46:597-673.

[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]

[Randhawa G, Kullar J, Rajkumar](#): Bioenhancers from mother nature and their applicability in modern medicine. *Int J Appl Basic Med Res*. 2011 Jan;1(1):5-10. [Reen R, Roesch S, Kiefer F et al](#): Piperine impairs cytochrome P4501A1 activity by direct interaction with the enzyme and not by down regulation of CYP1A1 gene expression in the rat hepatoma 5L cell line. *Biochem Biophys Res Commun* 1996. 218(2):562-9.

[Shoba G, Joy D, Joseph T et al](#): Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. *Planta Medica*, 1998. 64(4): 353–356. [Singh A, Duggal S](#): Piperine- Review of Advances in Pharmacology. *Int J Pharm Sci Nanotechnol*. 2009. 2:615–20.

[Singh V, Singh P, Mishra A et al](#): Piperine: delightful surprise to the biological world, made by plant “pepper” and a great bioavailability enhancer for our drugs and supplements. *World J Pharm Res* 2014; 3(6): 2084-2098.

[Srinivasan K](#): Black pepper and its pungent principle-piperine: A review of diverse physiological effects. *Critical Reviews in Food Science and Nutrition*. 2007. 47(8):735–48.

[Srinivasan K](#). (2013) *Biological Activities of Pepper Alkaloids*. In: Ramawat K., Mérillon JM. (eds) *Natural Products*. Springer, Berlin, Heidelberg. [Tatiraju D, Bagade V, Karambelkar P et al](#): Natural Bioenhancers: An overview. *J Pharm Phyto* 2013; 2 (3): 55-60.

[Wadhwa S, Singhal S, Rawat S](#): Bioavailability Enhancement by Piperine: A Review. *Asian J Biomed Pharma Sci*. 2014, 04(36): 1-8. [Wightman E, Reay J, Haskell C et al](#): Effects of resveratrol alone or in combination with piperine on cerebral blood flow parameters and cognitive performance in human subjects: a randomised, double-blind, placebo-controlled, cross-over investigation. *Br J Nutr*. 2014 Jul;112(2):203-13. [Zaveri M, Patel A, Khandhar A et al](#): Chemistry and Pharmacology of Piper Longum L. *Int J Pharm Sci Rev Res*. 2010, Dec; 5(1):67-76.