Vitamins (B_1, B_6, B_{12})

Vitamin B complex in neuro-metabolic resilience of mood and cognition under stress in students, professional, entrepreneurial, and menopausal populations

Abstract

Vitamin B complex, particularly thiamine (B_1), pyridoxine (B_6), and cobalamin (B_{12}), play essential roles in neuro-metabolic regulation and mood stability.

Acting as coenzymes in neurotransmitter synthesis, mitochondrial energy production, one-carbon metabolism, and myelin maintenance, these vitamins support both cognitive and emotional health.

Deficiencies in B_6 and B_{12} are linked to impaired serotonin, dopamine, and GABA synthesis, elevated homocysteine levels, and dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, leading to depression, anxiety, and sleep disturbances.

Clinical evidence demonstrates that B-vitamin supplementation reduces cortisol levels, improves memory performance, and alleviates emotional fatigue in high-stress populations.

Furthermore, synergistic combinations of B vitamins with 5-HTP, magnesium glycinate, L-Theanine, and Ashwagandha amplify effects on serotonin production, GABAergic modulation, stress buffering, and neuroprotection.

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This review summarizes the mechanistic pathways, clinical research evidence, and target populations for B-vitamin-based nutritional strategies, highlighting their role as foundational cofactors in mood regulation and stress resilience

Keywords

Vitamin B complex Depression, Anxiety, Insomnia, Neurotransmitter synthesis; One-carbon metabolism; HPA axis; Homocysteine; Cognitive performance; Stress resilience; Mood regulation; Students; Professionals; Entrepreneurs; Menopausal women.

The B-vitamin complex serves as a fundamental group of coenzymes essential for cellular metabolism and neural function.

This group includes B_1 (thiamine), B_2 (riboflavin), B_3 (niacin/Niacinamide), B_5 (pantothenic acid), B_6 (pyridoxine), B_7 (biotin), B_9 (folate), and B_{12} (cobalamin). Acting across neurotransmitter synthesis, energy metabolism, methylation reactions, and myelin maintenance, B vitamins are foundational, multi-target nutrients for emotional stability, stress resilience, and cognitive performance.

- Vitamin B_1 (Thiamine) - 1.2 mg
- Vitamin B_6 (Pyridoxine HCl) - 1.4 mg
- Vitamin B_{12} (Cobalamin) - 2.4 µg

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I Core Mechanisms of B_1 + B_6 + B_{12} in Neuro-Metabolic-Stress-Mood Regulation

1) Neurotransmitter System Modulation

- Thiamine (B_1) functions as a coenzyme (thiamine pyrophosphate, TPP) in pyruvate dehydrogenase and α-ketoglutarate dehydrogenase reactions, ensuring efficient ATP production via the TCA cycle. This energy support is critical for synthesizing key neurotransmitters including GABA, glutamate, and acetylcholine.
- Pyridoxal-5′-phosphate (PLP, active B_6) is an essential coenzyme in multiple neurotransmitter conversions, including:

- tryptophan → 5-HTP → serotonin
- glutamate → GABA
- dopamine → norepinephrine

- Cobalamin (B_{12}) supports the synthesis of S-adenosylmethionine (SAM), a key methyl donor in one-carbon metabolism. This pathway is vital for activating neurotransmitters via methylation, impacting serotonin and dopamine signaling efficiency.

✓ *Gibson GE, Hirsch JA, Cirio RT, Jordan BD, Fonzetti P, Elder J. Abnormal thiamine-dependent processes in Alzheimer's disease. Lessons from diabetes. Mol Cell Neurosci. 2016;73:89-101.*

✓ ***Dakshinamurti K, Stephens MC, Carlen PL.*** *Involvement of vitamin B6 in neurotransmitter synthesis and behavior. Nutr Res. 1990;10(1):1-22.*

✓ ***Kennedy DO.*** *B vitamins and the brain: mechanisms, dose and efficacy—a review. Nutrients. 2016;8(2):68.*

2) HPA Axis and Stress Response Regulation

- B_6 deficiency impairs the synthesis of GABA and serotonin, weakening negative feedback inhibition of hypothalamic CRH release, and leading to sustained elevations in cortisol.
- B_{12} deficiency is associated with elevated homocysteine (Hcy), which promotes inflammatory stress responses (↑ IL-6, ↑ TNF-α) and contributes to HPA axis overactivation.
- Adequate B_1 stabilizes neural energy metabolism, helping prevent “brain energy deficits” under chronic stress that can contribute to mood dysregulation.

✓ ***Liu F, Zhang Y, Guo X, Wang X, He Y.*** *Vitamin B6 intake is associated with lower depression and anxiety risk in US adults. Nutrients. 2021;13(5):1512.*

✓ ***Selhub J, Bagley LC, Miller J, Rosenberg IH.*** *B vitamins, homocysteine, and neurocognitive function in the elderly. Am J Clin Nutr. 2000;71(2):614S-620S.*

✓ ***Gibson GE, Hirsch JA, Cirio RT, Jordan BD, Fonzetti P, Elder J.*** *Abnormal thiamine-dependent processes in Alzheimer’s disease. Lessons from diabetes. Mol Cell Neurosci. 2016;73:89-101.*

3) Energy Metabolism and Mitochondrial Function

- Thiamine (B_1) is essential for shuttling glucose-derived pyruvate into the TCA cycle, preventing lactate accumulation and reducing “stress-induced fatigue.”
- Pyridoxine (B_6) plays a critical role in glycogenolysis and amino acid metabolism, providing substrate support during intense cognitive exertion.
- Cobalamin (B_{12}) participates in the methylmalonyl-CoA mutase reaction, facilitating the entry of fatty acids and odd-chain fatty acids into the TCA cycle for energy production.

- ✓ ***Jhala SS, Hazell AS.*** *Modeling neurodegenerative disease pathophysiology in thiamine deficiency: mechanisms and implications. Neurochem Int. 2011;58(3):248-255.*
- ✓ ***Dakshinamurti K, Stephens MC, Carlen PL.*** *Involvement of vitamin B6 in neurotransmitter synthesis and behavior. Nutr Res. 1990;10(1):1-22.*
- ✓ ***O'Leary F, Samman S.*** *Vitamin B12 in health and disease. Nutrients. 2010;2(3):299-316.*

4) Neuroprotection and Anti-Inflammatory Effects

- B_1 deficiency damages neural membrane phospholipids and myelin, triggering both peripheral and central nervous system inflammation.
- B_6 (PLP) reduces neuro-inflammation by lowering pro-inflammatory cytokines (IL-1β, TNF-α) and inhibiting overactivation of the kynurenine pathway, which is associated with neurotoxic metabolites.

- B_{12} supports myelin protein repair via methylation pathways and may help reverse subclinical neurodegenerative changes.

- ✓ *Gibson GE, Hirsch JA, Cirio RT, Jordan BD, Fonzetti P, Elder J. Abnormal thiamine-dependent processes in Alzheimer's disease. Lessons from diabetes. Mol Cell Neurosci. 2016;73:89-101.*
- ✓ *Parra M, Stahl S, Hellmann H. Vitamin B6 and its role in cell metabolism and physiology. Cells. 2018;7(7):84.*
- ✓ *Lindenbaum J, Healton EB, Savage DG, Brust JC, Garrett TJ, Podell ER, et al. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. N Engl J Med. 1988;318(26):1720-1728.*

II Clinical Consensus and Research Evidence

1) Mood and Cognitive Support

Low B_6 levels are inversely correlated with depression and anxiety risk, and supplementation with B_6 + B_{12} has been shown to improve mood and memory performance, especially in older adults and high-stress populations.

A. Mechanistic Pathways:

- Vitamin B_6 (PLP) is a coenzyme for key enzymes such as aromatic L-amino acid decarboxylase (AADC), involved in the biosynthesis of dopamine, norepinephrine,

and serotonin. Deficiency reduces the production of these inhibitory and modulatory neurotransmitters, contributing to mood instability and reduced attention.

- B_{12} + B_6 support one-carbon metabolism, reducing homocysteine (Hcy) levels, improving myelin integrity and synaptic function, and facilitating cognitive performance and memory consolidation.

B. Population Evidence:

- Observational studies consistently show that lower plasma B_6 levels are associated with more pronounced depressive symptoms. Supplementation with B-complex vitamins and folate-related cofactors has been linked to improved mood scores.

C. Keyora Formula Synergy:

- This formulation provides B_6 (1.4 mg) and B_{12} (2.4 μg) as essential enzymatic cofactors to support serotonin production from 5-HTP and myelin repair.
  When combined with magnesium glycinate (to stabilize GABA/NMDA signaling) and L-Theanine (to enhance alpha waves and reduce stress), the formula facilitates the entire cascade from precursor supply → neurotransmitter synthesis → synaptic efficiency.

2) Adjunctive Antidepressant Support

Several randomized controlled trials (RCTs) have shown that co-supplementation of B_6 with tryptophan or 5-HTP enhances serotonin synthesis and alleviates depressive symptoms.

A. Mechanistic Pathways:

- The conversion of 5-HTP to serotonin is catalyzed by AADC, a PLP (B_6)-dependent enzyme. Therefore, B_6 availability becomes the rate-limiting factor in serotonin biosynthesis. When dietary protein or 5-HTP is sufficient, B_6 enhances serotonin production efficiency, contributing to improved mood and anxiety regulation.

B. Evidence Base:

- Both clinical trials and review articles - including major professional textbooks—support the biological plausibility and practical efficacy of B_6 + tryptophan/5-HTP co-administration in mood modulation, especially among elderly or B-vitamin-deficient individuals.

C. Formula Synergy:

- This formula delivers 5-HTP (45 mg/day) together with B_6, creating a “substrate + coenzyme” pairing. Combined with magnesium’s modulatory effects on GABA/NMDA balance, this formulation supports the full transition from emotional reactivity → emotional stability.

3) Stress Recovery

B-complex supplementation has been shown to reduce cortisol levels and improve emotional fatigue in individuals with high occupational stress.

A. Mechanistic Pathways:

- B vitamins are key cofactors in glycolysis, the TCA cycle, and the electron transport chain, providing critical energy under stress. Through one-carbon metabolism, they also modulate the HPA axis and neurotransmitter dynamics, influencing cortisol rhythms, perceived fatigue, and mood responsiveness.

B. Population Evidence:

- A 90-day randomized controlled trial found that high-dose B-complex supplementation significantly reduced perceived stress and emotional fatigue scores in high-pressure occupational groups, alongside improvements in markers of occupational burnout.

C. Formula Synergy:

- This formulation includes B_1 + B_6 + B_{12}, supporting both energy production and neurotransmitter balance. Combined with Ashwagandha extract (to downregulate the HPA axis) and magnesium (to buffer sympathetic tone and cortisol), the formulation

simultaneously reduces “stress response intensity” and enhances “recovery capacity,” offering stable support for both baseline and peak stress periods.

4) Usage and Safety Notes

A. Safety Profile:

- The dosages of B_6 (1.4 mg), B_1 (1.2 mg), and B_{12} (2.4 μg) in this formulation align with the Recommended Daily Allowance (RDA), making it suitable for long-term foundational use with low risk. Together with 5-HTP, magnesium, and L-Theanine, the formulation forms a safe synergistic chain.
- Prolonged intake of very high-dose B_6 may cause sensory nerve disturbances; unsupervised high-dosage use is not recommended.

B. Timeline of Effects:

- Improvements in neurotransmitter-related symptoms typically begin within 2-4 weeks, while outcomes related to HPA axis regulation or sleep architecture often stabilize over 4-8 weeks.

C. Especially Beneficial For:

- Vegetarians, older adults, and individuals with elevated homocysteine, who are at higher risk of B_{12}/B_6 deficiency.

- Those experiencing chronic stress or poor sleep quality, who may benefit from enhanced neuroendocrine resilience.

✓ *Dakshinamurti K, Stephens MC, Carlen PL. Involvement of vitamin B6 in neurotransmitter synthesis and behavior. Nutr Res. 1990;10(1):1-22.*

✓ *Kennedy DO. B vitamins and the brain: mechanisms, dose and efficacy—a review. Nutrients. 2016;8(2):68.*

✓ *Selhub J, Bagley LC, Miller J, Rosenberg IH. B vitamins, homocysteine, and neurocognitive function in the elderly. Am J Clin Nutr. 2000;71(2):614S-620S.*

✓ *O'Leary F, Samman S. Vitamin B12 in health and disease. Nutrients. 2010;2(3):299-316.*

✓ *Hvas AM, Juul S, Bech P, Nexø E. Vitamin B6 level is associated with symptoms of depression. Psychother Psychosom. 2004;73(6):340-343.*

✓ *Stough C, Scholey A, Lloyd J, Spong J, Myers S, Downey LA. The effect of 90-day administration of a high dose vitamin B-complex on work stress. Hum Psychopharmacol. 2011;26(7):470-476.*

✓ *Shils ME, Shike M, Ross AC, Caballero B, Cousins RJ. Modern Nutrition in Health and Disease. 11th ed. LWW; 2012.*

III Target Population Overview - B Vitamins (B_1, B_6, B_{12})

1) High Cognitive Demand Individuals (e.g., students, programmers, researchers)

A. Metabolic Characteristics:

- Sustained mental activity requires continuous glucose-derived energy, stable neurotransmitter synthesis, and rapid synaptic plasticity.
- Thiamine (B_1) acts as a coenzyme for pyruvate dehydrogenase and α-ketoglutarate dehydrogenase, directly impacting the efficiency of glucose oxidation.
- Pyridoxal-5'-phosphate (PLP, active B_6) is a crucial coenzyme for the synthesis of dopamine, norepinephrine, and serotonin-neuro-transmitters that support attention and resistance to fatigue.
- Cobalamin (B_{12}) is involved in myelin formation and DNA repair, ensuring rapid neural signal transmission and memory consolidation.

B. Clinical Risks:

- B-vitamin deficiencies can result in reduced concentration, short-term memory decline, and impaired learning efficiency. High mental workload significantly increases B-vitamin utilization.

C. Supplementation Significance:

- Adequate B-vitamin intake helps maintain neurotransmitter balance and reduces symptoms of "brain fog" and mental fatigue.

D. Synergistic Formula Benefits:

- When combined with 5-HTP and magnesium glycinate, the formula provides dual support for neurotransmitter synthesis and energy metabolism, enhancing focus and cognitive clarity.

2) High-Stress Professionals (e.g., finance, healthcare, customer service)

A. Metabolic Characteristics:

- Chronic stress repeatedly activates the HPA axis, raising cortisol levels and causing substantial depletion of neurotransmitters and increased energy metabolism burden.
- B vitamins - particularly B_6 and B_{12} - are involved in one-carbon metabolism and methylation reactions, both essential for modulating neurotransmitter production (serotonin, GABA) during stress responses.
- Elevated homocysteine (Hcy) and emotional fatigue are common in high-stress individuals, increasing cardiovascular and depression risk.

B. Clinical Risks:

- Elevated Hcy and stress-related mood fatigue are prevalent, often contributing to heightened risks of cardiovascular issues and mood disorders.

C. Supplementation Significance:

- B vitamins help restore negative feedback control of the HPA axis, lower baseline cortisol levels, and improve emotional resilience and recovery speed.

D. Synergistic Formula Benefits:

- When paired with Ashwagandha extract (which downregulates the HPA axis) and L-Theanine (which stabilizes neural rhythms), the formulation supports both stress buffering and recovery pathways.

3) Individuals with Emotional Instability and Poor Sleep Quality

E. Metabolic Characteristics:

- B_6 is a coenzyme in the synthesis of serotonin and melatonin, directly influencing sleep latency and sleep architecture.
- B_{12} modulates tryptophan metabolism and can affect melatonin synthesis, helping to regulate circadian rhythms.

F. Clinical Risks:

- B_6 deficiency can reduce serotonin and GABA levels, leading to anxiety, irritability, and difficulty falling asleep.

G. Supplementation Significance:

- Co-supplementation of B_6 + B_{12} can stabilize mood, improve sleep continuity, and reduce mental fluctuations caused by circadian misalignment.

H. Synergistic Formula Benefits:

- When combined with 5-HTP, L-Theanine, and magnesium glycinate, the formula establishes a “serotonin-GABA-melatonin” tri-axis synergy to enhance emotional regulation and sleep restoration.

4) Individuals with a Monotonous Diet (High in Refined Carbohydrates)

A. Metabolic Characteristics:

- Diets high in refined carbohydrates increase the demand for B_1 and B_6, as these vitamins are essential coenzymes in carbohydrate metabolism (e.g., pyruvate dehydrogenase, transaminases).
- Chronic intake of high-glycemic-index foods lacking in B vitamins can lead to energy fluctuations, insulin dysregulation, and emotional instability.

B. Clinical Risks:

- Early signs may include fatigue and poor concentration; over time, these may progress to mood disturbances on a background of metabolic syndrome.

C. Supplementation Significance:

- B-vitamin supplementation improves glucose utilization efficiency, stabilizes blood sugar fluctuations, and reduces energy and mood volatility.

D. Synergistic Formula Benefits:

- When combined with magnesium glycinate, the formula helps stabilize energy metabolism and prevent blood sugar spikes and crashes that contribute to mental fatigue.

✓ *Kennedy DO. B vitamins and the brain: mechanisms, dose and efficacy—a review. Nutrients. 2016;8(2):68.*

✓ *Hvas AM, Juul S, Bech P, Nexø E. Vitamin B6 level is associated with symptoms of depression. Psychother Psychosom. 2004;73(6):340-343.*

✓ *Selhub J, Bagley LC, Miller J, Rosenberg IH. B vitamins, homocysteine, and neurocognitive function in the elderly. Am J Clin Nutr. 2000;71(2):614S-620S.*

✓ *Stough C, Scholey A, Lloyd J, Spong J, Myers S, Downey LA. The effect of 90-day administration of a high dose vitamin B-complex on work stress. Hum Psychopharmacol. 2011;26(7):470-476.*

IV Synergistic Mechanisms with Keyora Formula Components

- **With 5-HTP:**

  Vitamin B_6 enhances the conversion of 5-HTP into serotonin, supporting emotional stability and improving sleep initiation.

- **With L-Theanine:**

  Together, they enhance GABA activity and alpha brainwave production, promoting relaxation and focused attention.

- **With Magnesium Glycinate:**

  Thiamine (B_1) and pyridoxine (B_6) require magnesium ions as cofactors in both energy metabolism and neurotransmitter synthesis. Adequate magnesium amplifies the physiological efficacy of B vitamins.

- **With Ashwagandha:**

  B vitamins help lower the HPA axis activation threshold, while Ashwagandha buffers stress peaks. Their combination provides dual support for stress resistance and recovery.

1) Synergy in Neurotransmitter Biosynthesis

A. Vitamin B_6 (Pyridoxine)

functions as an essential coenzyme for multiple enzymes involved in neurotransmitter synthesis, especially:

- Aromatic L-amino acid decarboxylase (AADC): catalyzes 5-HTP → serotonin
- Glutamate decarboxylase (GAD): catalyzes glutamate → GABA

B. Synergy with 5-HTP:

Adequate B_6 significantly enhances the efficiency of 5-HTP's conversion into serotonin, increasing emotional stability and potentiating antidepressant effects.

C. Synergy with L-Theanine:

B_6 facilitates GABA synthesis, while L-Theanine modulates GABAergic signaling.

Together, they produce a more sustained calming effect.

D. Synergy with Magnesium Glycinate:

Magnesium enhances GABA_A receptor sensitivity, while B_6 increases GABA production - forming a dual mechanism that amplifies both GABA quantity and receptor responsiveness for stronger neuro-inhibitory modulation.

- ✓ *Birdsall TC. 5-Hydroxytryptophan: a clinically-effective serotonin precursor. Altern Med Rev. 1998;3(4):271-280.*
- ✓ *Dakshinamurti K, et al. Vitamin B6: role in neurotransmitter synthesis and gene expression. In: Shils ME et al., eds. Modern Nutrition in Health and Disease. 11th ed. Lippincott Williams & Wilkins, 2012.*

2) Synergistic Regulation of the HPA Axis and Stress Response

A. B vitamins - particularly B_5, B_6, and B_{12}

play key roles in supporting adrenal cortex function and modulating cortisol synthesis.

B. Synergy with Ashwagandha:

B vitamins improve the efficiency of stress hormone metabolism, while Ashwagandha helps reduce cortisol peak secretion. Together, they form a bidirectional stress-buffering system that enhances both hormone regulation and resilience to acute stressors.

C. Synergy with Magnesium Glycinate:

Magnesium can suppress ACTH (adrenocorticotropic hormone) secretion, while B vitamins enhance cellular energy metabolism. This combination helps prevent fatigue and burnout caused by chronic HPA axis overactivation.

- ✓ *Stough C, et al. The effects of 90 day administration of a high dose B-vitamin complex on work stress. Hum Psychopharmacol. 2011;26(7):470-476.*
- ✓ *Kennedy DO. B vitamins and the brain: mechanisms, dose and efficacy—a review. Nutrients. 2016;8(2):68.*

3) Synergy in Energy Metabolism and Anti-Fatigue Support

A. B vitamins (especially B_1, B_2, B_3, and B_5)

act as essential coenzymes in the tricarboxylic acid (TCA) cycle and electron transport chain, playing a central role in cellular energy production.

B. Synergy with Magnesium Glycinate:

Magnesium is a required ion for ATP synthesis, while B vitamins serve as coenzymes in the metabolism of carbohydrates, fats, and amino acids. Together, they work to enhance the rate of ATP generation, supporting sustained energy output.

C. Synergy with Ashwagandha:

In anti-fatigue pathways, B vitamins provide foundational support for energy metabolism, while Ashwagandha improves mitochondrial efficiency and reduces oxidative stress, forming a complementary mechanism for physical and mental endurance.

- ✓ *Kennedy DO. B vitamins and the brain: mechanisms, dose and efficacy—a review. Nutrients. 2016;8(2):68.*
- ✓ *Huskisson E, et al. The role of vitamins and minerals in energy metabolism and well-being. J Int Med Res. 2007;35(3):277-289.*

4) Synergy in Cognitive Function and Emotional Stability

A. Vitamins B_6, B_9 (folate), and B_{12}

help lower homocysteine (Hcy) levels, supporting cerebrovascular health and protecting against cognitive decline.

B. Synergy with L-Theanine:

B vitamins maintain neuronal structure and function, while L-Theanine enhances alpha brainwave activity. Together, they promote focused attention and cognitive resilience under stress.

C. Synergy with 5-HTP:

By improving the biochemical foundation for neurotransmitter balance, B vitamins enhance the mood-stabilizing and antidepressant effects of 5-HTP, amplifying emotional regulation outcomes.

- ✓ *Hvas AM, Juul S, et al. Vitamin B6 level is associated with symptoms of depression and anxiety in the general population. Psychother Psychosom. 2004;73(6):340-343.*
- ✓ *Malouf R, Grimley Evans J. Folic acid with or without vitamin B12 for cognition and dementia. Cochrane Database Syst Rev. 2008;(4):CD004514.*