

## **Attention Support**

**Promotes Focus & Concentration** 

### Directions:

Ages 6-8 years take 2 capsules daily, 9-13 years take 3 capsules daily, 14+ years take 4 capsules. Take with food.

Serving Size: 30 day supply for 9-13 year olds

# Attention Support Addressing Focus Naturally Dietary Supplement 90 Capsules

### Ingredients:

Folinic Acid (Folate) 300.00 mcg, L-5-methyltetrahydrofolate, calcium salt 300.00 mcg Methylcobalamin (Vitamin B-12) 1000.00 mcg, Riboflavin (Riboflavin 5 Phosphate) 15.00 mg Vitamin B-6 (Pyridoxal 5 Phosphate) 50.00 mg, Zinc (TRAACS® Zinc Bisglycinate Chelate) 23.00 mg, Magnesium L-Threonate 55.00 mg, Passionflower (Passiflora incarnata L.) Aerial Powder 25.00 mg, SATIEREAL® (Safranal Extract) 30.00 mg, Magnesium (TRAACS® Magnesium Bisglycinate Chelate) 50.00 mg

### Clinical Applications:

- Supports focus and attention
- Enhances executive function and cognitive processing
- Supports optimal neurotransmission
- Supports a healthy mood

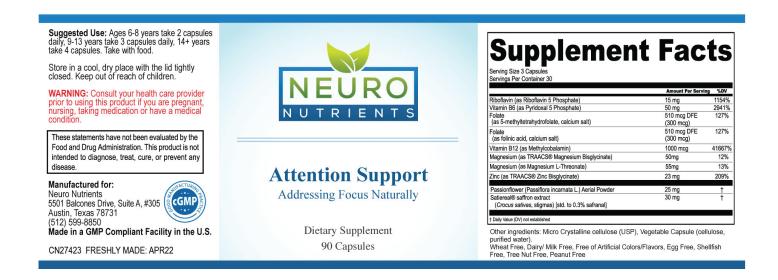
- Supports mental clarity and energy
- Promotes an alert and calm nervous system
- Supports optimizing known nutrient deficiencies in those with attention disorders

**SATIEREAL**® is a saffron extract (crocus sativus) from the stigma of the saffron flower. This is a highly concentrated, standardized, patented and propriety extract of saffron (standardized to >0.3% safranal) used in clinical research.



### Description:

Attention Support is a a powerful combination of evidence based nutraceuticals that have demonstrated efficacy in enhancing neurotransmitters that promote attention and focus in children and adults. This blend of bioactive B vitamins, calming minerals, and herbs is a natural choice to enhancing mental clarity, cognitive processing, and assisting in staying on task. Warning: Contact your physician or medical provider prior to use



### Formula Ingredient And Peer Reviewed Supportive References:

### SATIEREAL® Saffron Extract (crocus sativus)

Saffron is a spice that has been used in cooking for thousands of years. In some of the highest quality forms of research conducted in clinical nutrition medicine, saffron extract has shown numerous benefits for the brain and body (1). In a randomized, double blinded study, they gave children the stimulant medication, methylphenidate (also known as Daytrana or Quillivant), or saffron to treat ADHD, and after 6 weeks, they demonstrated the same efficacy in treatment (3). Several double-blind, randomized, placebo-controlled clinical trials have shown saffron can improve mild to moderate depression (2,5,7). One study showed the same efficacy using saffron as compared to a prescription antidepressant medication Citalopram (also known as Celexa)(5). Another therapeutic benefit saffron extract has shown is to reduce snacking, improve feelings of satiety, and support weight loss (6). The proposed mechanism of action for this herbal extract is its role in inhibiting serotonin re-uptake. It is plausible this mechanism of action has contributed to research results being consistent in demonstrating reproducible outcomes in the reduction of depressive symptoms (4,8).



- 1. Abu-Izneid T, Rauf A, Khalil AA, Olatunde A, Khalid A, Alhumaydhi FA, Aljohani ASM, Sahab Uddin M, Heydari M, Khayrullin M, Shariati MA, Aremu AO, Alafnan A, Rengasamy KRR. Nutritional and health beneficial properties of saffron (Crocus sativus L): a comprehensive review. Crit Rev Food Sci Nutr. 2022;62(10):2683-2706. doi: 10.1080/10408398.2020.1857682. Epub 2020 Dec 17. PMID: 33327732.
- 2. Akhondzadeh S, Tahmacebi-Pour N, Noorbala AA, Amini H, Fallah-Pour H, Jamshidi AH, Khani M. Crocus sativus L. in the treatment of mild to moderate depression: a double-blind, randomized and placebo-controlled trial. Phytother Res. 2005 Feb;19(2):148-51. doi: 10.1002/ptr.1647. PMID: 15852492.
- 3. Baziar S, Aqamolaei A, Khadem E, Mortazavi SH, Naderi S, Sahebolzamani E, Mortezaei A, Jalilevand S, Mohammadi MR, Shahmirzadi M, Akhondzadeh S. Crocus sativus L. Versus Methylphenidate in Treatment of Children with Attention-Deficit/Hyperactivity Disorder: A Randomized, Double-Blind Pilot Study. J Child Adolesc Psychopharmacol. 2019 Apr;29(3):205-212. doi: 10.1089/cap.2018.0146. Epub 2019 Feb 11. PMID: 30741567.
- 4. Dai L, Chen L, Wang W. Safety and Efficacy of Saffron (Crocus sativus L.) for Treating Mild to Moderate Depression: A Systematic Review and Meta-analysis. J Nerv Ment Dis. 2020 Apr;208(4):269-276. doi: 10.1097/NMD.000000000001118. PMID: 32221179.
- 5. Ghajar A, Neishabouri SM, Velayati N, Jahangard L, Matinnia N, Haghighi M, Ghaleiha A, Afarideh M, Salimi S, Meysamie A, Akhondzadeh S. Crocus sativus L. versus Citalopram in the Treatment of Major Depressive Disorder with Anxious Distress: A Double-Blind, Controlled Clinical Trial. Pharmacopsychiatry. 2017 Jul;50(4):152-160. doi: 10.1055/s-0042-116159. Epub 2016 Oct 4. PMID: 27701683.
- 6. Gout B, Bourges C, Paineau-Dubreuil S. Satiereal, a Crocus sativus L extract, reduces snacking and increases satiety in a randomized placebo-controlled study of mildly overweight, healthy women. Nutr Res. 2010 May;30(5):305-13. doi: 10.1016/j.nutres.2010.04.008. PMID: 20579522.
- 7. Kell G, Rao A, Beccaria G, Clayton P, Inarejos-García AM, Prodanov M. affron® a novel saffron extract (Crocus sativus L.) improves mood in healthy adults over 4 weeks in a double-blind, parallel, randomized, placebo-controlled clinical trial. Complement Ther Med. 2017 Aug;33:58-64. doi: 10.1016/j.ctim.2017.06.001. Epub 2017 Jun 13. PMID: 28735826.
- 8. Tóth B, Hegyi P, Lantos T, Szakács Z, Kerémi B, Varga G, Tenk J, Pétervári E, Balaskó M, Rumbus Z, Rakonczay Z, Bálint ER, Kiss T, Csupor D. The Efficacy of Saffron in the Treatment of Mild to Moderate Depression: A Meta-analysis. Planta Med. 2019 Jan;85(1):24-31. doi: 10.1055/a-0660-9565. Epub 2018 Jul 23. PMID: 30036891.



### Passionflower (Passiflora incarnata L.)

Passionflower has been used extensively in plant medicine and is best known for its anxiety reducing and calming effects on the nervous system (4,5). Anxiety disorders are typically treated with controlled medications (categorized as benzodiazepines) that can have unwanted sedative effects and impair the ability to perform job related tasks. Passionflower was studied in a randomized controlled trial with human subjects, and showed to be just as effective in treating anxiety as one of these benzodiazepine medications, called Oxazepam, however it had an advantage because it did not produce unwanted side effects of impaired job function (2). When given by medical providers alone for the treatment of anxiety, in a study with nearly 3,000 patients, passionflower showed very clinically significant improvement in anxiety scores after two weeks, compared to baseline (3). In addition, passionflower showed similar clinical benefit for treating ADHD compared to the stimulant medication, methylphenidate (also known as Quillivant or Daytrana), when given in a clinical trial. However, passionflower again showed an advantage in regards to side effects, as the stimulant medication group reported anxiety and decreased appetite (1). When given with an antidepressant (Sertraline, also known as Zoloft), passionflower was shown to be effective as an add on therapy in reducing anxiety (6).

- 1. Akhondzadeh S, Mohammadi MR, Momeni F. Passiflora incarnata in the treatment of attention-deficit hyperactivity disorder in children and adolescents. Therapy 2005;2(4):609-14.
- 2. Akhondzadeh S, Naghavi HR, Vazirian M, Shayeganpour A, Rashidi H, Khani M. Passionflower in the treatment of generalized anxiety: a pilot double-blind randomized controlled trial with oxazepam. Journal of clinical pharmacy and therapeutics. 2001;26:363–367.
- 3. Ansseau M, Seidel L, Crosset A, Dierckxsens Y, Albert A. A dry extract of Passiflora incarnata L. (Sedanxio) as first intention treatment of patients consulting for anxiety problems in general practice. Acta Psychiatrica Belgica 2012;112(3):5-11.
- 4. Elsas, S. M., Rossi, D. J., Raber, J., White, G., Seeley, C. A., Gregory, W. L., Mohr, C., Pfankuch, T., & Soumyanath, A. (2010). 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: international journal of phytotherapy and phytopharmacology, 17(12), 940–949. https://doi.org/10.1016/j.phymed.2010.03.002
- 5. Lolli LF, Sato CM, Romanini CV, Villas-Boas Lde B, Santos CA, de Oliveira RM. Possible involvement of GABA A-benzodiazepine receptor in the anxiolytic-like effect induced by Passiflora actinia extracts in mice. Journal of ethnopharmacology. 2007;111:308–314.



6. Nojoumi M, Ghaeli P, Salimi S, Sharifi A, Raisi F. Effects of Passion Flower Extract, as an Add-On Treatment to Sertraline, on Reaction Time in Patients with Generalized Anxiety Disorder: A Double-Blind Placebo- Controlled Study. Iran J Psychiatry. 2016 Jul;11(3):191-197. PMID: 27928252; PMCID: PMC5139955.

### Magnesium (L-threonate and bisglycinate)

Magnesium activates nerve channels in the brain that are fundamental to the process of learning, memory, and function (6). Magnesium helps lower one of the excitatory (or stimulating) neurotransmitters in our brain called glutamate. When glutamate is high, or in excessive levels in the brain, it can contribute to symptoms such as agitation, irritability, treatment resistant depression, headaches, insomnia, anxiety, and inattention (3,7). The supplemental forms of magnesium chosen for this formulation were critical to achieve the type of support intended. Magnesium bisglycinate is a form of magnesium that has been shown to have the highest rates of bioavailability, is more easily absorbed through the gut, and increases blood magnesium levels (1). Magnesium threonate has been found to be more easily absorbed into the brain, supports neurological function, and can even help repair neurological function that has been lost. Magnesium has been shown to improve executive function and cognitive processing, two symptoms in those with inattention disorders that are challenging and hallmarks of the disorder (4). In other compelling research, a study evaluating over 100 children with ADHD, found that 95% of them were magnesium deficient (2). In another study, magnesium was given with B6, and after an eight-week period, a significant reduction was seen in hyperactivity, aggressiveness, and inattention. When the study participants stopped the magnesium and B6 supplementation, the symptoms returned after two weeks (5). Attention Support contains both forms of magnesium (threonate and bisglycinate) and B6.

- 1. Blancquaert, L., Vervaet, C. Derave, W. Predicting and Testing Bioavailability of Magnesium Supplements. Nutrients. 2019 Jul; 11(7): 1663.
- 2. Kozielec T, Starobrat-Hermelin B. Assessment of magnesium levels in children with attention deficit hyperactivity disorder (ADHD). Magnes Res. 1997 Jun;10(2):143-8. PMID: 9368235.
- 3. Kris-Etherton, P. M., Petersen, K. S., Hibbeln, J. R., Hurley, D., Kolick, V., Peoples, S., Rodriguez, N., & Woodward-Lopez, G. (2021). Nutrition and behavioral health disorders: depression and anxiety. Nutrition reviews, 79(3), 247–260. https://doi.org/10.1093/nutrit/nuaa025
- 4. Liu, G., Weinger, J. G., Lu, Z. L., Xue, F., & Sadeghpour, S. (2016). Efficacy and Safety of MMFS-01, a Synapse Density Enhancer, for Treating Cognitive Impairment in Older Adults: A Randomized, Double-Blind, Placebo-Controlled Trial. Journal of Alzheimer's disease: JAD, 49(4), 971–990. https://doi.org/10.3233/JAD-150538



- 5. Mousain-Bosc M., Roche M., Polge A., Pradal-Prat D., Rapin J., Bali J.- P. Improvement of neurobehavioral disorders in children supplemented with magnesium-vitamin B6. I. Attention deficit hyperactivity disorders. Magnesium Research. 2006;19(1):46–52.
- 6. Slutsky I, Abumaria N, Wu LJ, Huang C, Zhang L, Li B, Zhao X, Govindarajan A, Zhao MG, Zhuo M, Tonegawa S, Liu G. Enhancement of learning and memory by elevating brain magnesium. Neuron. 2010 Jan 28;65(2):165-77. doi: 10.1016/j.neuron.2009.12.026. PMID: 20152124.
- 7. Zarate C, Duman RS, Liu G, Sartori S, Quiroz J, Murck H. New paradigms for treatment-resistant depression. Ann N Y Acad Sci. 2013 Jul;1292:21-31. doi: 10.1111/nyas.12223. PMID: 23876043; PMCID: PMC3936783.

### Zinc (bisglycinate)

Zinc is a critical mineral for the brain and body to develop and function optimally. Zinc is prevalent in the brain, where it binds to proteins, and contributes to how the brain is structured, develops, and how it functions (4,5). Studies have demonstrated blood zinc levels in patients with attention disorders are likely to be low (7). In a double-blind, placebo-controlled trial, they replaced zinc in children with ADHD, and it significantly reduced hyperactivity, impulsivity, and impaired socialization compared to placebo (3). Studies have shown zinc can also help ADHD stimulant medication be more effective, and in some cases, help lower the daily dose (1,2). The form of zinc in Attention Support was chosen due to its ability to absorb better in the body than other forms of zinc. The increased bioavailability of zinc bisglycinate increases blood levels of zinc more easily and is also typically better tolerated (6).

- 1. Akhondzadeh S., Mohammadi M.-R., Khademi M. Zinc sulfate as an adjunct to methylphenidate for the treatment of attention deficit hyperactivity disorder in children: a double blind and randomized trial [ISRCTN64132371] BMC Psychiatry. 2004;4, article 9 doi: 10.1186/1471-244x-4-9
- 2. Arnold LE, Disilvestro RA, Bozzolo D, et al. Zinc for attention-deficit/ hyperactivity disorder: placebo-controlled double-blind pilot trial alone and combined with amphetamine. J Child Adolesc Psychopharmacol. 2011;21(1):1-19. doi:10.1089/cap.2010.0073
- 3. Bilici M, Yildirim F, Kandil S, Bekaroğlu M, Yildirmiş S, Değer O, Ulgen M, Yildiran A, Aksu H. Double-blind, placebo-controlled study of zinc sulfate in the treatment of attention deficit hyperactivity disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2004 Jan;28(1):181-90. doi: 10.1016/j.pnpbp.2003.09.034. PMID: 14687872.



- 4. Black M. M. (1998). Zinc deficiency and child development. The American journal of clinical nutrition, 68(2 Suppl), 464S–469S. https://doi.org/10.1093/ajcn/68.2.464S
- 5. Colombo, J., Zavaleta, N., Kannass, K. N., Lazarte, F., Albornoz, C., Kapa, L. L., & Caulfield, L. E. (2014). Zinc supplementation sustained normative neurodevelopment in a randomized, controlled trial of Peruvian infants aged 6-18 months. The Journal of nutrition, 144(8), 1298–1305. https://doi.org/10.3945/jn.113.189365
- 6. Gandia P, Bour D, Maurette J-M, et al. A bioavailability study comparing two oral formulations of zinc (Zn bisglycinate vs. Zn gluconate) after a single administration to twelve healthy female volunteers. Int J Vitamin Nutr Res 2007;77(4):243-248
- 7. Ghoreishy, S.M., Ebrahimi Mousavi, S., Asoudeh, F. et al. Zinc status in attention-deficit/hyperactivity disorder: a systematic review and metaanalysis of observational studies. Sci Rep 11, 14612 (2021). https://doi.org/ 10.1038/ 541598-021-94124-5

### Vitamin B6 (pyridoxine 5 phosphate)

Vitamin B6 is important for helping us biosynthesize (or create) our neurotransmitters which play an important role in cognitive and brain development and function. B6 helps make one of the brains major inhibitory (or calming) neurotransmitters that have been shown to improve attentional processes (3). Disorders of B6 metabolism (being able to break down B6, so that the brain and body can use it) are more common in attention disorders and seizure disorders (1). Clinical trials have demonstrated supplementing with B6 and magnesium has reduced hyperactivity and aggression in children with ADHD, and improved school attention. When the study participants stopped the magnesium and B6 supplementation, the symptoms returned after two weeks (2).

- 1. Dolina S, Margalit D, Malitsky S, Rabinkov A. Attention-deficit hyperactivity disorder (ADHD) as a pyridoxine-dependent condition: urinary diagnostic biomarkers. Med Hypotheses. 2014;82(1):111-116. doi:10.1016/j. mehy.2013.11.018
- 2. Mousain-Bosc M., Roche M., Polge A., Pradal-Prat D., Rapin J., Bali J.- P. Improvement of neurobehavioral disorders in children supplemented with magnesium-vitamin B6. I. Attention deficit hyperactivity disorders. Magnesium Research. 2006;19(1):46–52
- 3. Novell, R., Esteba-Castillo, S., & Rodriguez, E. (2020). Efficacy and safety of a GABAergic drug (Gamalate® B6): effects on behavior and cognition in young adults with borderline-to-mild intellectual developmental disabilities and ADHD. Drugs in context, 9, 212601. https://doi.org/10.7573/ dic.212601



# Vitamin B12 (methylcobalamine), folate (5-methytretrahydrofolate and folinic acid), and B2 (riboflavin 5 phosphate)

DNA methylation, a way in which the body regulates gene expression, is supported through B vitamins, in particular vitamins B12, B2, and B9 (folate) (3). Attention disorders have been correlated with poor methylation (6). Attention Support includes the types of bioactive folates known to support growth, development, and mood disorders (1,8,9). Riboflavin supports the breakdown of folate into the active form, and is especially important for those with MTHFR gene mutations, which can impair folate bioavailability (5). Deficiencies in riboflavin can also contribute to headache disorders (2). The body does not make vitamin B12, and it has to be supplemented through the diet with B12 rich foods (7). Despite those eating foods high in B12 (such as animal protein) B12 is still absorbed better in supplemental form (7). Due to the complexity of how B12 is absorbed in the body, transported to the cells, and absorbed into the nervous system, Attention Support included a more bioavailable form of B12, at a higher dose, in the supplement formulation.

- 1. Alpert JE, Mischoulon D, Rubenstein GE, Bottonari K, Nierenberg AA, Fava M. Folinic acid (Leucovorin) as an adjunctive treatment for SSRI- refractory depression. Ann Clin Psychiatry. 2002;14(1):33-38. doi:10.1023/ a:1015271927517
- 2. Chen YS, Lee HF, Tsai CH, et al. Effect of Vitamin B2 supplementation on migraine prophylaxis: a systematic review and meta-analysis. Nutr Neurosci. 2021 Mar 29:1-12.
- 3. Collaboration HLT. Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomised trials. Homocysteine Lowering Trialists' Collaboration. BMJ. 1998 Mar 21;316(7135):894-8. PMID: 9569395; PMCID: PMC28491.
- 4. Coppen A, Bolander-Gouaille C. Treatment of depression: time to consider folic acid and vitamin B12. J Psychopharmacol. 2005;19(1):59-65. doi:10.1177/0269881105048899
- 5. Hustad S, Schneede J, Ueland PM. Riboflavin and Methylenetetrahydrofolate Reductase. Landes Bioscience; 2000-2013. Available from: https://www.ncbi.nlm.nih.gov/books/NBK6145/
- 6. Neumann, Al, et al. Association Between DNA Methylation and ADHD Symptoms From Birth To School Age: A Prospective Meta- Analysis. 2020, Translational Psychiatry, Volume 10, number 398
- 7. Office of Dietary Supplements Vitamin B12. https://ods.od.nih.gov/ factsheets/VitaminB12-HealthProfessional/. Accessed March 12, 2022.



- 8. Saha T, Chatterjee M, Verma D, Ray A, Sinha S, Rajamma U, Mukhopadhyay K. Genetic variants of the folate metabolic system and mild hyperhomocysteinemia may affect ADHD associated behavioral problems. Prog Neuropsychopharmacol Biol Psychiatry. 2018 Jun 8;84(Pt A):1-10. doi: 10.1016/j.pnpbp.2018.01.016. Epub 2018 Jan 31. PMID: 29407547.
- 9. Shelton RC, Sloan Manning J, Barrentine LW, Tipa EV. Assessing Effects of I-Methylfolate in Depression Management: Results of a Real-World Patient Experience Trial. Prim Care Companion CNS Disord. 2013;15(4):PCC.13m01520. doi:10.4088/PCC.13m01520