EMPowerplus™ Q96 is a micronutrient formula co-developed by Anthony F. Stephan. It is designed to promote mental wellbeing by providing a broad-based, balanced supply of micronutrients needed for healthy brain function and development.

Anthony Stephan's wife, Debbie, committed suicide in 1994. Two of their children, Autumn and Joseph, also struggled with mood disorders. In desperation, Anthony sought help from every possible source, and after two years made a breakthrough discovery. Using the micronutrient formulation, Autumn and Joseph have been well since 1996. Now, EMPowerplus™ Q96 is available to benefit millions of people in over one hundred and five countries.

The EMPowerplus™ Q96 formulation has been examined in a variety of human conditions. The formulation holds the distinction of being the most-researched micronutrient formula of its kind in the world.

Twenty-five published studies, including a double-blind placebo-controlled trial, have demonstrated both safety and effectiveness. In all, forty-four researchers and fifteen universities from four countries have participated in the research studies. All research is conducted and funded independently. These studies were completed under multiple labels, all of which are the EMPowerplus™ Q96 formulation.

In addition, a laboratory study conducted through the Canadian Centre for Behavioural Neuroscience demonstrated that rats, fed the formulation mixture, showed accelerated microscopic and functional recovery following experimentally induced brain lesions. These findings demonstrate the value of broad-based micronutrients in enhancing neuronal recovery following brain injury.

The unique EMPowerplus™ Q96 formulation, based on specialized technological advances in micronutrient delivery, allows the body to rapidly absorb and utilize these essential nutrients for optimum physical and mental health.

Empirical reports on EMPowerplus™ Q96 plus relevant reviews and commentaries

(June 2014)

1. Kaplan, B. J., Simpson, J. S. A., Ferre, R. C., Gorman, C., McMullen, D., & Crawford, S. G. (2001). Effective mood stabilization in bipolar disorder with a chelated mineral supplement. *Journal of Clinical Psychiatry*, 62, 936-944.

2. Popper, C. W. (2001). Do vitamins or minerals (apart from lithium) have mood-stabilizing effects? (Commentary). *Journal of Clinical Psychiatry*, 62, 933-935.

3. Simmons, M. (2003). Nutritional approach to bipolar disorder (Letter). *Journal of Clinical Psychiatry*, 64, 338.

4. Kaplan, B. J., Crawford, S. G., Gardner, B., & Farrelly, G. (2002). Treatment of mood lability and explosive rage with minerals and vitamins: Two case studies in children. *Journal of Child and Adolescent Psychopharmacology*, 12(3), 203-218.

5. Kaplan, B.J., Fisher, J.E., Crawford, S.G., Field, C.J., Kolb, B. (2004). Improved mood and behavior during treatment with a mineral-vitamin supplement: An open-label case series of children. *Journal of Child and Adolescent Psychopharmacology,* 14(1), 115-122.

6. Frazier, E.A., Fristad, M., Arnold, L.E. (2009). Multinutrient Supplement as Treatment: Literature Review and Case Report of a 12-year-old Boy with Bipolar Disorder. *Journal of Child and Adolescent Psychopharmacology*, 19: 453-460.

7. Rucklidge, J. J. (2009). Successful treatment of OCD with a micronutrient formula following partial response to CBT: A case study. *Journal of Anxiety Disorders*, 23: 836–840.

8. Gately, D., Kaplan, B.J. (2009). Database analysis of adults with bipolar disorder consuming a micronutrient formula. *Clinical Medicine Insights: Psychiatry,* 4:3-16**.** http://la-press.com/article.php?article_id=1384

9. Mehl-Madrona L, Leung B, Kennedy C, Paul S, Kaplan BJ (2010). Micronutrients versus standard medication management in autism: A naturalistic case-control study. *Journal of Child and Adolescent Psychopharmacology,* 20(2): 95-103. **http://www.liebertonline.com/doi/pdfplus/10.1089/cap.2009.0011**

10. Rucklidge JJ & Harrison (2010). Successful treatment of Bipolar Disorder II and ADHD with a micronutrient formula: A case study. *CNS Spectrums*, 15(5): 231-237.

11. Rucklidge JJ, Gately D, Kaplan BJ (2010). Database analysis of children and adolescents with Bipolar Disorder consuming a micronutrient formula, *BMC Psychiatry,* 10:74. http://www.biomedcentral.com/content/pdf/1471-244X-10-74.pdf

12. Rucklidge JJ, Taylor MR, Whitehead KA (2011). Effect of micronutrients on behaviour and mood in adults with ADHD: Evidence from an 8-week open label trial with natural extension. *Journal of Attention Disorders,* 15(1): 79-91.

13. Simpson JSA, Crawford SG, Goldstein ET, Field C, Burgess E, Kaplan BJ (2011). Systematic review of safety and tolerability of a complex micronutrient formula used in mental health. *BMC Psychiatry*, 11:62. http://www.biomedcentral.com/content/pdf/1471-244X-11-62.pdf

14. Rucklidge JJ, Johnstone J, Harrison R & Boggis A (2011). Micronutrients reduce stress and anxiety following a 7.1 earthquake in adults with Attention-Deficit/Hyperactivity Disorder. *Psychiatry Research,* 189: 281-87. doi:10.1016/j.psychres.2011.06.016

15. Rucklidge JJ, Blampied NM (2011). Post-earthquake psychological functioning in adults with Attention-Deficit/Hyperactivity Disorder: Positive effects of micronutrients on resilience. *New Zealand Journal of Psychology,* 40(4): 51-57.

16. Rucklidge JJ, Johnstone J, Harrison R (2011). Can micronutrients improve neurocognitive functioning in adults with ADHD and severe mood dysregulation? A pilot study: A pilot study. *Journal of Alternative and Complementary Medicine*, 17(12): 1-7.

17. Frazier EA, Fristad MA, Arnold LE (2012). Feasibility of a nutritional supplement as treatment for pediatric bipolar spectrum disorders. *Journal of Alternative and Complementary Medicine*, 18(7): 678-685.

18. Rucklidge JJ, 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 Psychopharmacoly: Clinical and Experimental,* 27(5): 440-54.

19. Rodway M, Vance A, Watters A, Lee H, Bos E, Kaplan BJ (2012), Efficacy and cost of micronutrient treatment of childhood psychosis. *BMJ Case Reports,* 2012 Nov 9. doi:10.1136/bcr-2012-007213. http://casereports.bmj.com/sevendays?fdate=11/05/2012&tdate=11/11/2012

20. Harrison R, Rucklidge JJ, Blampied N. (2013). Use of micronutrients attenuates cannabis and nicotine abuse as evidenced from a reversal design: A case study. *Journal of Psychoactive Drugs*, 45(2): 168-178.

21. Frazier EA, Gracious B, Arnold LE, Failla M, Chitchumroonchokchai C, Habash D, and Fristad MA. (2013). Nutritional and Safety Outcomes from an Open-Label Micronutrient Intervention for Pediatric Bipolar Spectrum Disorders. *Journal of Child and Adolescent Psychopharmacology*, 23(8): 558-67.

22. Rucklidge JJ (2013). Could Yeast Infections Impair Recovery From Mental Illness? A case study Using Micronutrients and Olive Leaf Extract for the Treatment of ADHD and Depression. *ADVANCES,* 27(3).

23. Rucklidge JJ., Johnstone J., Gorman B., Boggis A. and Frampton CA. (2014). Moderators of treatment response in adults with ADHD treated with a vitamin-mineral supplement. *Progress in Neuro-Psychopharmacoly and Biological Psychiatry*, 50: 163-171.

24. Rucklidge JJ., Frampton CA., Gorman B., and Boggis A. Vitamin-Mineral treatment of attention-deficit hyperactivity disorder in adults: double-blind randomized placebo-controlled trial. *The British journal of Psychiatry*, 1-10.doi: 10.1192/bjp. 113.132126.

25. Rucklidge JJ., Blampied N., Gorman B., and Sole E. Psychological functionining 1 year after a brief intervention using micronutrients to treat stress and anxiety related to the 2011 Christchurch earthquakes: a naturalistic follow-up. *Human Psychopharmacology: Clinical and Experimental*, 29(3): 230-43.

Review articles, and others relevant to broad-spectrum micronutrient treatment

1. 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).

2. Kaplan, BJ, Leung, B (2011). Micronutrient treatment of mental disorders. *Integrative Medicine: A Clinician's Journal,* 10(3):32-39.

3. Shaw, I., Rucklidge, J. J., Hughes, R. N. (2010). A possible biological mechanism for the B Vitamins altering behaviour in ADHD. *Pharmaceutical Medicine,* 24 (5): 1-6.

4. Rucklidge, J. J., Johnstone, J., Kaplan, B. J. (2009). Nutrient supplementation approaches in the treatment of ADHD. *Expert Review of Neurotherapeutics, 9*(4), 461-476.

5. Kaplan, BJ, Crawford, S., Field, C, and Simpson, JSA. (2007). Vitamins, minerals, and mood. *Psychological Bulletin, 133(5), 747-760.*

6. Kaplan, BJ and Shannon, S (2007). Nutritional aspects of child and adolescent psychopharmacology. *Psychiatric Annals, 37(7), 519-528. (reprinted in Pediatrics Annals,* 36(9), 600-609).

Abstracts of the above articles

1. **Kaplan, B. J., Simpson, J. S. A., Ferre, R. C., Gorman, C., McMullen, D., & Crawford, S. G. (2001). Effective mood stabilization in bipolar disorder with a chelated mineral supplement. *Journal of Clinical Psychiatry*, 62, 936-944.**

ABSTRACT

Background: To determine in open trials the therapeutic benefit of a nutritional supplement for bipolar disorder.

Method: The sample consisted of 11 patients with DSM-IV-diagnosed bipolar disorder aged 19 to 46 years, who were taking a mean of 2.7 psychotropic medications each at a study entry. Three additional patients dropped out prematurely. The intervention is a broad-based nutritional supplement of dietary nutrients, primarily chelated trace minerals and vitamins, administered in high doses. At study entry and periodically thereafter, patients were assessed with the Hamilton Rating Scale for Depression (HAM-D), the Brief Psychiatric Rating Scale (BPRS), and the Young Mania Rating Scale (YMRS).

Results: For those who completed the minimum 6-month open trial, symptom reduction ranged from 55%
to 66% on the outcome measures; need for psychotropic medications decreased by more than 50%. Paired t tests revealed treatment benefit on all measures for patients completing the trial: HAM-D mean score at entry =19.0, mean score at last visit = 5.4, $t = 5.59$, $df = 9$, $p < .01$; BPRS mean score at entry = 35.3, mean score at last visit = 7.4, $t = 2.57$, $df = 9$, $p < .05$; YMRS mean score at entry = 15.1, mean score at last visit = 6.0, $t = 4.11$, $df = 9$, $p < .01$. The effect size for the intervention was large (> .80) for each measure. The number of psychotropic medications decreased significantly to a mean ± SD of 1.0 ± 1.1 ($t = 3.54$, $df = 10$, $p < .01$). In some cases, the supplement replaced psychotropic medications and the patients remained well. The only reported side effect (i.e. nausea) was infrequent, minor, and transitory.

Conclusion: Some cases of bipolar illness may be ameliorated by nutritional supplementation. A randomized, placebo-controlled trial in adults with bipolar I disorder is currently underway, as well as open trials in children.

2. **Popper, C. W. (2001). Do vitamins or minerals (apart from lithium) have mood stabilizing effects? [Commentary]. *Journal of Clinical Psychiatry*, 62, 933-935.**

This is a commentary plus data from a case series; no abstract available

3. **Simmons, M. (2002). Nutritional approach to bipolar disorder. Letter to the Editor. *Journal of Clinical Psychiatry*, 64, 338.**

This is a letter to the editor with data from a case series; no abstract available

4. **Kaplan, B. J., Crawford, S. G., Gardner, B., & Farrelly, G. (2002). Treatment of mood lability and explosive rage with minerals and vitamins: Two case studies in children. *Journal of Child and Adolescent Psychopharmacology*, 12(3), 203-218.**

ABSTRACT

A micronutrient supplement containing a broad range of dietary minerals and vitamins is being examined for the treatment of mood lability in both adults and children (Kaplan et al. 2001; Popper 2001). During pilot work, two medication-free boys with mood lability and explosive rage were studied in an open-label treatment followed by reversal and retreatment. One child was an 8-year-

old with atypical obsessive- compulsive disorder, and the other was a 12-year-old with pervasive developmental delay. Both boys were monitored using the mood and temper items from the Conners Parent Rating.

Scale, as well as the Child Behavior Checklist. In addition, the boy with atypical obsessive-compulsive disorder was monitored with the child version of the Yale-Brown Obsessive Compulsive Scale. Both boys benefited from the micronutrient supplement when examined in ABAB designs: mood, angry outbursts, and obsessional symptoms improved when initially treated, returned when not taking the supplement, and remitted when the micronutrient supplement was reintroduced. Both boys have been followed and are stable on the nutritional supplement for over 2 years. These cases suggest that mood lability and explosive rage can, in some cases, be managed with a mixture of biologically active minerals and vitamins, without using lithium or other traditional psychopharmacologic agents.

5. **Kaplan, B.J., Fisher, J.E., Crawford, S.G., Field, C.J., Kolb, B. (2004). Improved mood and behavior during treatment with a mineral-vitamin supplement: An open-label case series of children. *Journal of Child and Adolescent Psychopharmacology,* 14(1), 115-122.**

ABSTRACT

Several studies have demonstrated that psychiatric symptoms such as depression, mood swings, and aggression may be ameliorated by supplementation with broad-based nutrient formulas containing vitamins, minerals, and sometimes essential fatty acids. These findings have been reported in young criminal offenders as well as in adults with mood disturbance and other psychiatric disorders. The purpose of the current case series was to explore the potential efficacy of a nutrient supplement in children. Childrenwith mood and behavioral problems (N = 11; 7 boys, 4 girls; 8–15 years old) participated; 9 completed this open-label trial. Parents completed the Child Behavior Checklist (CBCL), Youth Outcome Questionnaire (YOQ), and Young Mania Rating Scale (YMRS) at entry and following at least 8 weeks of treatment. Intent- to-treat analyses revealed decreases on the YOQ ($p < 0.001$) and the YMRS ($p < 0.01$) from baseline to final visit. For the 9 completers, improvement was significant on seven of the eight CBCL scales, the YOQ, and the YMRS (p values from 0.05–0.001). Effect sizes for all outcome measures were relatively large. The findings suggest that formal clinical trials of broad nutritional supplementation are warranted in children with these psychiatric symptoms.

6. **Frazier, E.A., Fristad, M., Arnold, L.E. (2009). Multinutrient Supplement as Treatment: Literature Review and Case Report of a 12-year-old Boy with Bipolar Disorder. *Journal of Child and Adolescent Psychopharmacology,*19:453-460*.***

ABSTRACT

Early-onset bipolar disorder has significant morbidity and mortality. Development of safe, effective treatments to which patients will adhere is critical. Pharmacologic interventions for childhood bipolar spectrum disorders are limited and are associated with significant risk for adverse events (Kowatch et al 2005). Diet and nutrition research suggests vitamins, minerals, and other nutrients are important underpinnings of general physical and mental health; further, they may even be useful in treating mood dysregulation by providing a more favorable risk-benefit ratio than contemporary psychotropic agents (Kaplan, Crawford, Field, & Simpson 2007). This article reviews the literature on multinutrient supplementation and mental health, and examines a case study of a 12-year-old boy with bipolar disorder and comorbid diagnoses treated for 6 years with conventional medication and finally a multinutrient supplement.

The multinutrient supplement in this case study is EMPowerplus (EMP+), a 36-ingredient supplement containing sixteen minerals, fourteen vitamins, three amino acids and three antioxidants. It was used to treat a 12-year-old boy initially diagnosed with bipolar disorder-not otherwise specified (BP-NOS) at age 6, whose diagnosis evolved by age 10 to bipolar I (BP-I), mixed, with psychotic features. He also met criteria for generalized anxiety disorder by age 8 and obsessive-compulsive disorder by age 10. After six years of conventional treatment (ages 6-12), he received fourteen months of EMP+. Symptom manifestation over seven years is described in conjunction with treatment history. EMP+ resulted in superior outcome to conventional treatment. This report adds to accumulating preliminary evidence that further basic science and clinical studies of multinutrient supplements are warranted.

7. **Rucklidge, J. J. (2009). Successful treatment of OCD with a micronutrient formula following partial response to CBT: A case study. *Journal of Anxiety Disorders*, 23: 836–840.**

ABSTRACT

Obsessive Compulsive Disorder (OCD) affects 0.5–2% of young people many of whom are resistant to conventional treatments. This case study describes an 18-year-old male with OCD who first underwent cognitive behavioral therapy (CBT) for a 1-year period with a modest response (his OCD had shifted from severe to moderate). Within a year, his anxiety had deteriorated back to the severe range and he now had major depression. He then entered an ABAB design trial using a nutritional formula consisting mainly of minerals and vitamins (together, known as micronutrients). After 8 weeks on the formula, his mood was stabilized, his anxiety reduced, and his obsessions were in remission. The treatment was then discontinued for 8 weeks, during which time his obsessions and anxiety worsened and his mood dropped. Reintroduction of the formula again improved the symptoms. This case illustrates the importance of considering the effect micronutrients have on mental illness.

8. **Gately, D., Kaplan, B.J. (2009). Database analysis of adults with bipolar disorder consuming a micronutrient formula. *Clinical Medicine: Psychiatry.* 4:3-16.** http://la-press.com/article.php?article_id=1384

ABSTRACT

Background: Bipolar disorder is a lifelong problem with imperfect available treatments. Recent research has shown potential benefit of nutritional treatment for mood symptoms. The goal of the current study was to determine whether adults with bipolar disorder reported treatment benefit from consuming a micronutrient formula.

Methods: Self-report data were available from 682 adults who reported a diagnosis of bipolar disorder; 81% were taking psychiatric medications. Those reporting additional diagnoses were excluded, as well as those who provided data <60 times during 180 days of using the micronutrients, leaving 358 for analysis.

Results: Mean symptom severity was 41% lower than baseline after 3 months (effect size = 0.78), and 45% lower after 6 months (effect size = 0.76) (both paired t-tests significant, $p < 0.001$). In terms of responder status, 53% experienced ≥50% improvement at 6 months. Half the sample were taking medications approved for bipolar disorder (lithium, anticonvulsants, atypical antipsychotics), and half were either medication-free or taking other medications: the magnitude of treatment benefi t did not differ between these two groups. Regression analyses indicated that decreased symptom severity over the 6 months was associated with increasing micronutrient dosage and with reducing medication. Symptom improvements were significant and sustained at 6 months, suggesting that benefits were not attributable to placebo/expectancy effects.

Conclusions: Further research on this micronutrient formula is warranted.

9. **Mehl-Madrona, L., Leung, B., Kennedy, C., Paul, S., Kaplan, B.J. (*2010).* Micronutrient versus standard medication management in autism: A naturalistic case-control study, *Journal of Child and Adolescent Psychopharmacology.* 20(2): 95-103.** http://www.liebertonline.com/doi/pdfplus/10.1089/cap.2009.0011

ABSTRACT

Autism spectrum disorder (ASD) is often accompanied by self-injurious behavior (SIB), aggression, and tantrums, symptoms that have reportedly improved with micronutrient (vitamins and minerals) treatment. The current study took advantage of naturally occurring differences in parental preferences for treatment approaches. The micronutrient group asked for treatment without pharmaceuticals (n=44, aged 2–28 years at entry [M=8.39±5.58]). Their records were matched with those of 44 similar children whose families requested conventional treatment (medication group). Both groups improved on both the Childhood Autism Rating Scale and the Childhood Psychiatric Rating Scale (all p values <0.0001). Both groups also exhibited significant decreases in total Aberrant Behavior Checklist scores, but the micronutrient group's improvement was significantly greater (p<0.0001). SIB Intensity was lower in the micronutrient group at the end of the study (p=0.005), and improvement on the Clinical Global Impressions scale was greater for the micronutrient group (p=0.0029). It is difficult to determine whether the observed changes were exerted through improvement in mood disorder or through an independent effect on autistic disorder. There were some advantages to treatment with micronutrients—lower activity level, less social withdrawal, less anger, better spontaneity with the examiner, less irritability, lower intensity SIB, markedly fewer adverse events, and less weight gain. Advantages of medication management were insurance coverage, fewer pills, and less frequent dosing.

10. **Rucklidge, J. J., & Harrison, R. (2010*).* Successful treatment of Bipolar Disorder II and ADHD with a micronutrient formula: A case study, *CNS Spectrums*. 15(5):231-237.**

ABSTRACT

Bipolar disorder with co-occurring attention-deficit/hyperactivity disorder (ADHD) is a challenge to treat. Ten previous reports have shown potential benefit of a micronutrient treatment (consisting mainly of vitamins and minerals) for various psychiatric symptoms, including mood and ADHD. This case study aimed to investigate the longer term impact of the micronutrients on both psychiatric and neurocognitive functioning in an off-on-off-on (ABAB) design with 1 year follow-up. A 21-year-old female with bipolar II disorder, ADHD, social anxiety, and panic disorder entered an open-label trial using a nutritional treatment following a documented 8 year history of on-going psychiatric symptoms not well managed by medications. After 8 weeks on the formula she showed significant improvements in mood, anxiety, and hyperactivity/impulsivity. Blood test results remained normal after 8 weeks on the formula. She did not report any adverse side effects associated with the treatment. She then chose to come off the formula; after 8 weeks her depression scores returned to baseline, and anxiety and ADHD symptoms worsened. The formula was reintroduced, showing gradual improvement in all psychiatric symptoms. This case represents a naturalistic ABAB design showing on-off control of symptoms. After 1 year, the patient is now in remission from all mental illness. Neurocognitive changes mirrored behavioral changes, showing improved processing speed, consistency in response speed, and verbal memory. A placebo response and expectancy effects cannot be ruled out although previous poor response to treatment and the duration of the current positive response decrease the likelihood that other factors better explain change. These consistently positive outcomes alongside an absence of side effects indicate that further research, particularly larger and more controlled trials, is warranted using this multinutrient approach.

11. **Rucklidge, J.J., Gately, D., Kaplan, B.J. (2010). Database analysis of children and adolescents with Bipolar Disorder consuming a micronutrient formula. BMC Psychiatry, 10:74 doi:10.1186/1471-244X-10-74.** http://www.biomedcentral.com/content/pdf/1471-244X 10-74.pdf

ABSTRACT

Background: Eleven previous reports have shown potential benefit of micronutrient treatment for psychiatric symptoms. The current study asked whether children (7-18 years) with pediatric bipolar disorder (PBD) benefited from the same micronutrient formula; the impact of Attention-Deficit/Hyperactivity Disorder (ADHD) on their response was also evaluated.

Methods: Data were available from 120 children whose parents reported a diagnosis of PBD; 79% were taking psychiatric medications that are used to treat mood disorders; 24% were also reported as ADHD. Using Last Observation Carried Forward (LOCF), data were analyzed from 3 to 6 months of micronutrient use.

Results: At LOCF, mean symptom severity of bipolar symptoms was 46% lower than baseline (effect size (ES) = 0.78) ($p < 0.001$). In terms of responder status, 46% experienced >50% improvement at LOCF, with 38% still taking psychiatric medication (52% drop from baseline) but at much lower levels (74% reduction in number of medications being used from baseline). The results were similar for those with both ADHD and PBD: a 43% decline in PBD symptoms (ES = 0.72) and 40% in ADHD symptoms (ES = 0.62). An alternative sample of children with just ADHD symptoms (n = 41) showed a 47% reduction in symptoms from baseline to LOCF (ES = 1.04). The duration of reductions in symptom severity suggests that benefits were not attributable to placebo/expectancy effects. Similar findings were found for younger and older children and for both sexes.

Conclusions: The data are limited by the open label design, the lack of a control group, and the inherent self-selection bias. While these data cannot establish efficacy, the results are consistent with a growing body of research suggesting that micronutrients appear to have therapeutic benefit for children with PBD with or without ADHD in the absence of significant side effects and may allow for a reduction in psychiatric medications while improving symptoms. The consistent reporting of positive changes across multiple sites and countries are substantial enough to warrant a call for randomized clinical trials using micronutrients

12. **Rucklidge, J.J., Taylor, M. R., Whitehead, K. A. (2011). Effect of Micronutrients on Behavior and Mood in Adults With ADHD: Evidence From an 8-week open label trial with natural extension. *Journal of Attention Disorders*. 2011;15(1):79-91.**

ABSTRACT

Objective: To investigate the impact of a 36-ingredient micronutrient formula consisting mainly of minerals and vitamins in the treatment of adults with both Attention-deficit/hyperactivity Disorder (ADHD) and severe mood dysregulation (SMD).

Method: 14 medication-free adults (9 men, 5 women; 18-55 years) with ADHD and SMD completed an 8- week open-label trial.

Results: A minority reported transitory mild side effects. Significant improvements were noted across informants (self, observer, clinician) on measures of inattention and hyperactivity/impulsivity, mood, quality of life, anxiety, and stress all with medium to very large effect sizes (all ps < .01); however, the mean of inattention remained in a clinical range whereas the means on measures of mood and hyperactivity/impulsivity were normalized. Follow-up data showed maintenance of changes or further improvement for those who stayed on the micronutrients.

Conclusions: Although this study, as an open trial, does not in itself prove efficacy, it provides preliminary evidence supporting the need for a randomized clinical trial of micronutrients as treatment for the more complex presentations of ADHD.

13. **Simpson JSA, Crawford SG, Goldstein ET, Field C, Burgess E, Kaplan BJ (2011). Systematic review of safety and tolerability of a complex micronutrient formula used in mental health. *BMC Psychiatry*. 11:62.** http://www.biomedcentral.com/content/pdf/1471-244X-11-62.pdf

ABSTRACT

Background: Theoretically, consumption of complex, multinutrient formulations of vitamins and minerals should be safe, as most preparations contain primarily the nutrients that have been in the human diet for millennia, and at safe levels as defined by the Dietary Reference Intakes. However, the safety profile of commercial formulae may differ from foods because of the amounts and combinations of nutrients they contain. As these complex formulae are being studied and used clinically with increasing frequency, there is a need for direct evaluation of safety and tolerability.

Methods: All known safety and tolerability data collected on one complex nutrient formula was compiled and evaluated.

Results: Data were assembled from all the known published and unpublished studies for the complex formula with the largest amount of published research in mental health. Biological safety data from 144 children and adults were available from six sources: there were no occurrences of clinically meaningful negative outcomes/effects or abnormal blood tests that could be attributed to toxicity. Adverse event (AE) information from 157 children and adults was available from six studies employing the current version of this formula, and only minor, transitory reports of headache and nausea emerged. Only one of the studies permitted a direct comparison between micronutrient treatment and medication: none of the 88 pediatric and adult participants had any clinically meaningful abnormal laboratory values, but tolerability data in the group treated with micronutrients revealed significantly fewer AEs and less weight gain.

Conclusions: This compilation of safety and tolerability data is reassuring with respect to the broad spectrum approach that employs complex nutrient formulae as a primary treatment.

14. **Rucklidge, J. J., Johnstone, J., Harrison, R., & Boggis, A. (2011). Micronutrients reduce stress and anxiety following a 7.1 earthquake in adults with Attention Deficit/Hyperactivity Disorder. *Psychiatry Research,* 189:281-87. doi:10.1016/j.psychres.2011.06.016**

ABSTRACT

The role of good nutrition for resilience in the face of stress is a topic of interest, but difficult to study. A 7.1 earthquake took place in the midst of research on a micronutrient treatment for Attention- Deficit/Hyperactivity Disorder (ADHD), providing a unique opportunity to examine whether individuals with ADHD taking micronutrients demonstrated more emotional resilience post-earthquake than individuals with ADHD not taking micronutrients. Thirty-three adults with ADHD were assessed twice following the earthquake using a measure of depression, anxiety and stress also completed at some point pre-earthquake (baseline). Seventeen were not taking micronutrients at the time of the earthquake (control group), 16 were (micronutrient group). While there were no between-group differences one week post-quake (Time 1), at two weeks post-quake (Time 2), the micronutrient group reported significantly less anxiety and stress than the controls (effect size 0.69). These between group differences could not be explained by other variables, such as pre-earthquake measures of emotions, demographics, psychiatric status, and personal loss or damage following the earthquake. The results suggest micronutrients may increase resilience to ongoing stress and anxiety associated with a highly stressful event in individuals with ADHD and are consistent with controlled studies showing benefit of micronutrients for mental health.

15. **Rucklidge JJ, Blampied NM (2011). Post-earthquake psychological functioning in adults with Attention- Deficit/Hyperactivity Disorder: Positive effects of micronutrients on resilience. *New Zealand Journal of Psychology,* 40(4):51-57.**

ABSTRACT

The September 2010 7.1 magnitude earthquake in Christchurch, New Zealand, provided an opportunity to study the after-effects of a major earthquake where death and injury were absent. It created a natural experiment into the protective effects on well-being of taking EMPowerplus (EMP+), a micronutrient supplement, in a group of 33 adults diagnosed with ADHD who had been assessed prior to the earthquake. Fortuitously, 16 were currently taking the supplement as part of on-going research at the time of the quake, while 17 were not (they had completed their trial of EMP+ or were waiting to begin consumption). The Depression Anxiety and Stress Scale (DASS-42) which had been administered at varying times before the earthquake on recruitment into the micronutrient study was re-administered by telephone 7-10 and again 14-18 days post-earthquake to volunteer, earthquake-exposed participants. A modified Brinley plot analysis of the individual DASS-42 scores showed that the 16 participants on the nutritional supplement were more resilient to the effects of the earthquake than the 17 individuals not taking the supplement. This effect was particularly marked for Depression scores.

16. **Rucklidge, J. J., Johnstone, J., Harrison, R. (2011). Can micronutrients improve neurocognitive functioning in adults with ADHD and Severe Mood Dysregulation? A pilot study. *Journal of Alternative and Complementary Medicine,* 17(12):1125-1131.**

ABSTRACT

Objectives: Little research has investigated how micronutrients (minerals and vitamins) affect cognitive functioning despite preliminary studies showing they may improve psychiatric functioning.

Intervention: This pilot study investigated the impact of a 36 ingredient micronutrient formula consisting mainly of vitamins and minerals on neurocognitive functioning in 14 adults with Attention-Deficit/Hyperactivity Disorder (ADHD) and severe mood dysregulation (SMD). *Design:* The formula was consumed in an open- label trial over an 8 week period.

Outcome Measures: The participants completed tests of memory (Wide Range Assessment of Memory and Learning) and executive functioning (Delis-Kaplan Executive Functioning System and Conners Continuous Performance Test) at baseline and at the end of the trial. A gender and age matched control group of 14 non-ADHD adults not taking the formula were assessed on the same tests 8 weeks apart in order to investigate the impact of practice on the results.

Results: There were no group differences in ethnicity, socio-economic status and estimated IQ. Significant improvement was observed in the ADHD group, but not the control group, across a range of verbal abilities including verbal learning, verbal cognitive flexibility and fluency, and verbal inhibition. These neurocognitive improvements were large and consistent with improved psychiatric functioning. No changes were noted above a practice effect in visual-spatial memory and there were no improvements noted in reaction time, working memory or rapid naming for either groups.

Conclusions: Although the pilot and open label design of the study limits the generalizability of the results, it supports a growing body of literature recognizing the importance of nutrients for mental health and cognition. The results also provide evidence supporting the need for randomized clinical trials of micronutrients as well as other experimental studies in order to better assess whether improved neurocognitive functioning may contribute to improved psychiatric symptoms.

17. **Frazier EA, Fristad MA, Arnold LE (2012). Feasibility of a nutritional supplement as treatment for pediatric bipolar spectrum disorders. *Journal of Alternative and Complementary Medicine.* 18(7):678-685.**

ABSTRACT

Objectives: Current psychotropic medications for childhood bipolar spectrum disorders (BPSD) are associated with significant adverse events. As nutrients play an important role in physical and mental health, they may be useful in treating mood disorders with few side effects. This open-label study explored the feasibility of testing therapeutic effects of a multinutrient supplement, EMPowerplus (EMP+), for pediatric BPSD. *Design*. EMP+ started at 1 capsule t.i.d. and escalated to a goal of 4 capsules t.i.d., which eight children attained. Four of these increased to the maximum dose, 5 capsules t.i.d. Mood symptoms were assessed seven times over eight weeks.

Subjects: Ten children, age 6-12 with BPSD were enrolled in 6.5 months. Seven participants completed the full trial. Three dropped out due to palatability and/or adherence issues.

Results: Mean medication adherence was 91%. With one-tailed nonparametric Fisher's Randomization Tests, intent-to-treat analyses demonstrated a 37% decrease in depression scores (p<0.06) and a 45% decrease in mania scores (p<0.01) from the start of treatment through final visit, suggesting improvement and possible treatment response. Study completers demonstrated significant decreasing trends in both depression and mania scores from baseline to final visit (p<0.05). Side effects were minor and transient, mostly temporary gastric discomfort.

Conclusions: Future randomized, placebo-controlled trials of EMP+ are warranted and feasible.

18. **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. *Hum Psychopharmacol Clin Exp*. DOI: 10.1002/hup.2246**

ABSTRACT

Objective: To compare two micronutrient (vitamins and minerals) formulas and assess their impact on emotions and stress related to the 6.3 earthquake on February 22nd 2011 in Christchurch, NZ.

Methods: 91 adults experiencing heightened anxiety or stress 2-3 months following the earthquake were randomized to Berocca™, CNE™ low dose (CNE4), or CNE™ high dose (CNE8), for 28 days and monitored weekly via on-line questionnaires and followed one month post-trial. A non-randomized control group (n=25) completed questionnaires at baseline and 4 weeks.

Results: All treatment groups experienced significant declines in psychological symptoms (p < .001). CNE™groups experienced greater reduction in intrusive thoughts as compared with Berocca™ (p = 0.05), with no group differences on other measures of psychological symptoms. However, CNE8 group reported greater improvement in mood, anxiety, and energy (p < .05) with twice as many reporting being "much" to "very much" improved and five times more likely to continue taking CNE™ post-trial than Berocca™ group. Treated participants had better outcomes on most measures over 4 weeks as compared to controls.

Conclusions: This study supports micronutrients as an inexpensive and practical treatment for acute stress following a natural disaster with a slight advantage to higher doses.

19. **Rodway M, Vance A, Watters A, Lee H, Bos E, Kaplan BJ (2012). Efficacy and cost of micronutrient treatment of childhood psychosis. *BMJ Case Reports*. doi:10.1136/bcr-2012-007213**

ABSTRACT

Psychosis is difficult to treat effectively with conventional pharmaceuticals, many of which have adverse long-term health consequences. In contrast, there are promising reports from several research groups of micronutrient treatment (vitamins, minerals, amino acids, and essential fatty acids) of mood, anxiety, and psychosis symptoms using a complex formula that appears to be safe and tolerable. We review previous studies using this formula to treat mental symptoms, and present an 11-year-old boy with a 3-year history of mental illness whose parents chose to transition him from medication to micronutrients. Symptom severity was monitored in three clusters: anxiety, obsessive compulsive disorder, and psychosis. Complete remission of psychosis occurred, and severity of anxiety and obsessional symptoms decreased significantly ($p < .001$); the improvements are sustained at 4-year follow-up. A cost comparison revealed that micronutrient treatment was <1% of his inpatient mental health care. Additional research on broad spectrum micronutrient treatment is warranted.

20. **Harrison R, Rucklidge JJ, Blampied N. Use of micronutrients attenuates cannabis and nicotine abuse as evidenced from a reversal design: A case study. *Journal of Psychoactive Drugs*.**

ABSTRACT

Background: Prior research shows that micronutrients, particularly amino acids, can assist individuals with substance dependence to quit various drugs of abuse, including cannabis, alcohol and cocaine.

Case Description: As part of a wider investigation of the impact of micronutrients (mostly vitamins and minerals) on psychiatric symptoms, such as Attention-Deficit/Hyperactivity Disorder (ADHD), depression, and anxiety, we observed that many participants reduced or eliminated use of alcohol, cigarettes and cannabis. One case using a single-case reversal (off-on-off-on-off) design is presented and shows not only on-off control of psychiatric symptoms as micronutrients are consumed or withdrawn, but also simultaneous on-off use of cannabis and cigarettes, despite not directly targeting this substance use as part of the treatment protocol.

Conclusions: This case adds to a growing body of research supporting the use of micronutrients in the treatment of psychiatric symptoms and suggests it may extend to substance dependence. Micronutrients, by assisting with mood regulation and reductions in anxiety, may assist with successful cessation of drug use. Alternatively, they may directly impact on the brain reward circuitry believed to be involved in the expression of addictions, thereby providing the appropriate precursors and cofactors necessary for adequate neurotransmitter synthesis. This case should continue to stimulate researchers to consider the role of nutrients, in particular vitamins and minerals, in drug treatment programmes and encourage more rigorous trials.

21. **Frazier EA, Gracious B, Arnold LE, Failla M, Chitchumroonchokchai C, Habash D, and Fristad MA. Nutritional and Safety Outcomes from an Open-Label Micronutrient Intervention for Pediatric Bipolar Spectrum Disorders. *Journal of Child and Adolescent Psychopharmacology*.**

ABSTRACT

Objective: Report safety, tolerability, serum micronutrient concentrations and their correlations with mood changes from an 8-week pilot feasibility study of a 36-ingredient multinutrient supplement, EMPowerplus (EMP+), for pediatric bipolar spectrum disorders (BPSD).

Methods: Ten children aged 6-12 received EMP+ escalating from 1 to 4 capsules t.i.d., with four children increased to the maximum suggested dose, 5 capsules t.i.d. Outcome measures were micronutrient concentrations in serum and red blood cells, vital signs, body mass index (BMI), dietary intake (Food Frequency Questionnaire and 24-hour dietary recall interview) and mood and global functioning ratings.
Results: Seven children (70%) completed the study. Three (30%) terminated early due to tolerability and compliance issues. Adverse effects were mild and transient, and chiefly initial insomnia or GI upset. No differences occurred in BMI (p = 0.310) or waist-hip ratio (WHR; p = 0.674) pre- to post-supplementation. Four of the tested serum vitamin concentrations increased from pre- to post-supplementation: vitamin A- retinol; vitamin B6; vitamin E-α-tocopherol; and folate (all p<0.05). The increase in serum 25-OH vitamin D approached significance (p=0.063). No differences were found in dietary intake pre- to post- supplementation, suggesting blood nutrient level increases were due to EMP+.
Conclusion: In this open prospective study, short-term use of EMP+ in children with BPSD appeared safe and well-tolerated, with a side effect profile preferable to first-line psychotropic drugs for pediatric bipolar spectrum disorders. A double-blind, randomized clinical trial is feasible, appears safe, and is warranted by open-label clinical outcomes and plausible mechanisms of action combined with documentation of increased serum concentrations of specific micronutrients.

22. **Rucklidge JJ (2013). Could Yeast Infections Impair Recovery From Mental Illness? A case study Using Micronutrients and Olive Leaf Extract for the Treatment of ADHD and Depression. *Advances,* 27(3).**

ABSTRACT

Prior research shows that micronutrients, particularly amino acids, can assist individuals with substance dependence to quit various drugs of abuse, including cannabis, alcohol, and cocaine. As part of a wider investigation of the impact of micronutrients (mostly vitamins and minerals) on psychiatric symptoms, such as Attention-Deficit/Hyperactivity Disorder (ADHD), depression, and anxiety, we observed that many participants reduced or eliminated use of alcohol, cigarettes, and cannabis. One case using a single-case reversal (off-on-off-on-off) design is presented and shows not only on-off control of psychiatric symptoms as micronutrients are consumed or withdrawn, but also simultaneous on-off use of cannabis and cigarettes, despite not directly targeting this substance use as part of the treatment protocol.

This case adds to a growing body of research supporting the use of micronutrients in the treatment of psychiatric symptoms and suggests it may extend to substance dependence. Micronutrients, by assisting with mood regulation and reductions in anxiety, may assist with successful cessation of drug use. Alternatively, they may directly impact on the brain reward circuitry believed to be involved in the expression of addictions, thereby providing the appropriate precursors and cofactors necessary for adequate neurotransmitter synthesis. This case should continue to stimulate researchers to consider the role of nutrients, in particular vitamins and minerals, in drug treatment programs and encourage more rigorous trials.

23. **Rucklidge JJ., Johnstone J., Gorman B., Boggis A. and Frampton CA. Moderators of treatment response in adults with ADHD treated with a vitamin-mineral supplement. Prog Neuro-Psychopharmacol Biol Psychiatry (2013).** http://dx.doi.org/10.1016/j.pnpbp.2013.12.014

ABSTRACT

Background: To date there has been no research investigating moderators of response to micronutrient treatment of mental illness, specifically baseline nutrient levels.
Method: We conducted analyses of data from a randomized placebo-controlled trial (RCT) of 80 adults (≥16 years) with Attention-Deficit/Hyperactivity Disorder (ADHD), whereby

participants were treated acutely (8 weeks) with micronutrients or placebo followed by an open-label (OL) phase of 8 weeks whereby all partic- ipants received micronutrients. To ensure that all participants had been exposed to the micronutrients for 8 weeks, only those who had adhered to the treatment protocol and completed 8 weeks on nutrients were included in the data analysis: from the group micronutrient arm, and from the group that had been randomized to the placebo group and hence had only received nutrients in the OL phase. Six outcomes were examined: change in ADHD symptoms (self/clinician), ADHD responder, Clinical Global Impression-Improvement (CGI-I), change in mood, and change in Global Assessment of Functioning (GAF). Demographic, developmental and psychiatric history, current clinical characteristics, and baseline nutrient levels were all considered as putative predictors.
Results: There were significant changes in all outcome variables after 8 weeks exposure to the micronutrients. Among the nutrients recorded at baseline, substantial deficiencies (27%)were only observed for vitamin D.

24. **Rucklidge JJ., Frampton CA., Gorman B., and Boggis *A.* Vitamin-Mineral treatment of attention-deficit hyperactivity disorder in adults: double-blind randomized placebo-controlled trial. The British journal of Psychiatry 1-10.doi: 10.1192/bjp. 113.132126**

ABSTRACT

Background: The role of nutrition in the treatment of attention-deficit hyperactivity disorder (ADHD) is gaining international attention; however, treatments have generally focused only on diet restriction or supplementing with one nutrient at a time.
Aims: To investigate the efficacy and safety of a broad-based micronutrient formula consisting mainly of vitamins and minerals, without omega fatty acids, in the treatment of ADHD in adults.
Method: This double-blind randomised controlled trial assigned80 adults with ADHD in a 1:1 ratio to either micronutrients (n=42) or placebo (n=38) for 8 weeks (trial registered with the Australian New Zealand Clinical Trials Registry: ACTRN12609000308291).
Results: Intent-to-treat analyses showed significant between-group differences favouring active treatment on self- and observer- but not clinician-ADHD rating scales. However, clinicians rated those receiving
micronutrients as more improved than those on placebo both globally and on ADHD symptoms. Post-hoc analyses showed that for those with moderate/severe depression at baseline, there was a greater change in mood favouring active treatment over placebo. There were no group differences in adverse events.
Conclusions: This study provides preliminary evidence of efficacy for micronutrients in the treatment of ADHD symptoms in adults, with a reassuring safety profile.
Declaration of interest: None.

25. **Rucklidge JJ., Blampied N., Gorman B., and Sole E. Psychological functionining 1 year after a brief intervention using micronutrients to treat stress and anxiety related to the 2011 Christchurch earthquakes: a naturalistic follow-up. *Human Psychopharmacology: Clinical and Experimental*, 29(3): 230-43.**

ABSTRACT

Objective: We investigated whether micronutrients given acutely following the Christchurch earthquakes continued to confer benefit 1 year following the treatment.
Methods: Sixty-four adults from the original 91 participants experiencing heightened anxiety or stress 2-3 months following the 22nd February 2011 earthquake and who had been randomized to receive three different doses of micronutrients completed on-line questionnaires assessing mood, anxiety, stress, and symptoms associated with post-traumatic stress disorder 1 year after completing the initial study. Twenty-one out of 29 nonrandomized controls who did not receive the

treatment also completed the questionnaires.
Results: Both the treated and control groups experienced significant improvement in psychological functioning compared with end-of-trial. However, treated participants had better long-term outcomes on most measures compared with controls (ES = 0.69-1.31). Those who stayed on micronutrients through to follow-up or stopped all treatment reported better psychological functioning than those who switched to other treatments including medications. About 10% of the sample continued to have post-traumatic stress disorder symptoms.
Conclusions: Disaster survivors improve psychologically over time regardless of receiving intervention; however, those taking micronutrients during the acute phase following a disaster show better outcomes, identifying micronutrients as a viable treatment for acute stress following a natural disaster with maintenance of benefits
1 year later.

Abstracts of Review and Related Articles

1. **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).**

ABSTRACT

Ingesting minerals and vitamins in combination makes physiological sense, and research on the use of broad spectrum formulations for psychiatric symptoms is increasing rapidly. This review covers formulas consisting of at least four vitamins and/or minerals, and includes four experimental designs: randomized controlled trials (RCTs), open-label trials (OL), case-control studies, and case studies with within-subject crossovers (ABAB). Nevertheless, there is evidence for the efficacy of micronutrients in the treatment of stress and antisocial behaviours as well as depressed mood in nonclinical and elderly populations. Many reports studied mood changes in healthy populations, making it difficult to generalize to clinical samples. There is also preliminary support for the treatment of autism with micronutrients. However, despite preliminary positive findings, there is less data available to support efficacy of micronutrient formulas in treating bipolar disorder, ADHD, and substance abuse/dependence and no clinical trials have been done with clinically depressed or anxious samples, psychosis or eating disorders.

2. **Shaw, I., Rucklidge, J. J., Hughes, R. N. (2010). A possible biological mechanism for the B Vitamins altering behaviour in ADHD. *Pharmaceutical Medicine,* 24 (5): 1-6.**

ABSTRACT

There is a growing body of recent evidence showing that micronutrients (combinations of minerals, vitamins and amino acids) improve the symptoms of Attention-Deficit/Hyperactivity Disorder (ADHD). Dopamine (DA) agonists, such as methylphenidate, have long been identified as effective in treating ADHD symptoms, by inhibiting DA transporter function. This paper explores the role that B vitamins might have in the treatment of ADHD symptoms by investigating the structural similarities between B vitamins and methylphenidate. We suggest that the presence of B vitamins and their postulated structure activity relationships (SARs) with DA may be responsible for the observed pharmacological effect. This pharmacological activity is likely to be via their competitive binding to the DAT dopamine binding site with a concomitant increase in synaptic DA concentration which in turn might activate the postsynaptic dopamine receptor and thus ameliorate the symptoms of ADHD. Further research is required to assess the validity of the intriguing possibility that B vitamins and methylphenidate share a common neurochemical mechanism of action.

3. **Kaplan, BJ, Leung, B (July 2011). Micronutrient treatment of mental disorders. *Integrative Medicine: A Clinician's Journal.***

ABSTRACT

Problem: Studying the effect of individual micronutrients on health has been the norm in the research literature for over a century. It is only recently that a significant shift has been made in traditional medical journals toward accepting the importance of using a complex nutrient formula for intervention research. Acceptance of this shift is not trivial, as conventional scientific methodology previously branded such interventions 'confounded' experiments. But of course broad spectrum supplementation is based on fundamental laws of physiology, and important treatment benefits are now emerging in the area of mental health as a result of this shift in attitude.

Review: The focus of this review is the growing body of literature on a broad-based micronutrient

formula showing beneficial effects, particularly for mood and anxiety symptoms.
Results. Positive results have been reported in 13 publications thus far, in multiple settings, and with many types of designs and analyses, including case reports, case studies, case series in both research and clinical settings, and a retrospective database analysis.
Conclusions: In addition to the review of these studies, seven conceptual models are presented to help understand the mechanism(s) by which micronutrients might be expected to influence mental health function. Without some understanding of the biological basis for micronutrient interventions for mental health, the benefits tend to be dismissed as being mysterious, when in fact they likely reflect fundamental physiological principles of brain function.

4. **Rucklidge, J. J., Johnstone, J., & Kaplan, B. J. (2009). Nutrient supplementation approaches in the treatment of ADHD. *Expert Review of Neurotherapeutics, 9*(4): 461-476.**

ABSTRACT

Attention-Deficit/Hyperactivity Disorder (ADHD) is a chronic, debilitating psychiatric illness that often co- occurs with other common psychiatric problems. Although empirical evidence supports pharmacological and behavioral treatments, side effects, concerns about safety, and fears about long-term use all contribute to families searching for alternative methods of treating the symptoms of ADHD. This review presents the published evidence on supplementation, including single ingredients (e.g. minerals, vitamins, amino acids, essential fatty acids), botanicals and multi-ingredient formulae in the treatment of ADHD symptoms. In most cases, evidence is sparse, mixed and lacking information. Of those supplements where we found published studies, the evidence is best for zinc (two positive randomized control trials); there is mixed evidence for carnitine, pycnogenol and essential fatty acids, and more research is needed before drawing conclusions about vitamins, magnesium, iron, SAM-e, tryptophan, and *Gingko Biloba* with *Ginseng*. To date, there is no evidence to support the use of St. John's wort, tyrosine, or phenylalanine in the treatment of ADHD symptoms. Multi-ingredient approaches are an intriguing yet under-researched area; we discuss the benefits of this approach considering the heterogeneous nature of ADHD.

5. **Kaplan, BJ, Crawford, S., Field, C, and Simpson, JSA. (2007). Vitamins, minerals, and mood. *Psychological Bulletin, 133(5), 747-760.***

ABSTRACT

In this article, the authors explore the breadth and depth of published research linking dietary vitamins and minerals (micronutrients) to mood. Since the 1920s, there have been many studies on individual vitamins (especially B vitamins and Vitamins C, D, and E), minerals (calcium, chromium, iron, magnesium, zinc, and selenium), and vitamin-like compounds (choline). Recent investigations with multi-ingredient formulas are especially promising. However, without a reasonable conceptual framework for understanding mechanisms by which micronutrients might influence mood, the published literature is too readily dismissed. Consequently, 4 explanatory models are presented, suggesting that mood symptoms may be expressions of inborn errors of metabolism, manifestations of deficient methylation reactions, alterations of gene expression by nutrient deficiency, and/or long-latency deficiency diseases. These models provide possible explanations for why micronutrient supplementation could ameliorate some mental symptoms.

6. **Kaplan, BJ and Shannon, S (2007). Nutritional aspects of child and adolescent psychopharmacology. *Psychiatric Annals, 37(7), 519-528. (reprinted in Pediatrics Annals, (2007)*, 36(9), 600-609).**

No abstract available.