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SUMMARY OF CLINICAL STUDIES

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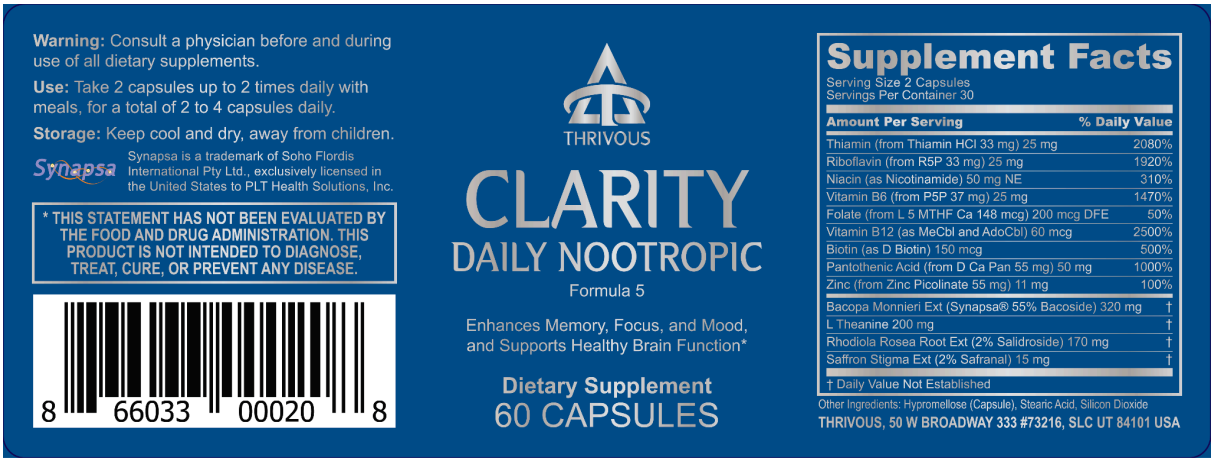

Table of Contents

Bacopa Monnieri to Enhance Memory 2

L Theanine to Enhance Relaxation 5

Rhodiola Rosea to Enhance Focus, Mood, and Energy 6

Saffron to Enhance Mood 8

Vitamin B Complex to Support Healthy Brain Function 11

Zinc to Enhance Mood 17

Bacopa Monnieri to Enhance Memory

Bacopa Monnieri supplements (dosage standardized to at least 120 mg bacoside as measured by UV-Vis) daily for at least two to three months may enhance memory up to 35%, according to these clinical studies on humans:

- An acute, double-blind, placebo-controlled cross-over study of 320 mg and 640 mg doses of Bacopa monnieri (CDRI 08) on multitasking stress reactivity and mood. In 2014, this study found that Bacopa "produced some adaptogenic and nootropic effects". 17 participants used 320 mg or 640 mg of 55% bacoside extract (at least 176 mg bacoside as measured by UV-Vis) once. Supplementation of the lower dose was more effective for improving memory, and it increased memory about 9% at 1 hour and about 5% at 2 hours (letter search task compared to placebo).

- An acute, double-blind, placebo-controlled crossover study of 320 mg and 640 mg doses of a special extract of Bacopa monnieri (CDRI 08) on sustained cognitive performance. In 2013, this study found that Bacopa "improved performance at the first, second, and fourth repetition post-dosing on the [Cognitive Demand Battery]". 24 participants used 320 mg or 640 mg of 55% bacoside extract (at least 176 mg bacoside as measured by UV-Vis) once.

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Supplementation of the higher dose was not more effective, and both doses improved cognitive parameters loosely associated with memory at 2 hours.

- Effects of 12-Week Bacopa monnieri Consumption on Attention, Cognitive Processing, Working Memory, and Functions of Both Cholinergic and Monoaminergic Systems in Healthy Elderly Volunteers. In 2012, this study found that Bacopa “can improve attention, cognitive processing, and working memory”. 60 participants used 300 mg or 600 mg of 5% bacoside extract (at least 15 mg bacoside as measured by HPLC) daily. Supplementation of the lower dose was more effective, and it increased memory about 14% at 12 weeks (quality of working memory and speed of memory tasks compared to placebo).

- Does Bacopa monnieri improve memory performance in older persons? Results of a randomized, placebo-controlled, double-blind trial. In 2010, this study found that "Bacopa significantly improved memory acquisition and retention". 36 participants used 300 mg of 40% bacoside extract (120 mg bacoside) daily. Supplementation increased memory about 35% at 3 months (delayed recall task compared to placebo).

- Effects of a standardized Bacopa monnieri extract on cognitive performance, anxiety, and depression in the elderly: a randomized, double-blind, placebo-controlled trial. In 2008, this study found that Bacopa "has potential for safely enhancing cognitive performance". 24 participants used 300 mg of 50% bacoside extract (150 mg bacoside as measured by UV-Vis) daily. Supplementation increased memory about 6% at 6 weeks and about 18% at 12 weeks (delayed recall task compared to placebo).

- Examining the nootropic effects of a special extract of Bacopa monniera on human cognitive functioning: 90 day double-blind placebo-controlled randomized trial. In 2008, this study found that Bacopa "significantly improved performance on the 'Working Memory' factor, more specifically spatial working memory accuracy [and] the number of false-positives recorded in the Rapid visual information processing task was also reduced". 33 participants used 300 mg of 55% bacoside extract (165 mg bacoside as measured by UV-Vis) daily. Supplementation increased memory about 2% at 3 months (working memory task compared to placebo).

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- Efficacy and Tolerability of BacoMind® on Memory Improvement in Elderly Participants - A Double Blind Placebo Controlled Study. In 2008, this study found that Bacopa “improved the cognitive functions such as attention and verbal memory”. Participants used 450 mg of 40% bacoside extract (180 mg bacoside) daily. Supplementation increased memory at 12 weeks.

- BacoMind®: A Cognitive Enhancer in Children Requiring Individual Education Programme. In 2008, this study found that Bacopa improved “working memory and short term verbal memory … logical memory, memory related to personal life … [and] visual as well as auditory memory”. 28 participants used 225 mg of 40% bacoside extract (90 mg bacoside) daily. Supplementation increased memory about 18% at 4 months (memory scale test compared to placebo).

- Randomized controlled trial of standardized Bacopa monniera extract in age-associated memory impairment. In 2006, this study found that Bacopa "is efficacious in subjects with age-associated memory impairment". 20 participants used 250 mg of 55% bacoside extract (137.5 mg bacoside as measured by UV-Vis) daily. Supplementation increased memory about 3% at 1 month, 10% at 2 months, and 10% at 3 months (total memory test compared to placebo). Effect ended within 1 month after supplementation ended.

- Chronic effects of Brahmi (Bacopa monnieri) on human memory. In 2002, this study found that Bacopa "decreases the rate of forgetting of newly acquired information". 37 participants used 300 mg (450 mg for those over 90 kg) of 55% bacoside extract (at least 165 mg bacoside as measured by UV-Vis) daily. Supplementation increased memory about 25% at 3 months (delayed word pairs task compared to placebo). Effect ended within 6 weeks after supplementation ended.

- The chronic effects of an extract of Bacopa monniera (Brahmi) on cognitive function in healthy human subjects. In 2001, this study found that Bacopa "may improve higher order cognitive processes that are critically dependent on the input of information from our environment such as learning and memory". 23 participants used 300 mg of 55% bacoside extract (165 mg bacoside as measured by UV-Vis) daily. Supplementation was ineffective at 5 weeks, and

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increased memory at 12 weeks (proactive interference task compared to placebo).

These clinical study reviews confirm that Bacopa Monnieri supplements may enhance memory:

- Meta-analysis of randomized controlled trials on cognitive effects of Bacopa monnieri extract. In 2014, this meta-analysis found that Bacopa "has the potential to improve cognition, particularly speed of attention".

- Cognitive effects of two nutraceuticals Ginseng and Bacopa benchmarked against modafinil: a review and comparison of effect sizes. In 2013, this meta-analysis found that "neurocognitive enhancement from [Bacopa] can produce cognition enhancing effects of similar magnitude to those from pharmaceutical interventions". Cohen power analysis quantifies magnitude of effect on a scale of 0 to 1, where 0 is no effect, .2 is small effect, .5 is medium effect, and .8 is large effect. The meta-analysis found that magnitude of effect for Modafinil (a particularly popular nootropic) is .77, which is an approximately large effect. And the meta-analysis found that Bacopa magnitude of effect is .95, which is a large effect and substantially larger than that of the pharmaceutical, Modafinil, although for a different cognitive function.

L Theanine to Enhance Relaxation

L Theanine supplements may enhance relaxation without sedation, according to these clinical studies on humans:

- Anti-stress effect of theanine on students during pharmacy practice: positive correlation among salivary α-amylase activity, trait anxiety and subjective stress. In 2013, this study found that L-Theanine “intake suppressed initial stress response of students assigned for a long-term commitment of pharmacy practice.”

- Effects of l-theanine on attention and reaction time response. In 2011, this study found that L-Theanine “clearly has a pronounced effect on attention performance

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and reaction time response in normal healthy subjects prone to have high anxiety."

- L-Theanine reduces psychological and physiological stress responses. In 2007, this study found that "oral intake of [L-Theanine] could cause anti-stress effects via the inhibition of cortical neuron excitation."

- The acute effects of L-theanine in comparison with alprazolam on anticipatory anxiety in humans. In 2004, this study found that L-Theanine "may have some relaxing effects under resting conditions."

- Effects of Theanine on the Release of Brain Alpha Wave in Adult Males. In 2003, this study found that L-Theanine "containing tablets promote the release of alpha waves related to mental relaxation and concentration in young adult males."

Rhodiola Rosea to Enhance Focus, Mood, and Energy

Rhodiola Rosea supplements (dosage standardized to at least 1 mg salidroside daily as measured by HPLC) may enhance focus, mood, and energy according to these clinical studies on humans:

- Burnout: A Multicenter Exploratory Clinical Trial With a Proprietary Extract of Rhodiola rosea in Patients With Burnout Syndrome. In 2018, this study found that emotional exhaustion scores improved throughout the intervention. 118 participants used 400 mg Rhodiola daily for 12 weeks.

- Rhodiola rosea versus sertraline for major depressive disorder: A randomized placebo-controlled trial. In 2015, this study found that Rhodiola, "although less effective than sertraline, [Rhodiola] may possess a more favorable risk to benefit ratio for individuals with mild to moderate depression". Participants used 340 mg of 1.95% salidroside extract (~7 mg salidroside) daily for 12 weeks.

- Therapeutic effects and safety of Rhodiola rosea extract WS® 1375 in subjects with life-stress symptoms--results of an open-label study. In 2012, this study found that Rhodiola "is safe and effective in improving life-stress symptoms to a

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clinically relevant degree". Participants used 400 mg of WS-1375 extract (>4 mg salidroside) daily for 4 weeks.

- The influence of adaptogens on ultraweak biophoton emission: a pilot-experiment. In 2009, this study found that "after supplementation, a significant decrease concerning the experienced level of fatigue in the Rhodiola group was observed". Participants used 288 mg of 2.3% salidroside extract (~7 mg salidroside) daily for 1 week.

- Clinical trial of Rhodiola rosea L. extract SHR-5 in the treatment of mild to moderate depression. In 2007, this study found that Rhodiola "shows anti-depressive potency in patients with mild to moderate depression". Participants used 340 to 680 mg of SHR-5 extract (>3 to >7 mg salidroside) daily for 6 weeks. The higher dose was more effective.

- Acute Rhodiola rosea intake can improve endurance exercise performance. In 2004, this study found that Rhodiola "can improve endurance exercise capacity in young healthy volunteers". Participants used 200 mg of 1% salidroside extract (~3 mg salidroside) once or daily for 4 weeks. Both time periods were effective.

- A randomized trial of two different doses of a SHR-5 Rhodiola rosea extract versus placebo and control of capacity for mental work. In 2003, this study found that Rhodiola had "a pronounced antifatigue effect". Participants used 370 to 555 mg of 2.4% salidroside extract (~9 to ~13 mg salidroside) once. The higher dose was not more effective.

- A double-blind, placebo-controlled pilot study of the stimulating and adaptogenic effect of Rhodiola rosea SHR-5 extract on the fatigue of students caused by stress during an examination period with a repeated low-dose regimen. In 2000, this study found that "the most significant improvement in the [Rhodiola] group was seen in physical fitness, mental fatigue and neuro-motoric tests ... [and] the self-assessment of the general well-being was also significantly better". Participants used 100 mg of SHR-5 extract (>1 mg salidroside) daily for 3 weeks.

- Rhodiola rosea in stress induced fatigue--a double blind cross-over study of a standardized extract SHR-5 with a repeated low-dose regimen on the mental

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performance of healthy physicians during night duty. In 2000, this study found that Rhodiola "can reduce general fatigue under certain stressful conditions". Participants used 170 mg of 2.6% salidroside extract (~4 mg salidroside) daily for 2 weeks.

This clinical study identifies salidroside and tyrosine, and not rosavin, as bioactive components in Rhodiola Rosea extract:

- Comparative study of Rhodiola preparations on behavioral despair of rats. In 2008, this animal study found that "Rhodioloside [salidroside], and tyrosol were identified as active principles of the extract, whereas rosavin, rosarin, rosin, cinnamic alcohol, cinnamaldehyde, cinnamic acid were inactive".

Saffron to Enhance Mood

Saffron supplements (extracts standardized to 2% safranal) may enhance mood according to these clinical studies on humans:

- A placebo controlled randomized clinical trial of Crocus sativus L. (saffron) on depression and food craving among overweight women with mild to moderate depression. In 2020, this study found that saffron supplementation significantly improved mood compared to placebo. 73 participants used 30 mg saffron daily for 12 weeks. Supplementation improved mood scores compared to placebo, although it had no significant effect on food craving. Participants in the saffron group also reported fewer side effects.

- Crocus Sativus L. (saffron) versus sertraline on symptoms of depression among older people with major depressive disorders-a double-blind, randomized intervention study. In 2019, this study found that saffron supplementation significantly improved mood. 50 participants used 60 mg saffron daily for 6 weeks. Supplementation improved mood over time with results comparable to a pharmaceutical control.

- Saffron improved depression and reduced homocysteine level in patients with major depression: A Randomized, double-blind study. In 2018, this study found

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that saffron supplementation improved mood and reduced homocysteine levels. 40 participants used 30 mg saffron daily for 4 weeks alongside fluoxetine. Supplementation reduced homocysteine levels compared to the control group while mood improved over the course of the study.

- Efficacy of Crocus sativus (saffron) in treatment of major depressive disorder associated with post-menopausal hot flashes: a double-blind, randomized, placebo-controlled trial. In 2018, this study found that saffron supplementation improved mood and reduced hot flash interference compared to placebo. 60 participants used 30 mg saffron daily for 6 weeks. Supplementation significantly improved mood and reduced the impact of hot flashes on daily activities, with no significant difference in adverse events between groups.

- The effects of alcoholic extract of saffron (Crocus satious L.) on mild to moderate comorbid depression-anxiety, sleep quality, and life satisfaction in type 2 diabetes mellitus: A double-blind, randomized and placebo-controlled clinical trial. In 2018, this study found that saffron supplementation improved mood and sleep quality compared to placebo. 54 participants used 30 mg saffron daily for 8 weeks. Supplementation significantly improved mood and sleep measures, while life satisfaction and physical measures remained unchanged.

- Crocus sativus L. versus Citalopram in the Treatment of Major Depressive Disorder with Anxious Distress: A Double-Blind, Controlled Clinical Trial. In 2017, this study found that saffron supplementation significantly improved mood scores. 66 participants used 30 mg saffron daily for 6 weeks. Supplementation significantly improved mood measures, with results comparable to the pharmaceutical control and similar rates of side effects.

- A double-blind, randomized and placebo-controlled trial of Saffron (Crocus sativus L.) in the treatment of anxiety and depression. In 2016, this study found that saffron supplementation significantly improved mood compared to placebo. 60 participants used saffron extract for 12 weeks. Supplementation significantly improved mood scores compared to placebo, with few reported side effects.

- A randomized, double-blind, clinical trial comparing the efficacy and safety of Crocus sativus L. with fluoxetine for improving mild to moderate depression in

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post percutaneous coronary intervention patients. In 2014, this study found that saffron supplementation significantly improved mood. 40 participants used 30 mg saffron daily for 6 weeks. Supplementation improved mood with results comparable to the pharmaceutical control and similar rates of side effects.

- Comparison of petal of Crocus sativus L. and fluoxetine in the treatment of depressed outpatients: a pilot double-blind randomized trial. In 2007, this study found that saffron supplementation significantly improved mood. 40 participants used 30 mg saffron petal extract daily for 8 weeks. Supplementation improved mood with results comparable to the pharmaceutical control and similar rates of side effects.

- Crocus sativus L. (petal) in the treatment of mild-to-moderate depression: a double-blind, randomized and placebo-controlled trial. In 2006, this study found that saffron supplementation significantly improved mood compared to placebo. 40 participants used 30 mg saffron petal extract daily for 6 weeks. Supplementation improved mood scores compared to placebo with no significant difference in observed side effects.

- Crocus sativus L. in the treatment of mild to moderate depression: a double-blind, randomized and placebo-controlled trial. In 2005, this study found that saffron supplementation significantly improved mood compared to placebo. 40 participants used 30 mg saffron daily for 6 weeks. Supplementation significantly improved mood scores compared to placebo with no significant difference in observed side effects.

- Hydro-alcoholic extract of Crocus sativus L. versus fluoxetine in the treatment of mild to moderate depression: a double-blind, randomized pilot trial. In 2005, this study found that saffron supplementation improved mood. 40 participants used 30 mg saffron extract daily for 6 weeks. Supplementation improved mood with results comparable to the pharmaceutical control and similar rates of side effects.

- Comparison of Crocus sativus L. and imipramine in the treatment of mild to moderate depression: a pilot double-blind randomized trial [ISRCTN45683816]. In 2004, this study found that saffron supplementation improved mood. 30 participants used 30 mg saffron daily for 6 weeks. Supplementation improved

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mood with results comparable to the pharmaceutical control, with fewer reported side effects.

These meta-analyses confirm that Saffron may enhance mood:

- Effect of Saffron Versus Selective Serotonin Reuptake Inhibitors (SSRIs) in Treatment of Depression and Anxiety: A Meta-analysis of Randomized Controlled Trials. In 2025, this meta-analysis found that saffron supplementation produced mood improvements, with fewer reported adverse events than pharmaceuticals. The analysis included 12 clinical trials evaluating mood outcomes. Overall results showed no significant difference between saffron and pharmaceuticals in improving mood measures.

- Effect of saffron supplementation on symptoms of depression and anxiety: a systematic review and meta-analysis. In 2019, this meta-analysis found that saffron supplementation significantly improved mood compared to placebo. The analysis included 23 clinical studies evaluating saffron supplementation in both clinical and general populations. Overall results showed a large positive effect on mood measures.

Vitamin B Complex to Support Healthy Brain Function

Between approximately 2% and 12% of people in the United States consume less than the estimated average requirement for B Vitamins from natural sources and fortified foods, and larger unknown percentages consume less than optimal amounts, according to these studies:

- Second National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population. In 2012, this study observed that “dietary deficiencies are well documented, and they have characteristic signs and symptoms. In addition, recent findings have determined that less than optimal biochemical concentrations (representing suboptimal status) have been associated with risks of adverse health effects”.

- Foods, Fortificants, and Supplements: Where Do Americans Get Their Nutrients?

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In 2011, this study observed that “without enrichment and/or fortification and supplementation, many Americans did not achieve the recommended micronutrient intake levels set forth in the Dietary Reference Intake”.

Vitamin B Complex supplements (dosage above the recommended daily intake, and below the upper limit of daily intake likely to pose no risk of adverse effects) may support healthy brain function according to these clinical studies on humans:

- Intake of niacin, folate, vitamin B-6, and vitamin B-12 through young adulthood and cognitive function in midlife: the Coronary Artery Risk Development in Young Adults (CARDIA) study. In 2017, this cohort study found that “higher intake of B vitamins throughout young adulthood was associated with better cognitive function in midlife”.

- The Effects of Four-Week Multivitamin Supplementation on Mood in Healthy Older Women: A Randomized Controlled Trial. In 2016, this double-blind, placebo-controlled study found that “multivitamin supplementation [including high dose B Complex] improved ratings of stress, with a trend to reduce mental fatigue”.

- Effects of Multivitamin Supplements on Cognitive Function, Serum Homocysteine Level, and Depression of Korean Older Adults With Mild Cognitive Impairment in Care Facilities. In 2016, this double-blind, placebo-controlled study found that “multivitamin supplements [consisting exclusively of partial B Complex] can be utilized for improving cognitive ability and for decreasing depression”.

- Multivitamins and minerals modulate whole-body energy metabolism and cerebral blood-flow during cognitive task performance: a double-blind, randomised, placebo-controlled trial. In 2016, this double-blind, placebo-controlled study found that “brain function and metabolism are amenable to micronutrient supplementation [including high dose B Complex], even in adults who are assumed to have nutritional status typical of the population”.

- 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. In 2015, this double-blind, placebo-controlled study

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found that “supplementation [including high dose B Complex] may have beneficial effects on mood, underpinned by elevated B-vitamins and lowered homocysteine in healthy young adults”.

- Acute mood but not cognitive improvements following administration of a single multivitamin and mineral supplement in healthy women aged 50 and above: a randomised controlled trial. In 2015, this placebo-controlled study found that “supplementation with a single multivitamin, mineral and herbal supplement [including high dose B Complex] reduces stress several hours after intake in healthy older people”.

- Effects of multivitamin, mineral and herbal supplement on cognition in younger adults and the contribution of B group vitamins. In 2014, this double-blind, placebo-controlled study found that “supplementation [including high dose B Complex] may be useful for maintaining levels of B vitamins [and] the effects of multivitamins on speeded attention such as the stroop task in young [male] adults warrant further investigation”.

- The effects of multivitamin supplementation on diurnal cortisol secretion and perceived stress. In 2013, this double-blind, placebo-controlled study found “a significant interaction … between treatment group and study visit for the Cortisol Awakening Response (CAR) … a possible interpretation of the elevation in CAR associated with multivitamin supplementation [including high dose B Complex] is that this represents an adaptive response to everyday demands in healthy participants … the finding of correlation between CAR and serum B-vitamin levels in the blood in the current study provides strong evidence to suggest that B-vitamins were at least a necessary constituent required to modulate the CAR response”.

- The effects of multivitamin supplementation on mood and general well-being in healthy young adults. A laboratory and at-home mobile phone assessment. In 2013, this study found “significantly reduced stress, physical fatigue and anxiety in the [multivitamin including high dose B Complex] group in comparison to placebo across a number of time points”.

- Participant experiences from chronic administration of a multivitamin versus

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placebo on subjective health and wellbeing: a double-blind qualitative analysis of a randomised controlled trial. In 2012, this double-blind, placebo-controlled study found "a range of subjective beneficial effects that are consistent with quantitative data from previously published randomised controlled trials examining the effects of multivitamins and [high dose] B vitamin complexes on mood and well-being".

- Effects of a multivitamin, mineral and herbal supplement on cognition and blood biomarkers in older men: a randomised, placebo-controlled trial. In 2012, this double-blind, placebo-controlled study found that "Levels of vitamin B(12) and folate were significantly increased with a concomitant decrease in homocysteine, indicating that relatively short-term supplementation with a multivitamin [including high dose B Complex] can benefit these risk factors for cognitive decline [and] daily multivitamin supplementation may improve episodic memory in older men at risk of cognitive decline".

- Memory improvements in elderly women following 16 weeks treatment with a combined multivitamin, mineral and herbal supplement: A randomized controlled trial. In 2012, this double-blind, placebo-controlled study found that "Sixteen weeks supplementation with a combined multivitamin, mineral and herbal formula [including high dose B Complex] may benefit working memory in elderly women at risk of cognitive decline".

- Neurocognitive effects of multivitamin supplementation on the steady state visually evoked potential (SSVEP) measure of brain activity in elderly women. In 2012, this double-blind, placebo-controlled study found that "in the elderly, multivitamin supplementation [including high dose B Complex] may enhance neural efficiency during memory retrieval".

- The effects of multivitamins on cognitive performance: a systematic review and meta-analysis. In 2012, this meta-analysis of supplementation including Vitamin B Complex found that "multivitamins were found to enhance immediate free recall memory but no other cognitive domains".

- The effect of 90 day administration of a high dose vitamin B-complex on work stress. In 2011, this double-blind, placebo-controlled study found that "[high dose] vitamin B complex treatment groups reported significantly lower personal strain

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and a reduction in confusion and depressed/dejected mood after 12 weeks".

- Vitamins and psychological functioning: a mobile phone assessment of the effects of a B vitamin complex, vitamin C and minerals on cognitive performance and subjective mood and energy. In 2011, this double-blind, placebo-controlled study found that "participants in the vitamin/mineral [including B Complex] group rated themselves as having greater 'physical stamina' [and] they also rated themselves as having had greater 'concentration' and 'mental stamina' [and] participants in this group also reported greater subjective 'alertness' … healthy members of the general population may benefit from augmented levels of vitamins/minerals via direct dietary supplementation".

- The effect of multivitamin supplementation on mood and stress in healthy older men. In 2011, this double-blind, placebo-controlled study found that "supplementation with a multivitamin, mineral and herbal formulation [including high dose B Complex] may be useful in improving alertness and reducing negative mood symptoms and may also improve feelings of general day-to-day well-being".

- Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males. In 2010, this double-blind, placebo-controlled study found that "healthy members of the general population may benefit from augmented levels of vitamins/minerals [including high dose B Complex] via direct dietary supplementation [and] supplementation led to improved ratings of stress, mental health and vigour and improved cognitive performance during intense mental processing".

- Effects of a multi-vitamin/mineral supplement on cognitive function and fatigue during extended multi-tasking. In 2010, this double-blind, placebo-controlled study found that "the vitamin/mineral [including B Complex] group exhibited an attenuation of the negative effects of extended task completion on mood/fatigue. Multi-tasking performance for this group was also improved in terms of accuracy across all tasks, and on two of the individual tasks (Mathematical Processing and Stroop) in terms of both faster and more accurate responses [and] healthy members of the general population may benefit from augmented levels of vitamins/minerals via direct dietary supplementation".

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- Cognitive and mood effects in healthy children during 12 weeks' supplementation with multi-vitamin/minerals. In 2008, this double-blind, placebo-controlled study found that “vitamin/mineral supplementation [including low dose B Complex] has the potential to improve brain function in healthy children”.

- Effect of B vitamins-fortified foods on primary school children in Beijing. In 2006, this study found that "The effect of B vitamin compound supplementation is better than that of single riboflavin supplementation ... [and] micronutrient supplementation appears to assist children's study abilities".

These clinical study reviews confirm that Vitamin B Complex supplements may support healthy brain function:

- B Vitamins and the Brain: Mechanisms, Dose and Efficacy – A Review. In 2016, this review concluded that “administration of the entire B-vitamin group, rather than a small sub-set, at doses greatly in excess of the current governmental recommendations, would be a rational approach for preserving brain health”.

- Effects of vitamin and mineral supplementation on stress, mild psychiatric symptoms, and mood in nonclinical samples: a meta-analysis. In 2013, this meta-analysis of eight studies found that “micronutrient supplementation has a beneficial effect on perceived stress, mild psychiatric symptoms, and aspects of everyday mood in apparently healthy individuals [and] supplements containing high doses of B vitamins may be more effective in improving mood states”.

- Vitamins and cognition: what is the evidence? In 2011, this analysis found that “whereas studies involving supplementation with single vitamins, or restricted ranges of vitamins, have demonstrated equivocal results, evidence from studies involving the administration of broader ranges of vitamins, or multivitamins, suggest potential efficacy in terms of cognitive and psychological functioning”.

These clinical studies and reviews indicate that the L-5-Methyltetrahydrofolate form of Vitamin B9 may present a lower risk of adverse effects and greater bioavailability than alternative forms of Vitamin B9:

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- Folate, folic acid and 5-methyltetrahydrofolate are not the same thing. In 2014, this review observed that “using [Folate] instead of folic acid reduces the potential for masking haematological symptoms of vitamin B12 deficiency, reduces interactions with drugs that inhibit dihydrofolate reductase and overcomes metabolic defects caused by methylenetetrahydrofolate reductase polymorphism”.

- Treatment with Mefolinate (5-Methyltetrahydrofolate), but Not Folic Acid or Folinic Acid, Leads to Measurable 5-Methyltetrahydrofolate in Cerebrospinal Fluid in Methylenetetrahydrofolate Reductase Deficiency. In 2016, this study found that “only treatment with oral [5-Methyltetrahydrofolate] … resulted in an increase in [cerebrospinal fluid 5-Methyltetrahydrofolate]”.

- Antioxidant activity comparison between [6S]-5-methyltetrahydrofolic acid calcium salt and the related racemate form. In 2013, this study found that “the [L-5-Methyltetrahydrofolate] form had higher antioxidant activity than its racemate form”.

This clinical study review indicates that a combination of the Adenosylcobalamin and Methylcobalamin forms of Vitamin B12 may provide the broadest bioavailability:

- Treatment of vitamin B12 deficiency-methylcobalamine? Cyancobalamine? Hydroxocobalamin?-clearing the confusion. In 2015, this review observed that “it is important to treat vitamin B12 deficiency with a combination of [Methylcobalamin] and [Adenosylcobalamin] ”.

Zinc to Enhance Mood

Approximately 10% of people in the United States consume less than the estimated average requirement for Zinc from natural sources and fortified foods, and a larger unknown percentage consumes less than optimal amounts, according to these studies:

- Second National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population. In 2012, this study observed that “dietary deficiencies are well documented, and they have characteristic signs and symptoms. In addition,

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recent findings have determined that less than optimal biochemical concentrations (representing suboptimal status) have been associated with risks of adverse health effects".

- Foods, Fortificants, and Supplements: Where Do Americans Get Their Nutrients? In 2011, this study observed that "without enrichment and/or fortification and supplementation, many Americans did not achieve the recommended micronutrient intake levels set forth in the Dietary Reference Intake".

Zinc supplements (dosage at 7 mg to 30 mg daily, or half to triple the recommended daily intake, and below the upper limit of daily intake likely to pose no risk of adverse effects) may enhance mood according to these clinical studies on humans:

- Zinc Monotherapy Increases Serum Brain-derived Neurotrophic Factor (BDNF) Levels And Decreases Depressive Symptoms In Overweight Or Obese Subjects: A Double-blind, Randomized, Placebo-controlled Trial. In 2015, this study found that "Zinc monotherapy improves mood in overweight or obese subjects".

- Effects Of Zinc Supplementation On Efficacy Of Antidepressant Therapy, Inflammatory Cytokines, And Brain-derived Neurotrophic Factor In Patients With Major Depression. In 2014, this study found that "Zinc supplementation in conjunction with antidepressant drugs might be beneficial for reducing depressive symptoms".

- Effect Of Zinc Supplementation On Mood States In Young Women: A Pilot Study. In 2010, this study found that Zinc "supplementation may be effective in reducing anger and depression".

- Zinc Supplementation Augments Efficacy Of Imipramine In Treatment Resistant Patients: A Double Blind, Placebo-controlled Study. In 2009, this study found that "zinc supplementation significantly reduced depression scores and facilitated the treatment outcome in antidepressant treatment resistant patients".

This clinical study indicates that the Picolinate form of Zinc may provide greater bioavailability than alternative forms of Zinc:

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- Comparative absorption of zinc picolinate, zinc citrate and zinc gluconate in humans. In 1987, this study found that “zinc absorption in humans can be improved by complexing zinc with picolinic acid”.

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