

Below, we have compiled a list of ALL the micronutrient formulas that have been studied to treat a psychiatric or psychological problem. This is an updated version, as of August 1, 2022, of the information listed in chapter 11 of *The Better Brain* by Kaplan and Rucklidge, published in April 2021.

Each product listed below has at least one positive RCT to support its use – all the research behind each of the products has been cited.

1. **EMPower™, EMPowerplus™, and EMPowerplus Advanced™ (EMP):** www.truehope.com (ADHD, PMS, symptoms associated with trauma, stress, anxiety):

For those taking the current EMP formulation for the treatment of psychiatric symptoms, the recommended dose on the bottle is two capsules twice a day. However, the dose more typically used in research has been four twice a day. For those using these products for assisting with managing stress, our research after the earthquakes and floods showed that a therapeutic dose may be lower, such as four a day.

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<https://doi.org/10.1136/bcr-2012-007213>
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2. **Daily Essential Nutrients***™ (DEN): www.hardynutritionals.com (ADHD, smoking cessation, emotional dysregulation, symptoms associated with trauma, aggression, stress, anxiety)

***Prior to 2013, there was just one formula and it was manufactured by TrueHope. From 2013 onward, Hardy Nutritionals produced Daily Essential Nutrients while TrueHope continued to produce EMP+. Therefore, the ingredients of DEN are very similar to EMP+ in both breadth and dose. Some modifications have been made to both formulas over the ensuing decade. For updated information on current formulas, see the manufacturers' websites.**

A full daily dose for improving psychiatric symptoms with DEN is four capsules three times a day (twelve/day) and this is the dose that has been the most used in the cited research. Hardy Nutritionals has a product called Optimal Balance® designed for people just seeking a little additional nutrient support to manage stress or insomnia. The typical daily dose is three twice a day (six/day).

DEN is a better choice than Optimal Balance® for those with more serious psychiatric problems and/or if taking the nutrients alongside psychiatric medications, where they may want to consult with the company product specialists regarding their own situation.

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47. Johnstone, J. M., Leung, B., Gracious, B., Perez, L., Tost, G., Savoy, A., . . . Arnold, L. E. (2019). Rationale and design of an international randomized placebo-controlled trial of a 36-ingredient micronutrient supplement for children with ADHD and irritable mood: The Micronutrients for ADHD in Youth (MADDY) study. *Contemporary clinical trials communications*, 16, 100478-100478. doi:10.1016/j.conctc.2019.100478 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6859218/>
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52. Robinette, LM; Hatsu, I; Johnstone JM; Tost, G; Bruton, AM; Eiterman, LP; Leung, BMY; Odie, JB;

- Orchard, T; Gracious, BL; Arnold, LE. (2022). Fruit and Vegetable Intake are Inversely Associated with Severity of ADHD and Emotional Dysregulation Symptoms in a Pediatric Population: The MADDY Study. *Nutritional Neuroscience*. <https://pubmed.ncbi.nlm.nih.gov/35535573/>
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55. Lu, S; Bruton, AM; Millington, E; Alexander, E; Camden, K; Johnstone, JM; Hatsu, I; Arnold, LE; Leung, B (2022). Parents' Priorities and Preferences for Treatment of their Children with ADHD: Qualitative Inquiry in the MADDY Study, a Multinutrient Intervention Trial. *Child: Care, Health & Development*. <https://doi.org/10.1111/cch.12995>

Both DEN and EMP are available as powders for mixing into juice, for those who cannot swallow capsules. Also, some people are very sensitive to the smell of dietary supplements. If the smell of the capsules is a problem, try keeping them in the fridge or freezer. Pre-pubertal children may take a lower dose (4 twice a day), although research studies have sometimes gone up to the full adult dose for treating childhood ADHD. As children enter their teenage years, research has shown that the dose may need to be increased to maintain symptom control.

Finally, the doses mentioned above are mostly based on research with people who were *not* taking any psychiatric medications (e.g., antidepressants, anxiolytics, stimulants) because up to this point, most studies have *excluded* people taking these medications.

The large number of pills does not imply that the micronutrient dosing is high. Many commercial products contain a broad spectrum of micronutrients in one or two capsules daily, but the nutrients are present in chemical forms that are poorly absorbed. One way to enhance bioavailability of the minerals is to deliver them in chelated forms (chelation promotes passage from the gut into the blood stream, where the minerals dissociate from the chelates), but the chelated minerals are bulky and cannot be condensed into one or two capsules. Furthermore, some broad-spectrum formulations also provide macro-minerals, such as calcium, magnesium, and phosphorus, which are often under-represented in diets and are required in much larger bulk quantities than micronutrients. Products containing chelated microminerals and bulky macrominerals require more pills each day, are more expensive, but will likely be more effective than regular formulations.

3. **Brain Child Spectrum Support/ANRC Essentials** (autism):
<http://www.brainchildnutritional.com/spectrum-support-vitamins.html/> or
<http://www.autismnrc.org/anrc-essentials>

Professor Jim Adams at Arizona State University has conducted a number of studies using nutrients for the treatment of autism, using three products: Spectrum Support II/III™, Syndion™, and ANRC Essentials Plus™ (a revised version of Syndion™). Spectrum Support comes as a capsule or colloidal suspension--the standard dose is two capsules (or two teaspoons) twice a day. For ANRC Essentials Plus™, the company provides information on how to gradually increase to the optimal dose based on body weight. The formula comes either as capsules or a powder to mix with your favorite juice (they suggest orange, mango, or cranberry).

- Adams, J. B., & Holloway, C. (2004). Pilot study of a moderate dose multivitamin/mineral supplement for children with autism spectrum disorder. *Journal of Alternative and Complementary Medicine*, 10(6), 1033-1039. <http://online.liebertpub.com/doi/abs/10.1089/acm.2004.10.1033>
- Adams, J. B., Audhya, T., McDonough-Means, S., Rubin, R. A., Quig, D., Geis, E., Gehn, E., Loresto, M., Mitchell, J., Atwood, S., Barnhouse, S., & Lee, W. (2011). Effect of a vitamin/mineral supplement on children and adults with autism. *BMC Pediatrics*, 11, 111. <https://doi.org/10.1186/1471-2431-11-111>
- Adams, J. B., Audhya, T., Geis, E., Gehn, E., Fimbres, V., Pollard, E., Mitchell, J., Ingram, J., Hellmers, R., Laake, D., Matthews, J., Li, K., Naviaux, J., Naviaux, R., Adams, R., Coleman, D., & Quig, D. (2018). Comprehensive Nutritional and Dietary Intervention for Autism Spectrum Disorder—A Randomized, Controlled 12-Month Trial. *Nutrients*, 10(3), 369. <http://www.mdpi.com/2072-6643/10/3/369>

4. **Forceval** (aggression in prisoners): <http://www.forceval.co.uk>

Forceval is available in a capsule or in effervescent tablets and is a licensed medicine in the UK. The recommended dose is one capsule daily. The main target for the formula is to combat malnutrition. However, Forceval has been used along with fish oil for omega 3s to successfully reduce aggression in people incarcerated in prisons. There were no adverse reactions.

- Gesch CB., Hammond SM, Hampson SE, et al. (2002). *The British Journal of Psychiatry*, 181(1) 22-28; doi: 10.1192/bjp.181.1.22

5. **Bayer's Berocca** (stress/anxiety/mood): <http://www.berocca.com/en/home.php>

Berocca is the most studied B-complex formula for reduction of stress. It can be taken as a capsule or an effervescent tablet that you add to water. It has been studied primarily in people drawn from the general population. No concerning side effects have been reported.

- Carroll, D., Ring, C., Suter, M., & Willemsen, G. (2000). The effects of an oral multivitamin combination with calcium, magnesium, and zinc on psychological well-being in healthy young male volunteers: a double-blind placebo-controlled trial. *Psychopharmacology*, 150(2), 220-225. <https://doi.org/doi:10.1007/s002130000406>
- Schlebush, L., Bosch, B. A., Polglase, G., Kleinschmidt, I., Pillay, B. J., & Cassimjee, M. H. (2000). A double-blind, placebo-controlled, double-centre study of the effects of an oral multivitamin-mineral combination on stress. *South African Medical Journal*, 90(12), 1216-1223. <https://www.ncbi.nlm.nih.gov/pubmed/11234653>
- Kennedy, D. O., Haskell, C. F., Robertson, B., Reay, J., Brewster-Maund, C., Luedemann, J., Maggini, S., Ruf, M., Zangara, A., & Scholey, A. B. (2008). Improved cognitive performance and mental fatigue following a multi-vitamin and mineral supplement with added guarana (*Paullinia cupana*). *Appetite*, 50(2-3), 506-513. <https://doi.org/10.1016/j.appet.2007.10.007>
- Kennedy, D., Veasey, R., Watson, A., Dodd, F., Jones, E., Maggini, S., & Haskell, C. (2010). Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males. *Psychopharmacology*, 211(1), 55-68. <https://doi.org/doi:10.1007/s00213-010-1870-3>
- Rucklidge, J. J., Andridge, R., Gorman, B., Blampied, N., Gordon, H., & Boggis, A. (2012). Shaken but unstirred? Effects of micronutrients on stress and trauma after an earthquake: RCT evidence comparing formulas and doses. *Human Psychopharmacology*, 27(5), 440-454. <https://doi.org/10.1002/hup.2246>
- Scholey, A., Bauer, I., Neale, C., Savage, K., Camfield, D., White, D., Maggini, S., Pipingas, A., Stough, C., & Hughes, M. (2013). Acute effects of different multivitamin mineral preparations with and without Guarana on mood, cognitive performance and functional brain activation. *Nutrients*, 5(9), 3589-3604. <https://doi.org/10.3390/nu5093589>
- White, D., Cox, K., Peters, R., Pipingas, A., & Scholey, A. (2015). Effects of Four-Week Supplementation with a Multi-Vitamin/Mineral Preparation on Mood and Blood Biomarkers in Young

Adults: A Randomised, Double-Blind, Placebo-Controlled Trial. *Nutrients*, 7(11), 5451.
<http://www.mdpi.com/2072-6643/7/11/5451>

6. **Swisse Ultivite** (stress/mood): <http://www.swisse.com/au/vitamins-and-supplements/mens-health/73/swisse-mens-ultivite-f1>

Swisse Ultivite™ is available in both a women and men's version and is taken as one capsule daily with a meal. Several studies support its use for reduction of stress in otherwise healthy people. No side effects were reported.

- Harris, E., Kirk, J., Rowsell, R., Vitetta, L., Sali, A., Scholey, A., & Pipingas, A. (2011). The effect of multivitamin supplementation on mood and stress in healthy older men. *Human Psychopharmacology*, 26(8), 560-567. <https://doi.org/10.1002/hup.1245>
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7. **Blackmores Executive B** (stress): <http://www.blackmores.com.au/products/executive-b-stress-formula>

Blackmores is taken as one capsule twice a day with meals. One study showed improved work-related stress. It is also available as an immediate-release and sustained-release capsule. No side effects have been reported.

- Stough, C., Scholey, A., Lloyd, J., Spong, J., Myers, S., & Downey, L. A. (2011). The effect of 90 day administration of a high dose vitamin B-complex on work stress. *Human Psychopharmacology: Clinical and Experimental*, 26(7), 470-476. <https://doi.org/10.1002/hup.1229>

8. **Enlyte** (depression): <https://www.enlyterx.com/>

There has been one study using Enlyte to treat people with a variant of the *MTHFR* gene who also had major depression. The treatment consists of one capsule taken on an empty stomach. It is available by prescription and may be covered by insurance in the US. No reported side effects.

- Mech A, Farah A. Correlation of clinical response with homocysteine reduction during therapy with reduced B vitamins in patients with MDD who are positive for MTHFR C677T or A1298C

polymorphism: a randomized, double-blind, placebo-controlled study. *Journal of Clinical Psychiatry*. 2016 May;77(5):668-71. doi:10.4088/JCP.15m10166.

9. **Optivite** (premenstrual symptoms): www.optimox.com

Optivite was first studied in the 1980s and as far as I am aware, there have been no new studies for the last two decades. The product is still available for purchase. The studies suggested between six and twelve capsules a day. The bottle recommends two-to-six tablets daily with meals. The main concern raised about taking a dose above ten capsules is that it delivers vitamin B6 in a range that can produce some neurological side effects, including tingling of limbs. Fortunately, the side effect is reversible once you stop taking the pills.

- Chakmakjian, Z. H., Higgins, C. E., & Abraham, G. E. (1985). The effect of a nutritional supplement, Optivite for women, on premenstrual tension syndromes. II. Effect on symptomatology, using a double blind cross-over design. *The Journal of Applied Nutrition*, 37(1), 12-17.
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Finally, there are some **excellent reviews** and **letters to editors** including:

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- Gardner, A., Kaplan, B. J., Rucklidge, J. J., Jonsson, B. H., & Humble, M. B. (2010). The potential of nutritional therapy. *Science (letter)*, 327, 268.
- Kaplan, B. J., Nikkel, G., Nikkel, B., & Rucklidge, J. J. (2013). Keeping Academic Psychiatry Relevant. *British Journal of Psychiatry (letter)*. http://bjp.rcpsych.org/content/201/6/421/reply#bjprcpsych_el_53864
- Rucklidge, J. J., & Kaplan, B. J. (2013). Broad-spectrum micronutrient formulas for the treatment psychiatric symptoms: A systematic review. *Expert Review of Neurotherapeutics*, 13(1), 49-73.
- Rucklidge, J. J., Johnstone, J., & Kaplan, B. J. (2013). Single bullet madness - why do we continue to perpetuate this fallacy? (letter). *British Journal of Psychiatry*, 203, 154-155. http://bjp.rcpsych.org/content/202/6/398/reply#bjprcpsych_el_54588
- Popper, C. W. (2014). Single-Micronutrient and Broad-Spectrum Micronutrient Approaches for Treating Mood Disorders in Youth and Adults. *Child and Adolescent Psychiatric Clinics of North America*, 23(3), 591-672. doi:10.1016/j.chc.2014.04.001
- Rucklidge, J. J., Harris, A., & Shaw, I. (2014). Are the amounts of vitamins in commercially available dietary supplement formulations relevant for the management of psychiatric disorders in children? *New Zealand Journal of Medicine*, 127, 73-85. <https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2014/vol-126-no-1392/article-rucklidge>
- Rucklidge, J. J., & Mulder, R. T. (2015). Could nutrition help behaviours associated with personality disorders? A narrative review. *Personality and Mental Health*. <http://onlinelibrary.wiley.com/doi/10.1002/pmh.1325/epdf>
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Mainstream in Psychiatry: A Consensus Position Statement from The International Society for Nutritional Psychiatry Research (ISNPR). *Lancet Psychiatry*, 2, 271-274.

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