Keyora MoodFlow 8 in 1

Nutritional Neuro-Psychiatric Intervention for Mood, Sleep, and Cognitive Resilience in Students, Professionals, Entrepreneurs, and Menopausal Women under Stress

Abstract

Keyora MoodFlow 8 in 1 is a comprehensive nutritional formulation designed to address stress-related emotional, cognitive, and sleep disturbances through a multi-axis regulatory strategy.

The formulation integrates eight clinically supported bio-actives - including 5-hydroxytryptophan (5-HTP), L-Theanine, magnesium glycinate, vitamin B complex, and Ashwagandha - each contributing distinct yet complementary neurobiological mechanisms.

Mechanistically, the formula enhances serotonergic and GABAergic transmission, supports melatonin synthesis, regulates the hypothalamic-pituitary-adrenal (HPA) stress axis, and promotes neuroplasticity in prefrontal-limbic circuits.

Clinical evidence indicates its efficacy in alleviating depressive and anxiety symptoms, improving sleep quality, and sustaining cognitive flexibility in high-stress populations.

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Positioned within the framework of nutritional psychiatry, MoodFlow offers a synergistic, non-pharmacological intervention tailored for students, professionals, entrepreneurs, and menopausal women - populations characterized by heightened stress vulnerability. Its safety profile aligns with validated clinical doses of individual components, supporting long-term applicability.

Conclusion: Keyora MoodFlow 8 in 1 represents a scientifically grounded, multi-component intervention addressing the interconnected triad of mood, sleep, and cognition, with clear applicability across stress-prone populations.

Keywords

Depression, Anxiety, Insomnia, Neurotransmitter synthesis, HPA axis; Homocysteine, Stress resilience, Mood regulation, Sleep quality, Cognitive performance, Magnesium glycinate, 5-Hydroxytryptophan (5-HTP), Ashwagandha, L-Theanine, Vitamin B complex, Students; Professionals; Entrepreneurs; Menopausal women.

Emotional stability, restorative sleep, and effective stress resilience are the three core pillars of brain health and optimal cognitive performance.

Prolonged stress, irregular sleep–wake cycles, and nutrient insufficiency can impair neurotransmitter synthesis, over-activate the stress response, and disrupt circadian

rhythms - leading to a cascade of symptoms such as anxiety, depression, irritability, insomnia, and cognitive decline.

Keyora MoodFlow 8 in 1 is designed around an evidence-based **"Tri-Axis Regulation"** strategy, integrating eight core nutrients into a synergistic intervention model:

- Neurotransmitter Enhancement Axis - Supplementation with 5-HTP and key coenzymes (B6, B1, B12) to facilitate the synthesis of serotonin (5-HT) and gamma-aminobutyric acid (GABA), restoring neurochemical balance and emotional stability.
- Stress Buffer Axis - Synergistic action of Ashwagandha and magnesium glycinate to modulate the hypothalamic-pituitary-adrenal (HPA) axis, reduce peak cortisol levels, and protect the nervous system from chronic stress-induced damage.
- Sleep Rhythm Axis - Optimization of the 5-HT → melatonin synthesis pathway combined with L-Theanine - induced alpha wave modulation to improve sleep latency and deep sleep proportion. Vitamin D is included to further support neurotransmitter synthesis, circadian regulation, and immune modulation - ensuring integrated support for both mood and sleep health.

Each ingredient in the formula is backed by clinical research for its role in improving mood, reducing stress, and enhancing sleep quality. Dosage and safety are calibrated for long-term daily use.

I Nutrient Advantage Summary

Keyora MoodFlow 8 in 1 incorporates eight clinically validated core nutrients, each scientifically selected and dosed to ensure safety and efficacy in long-term supplementation. The formulation is strategically structured to act on three key regulatory axes - neurotransmitter metabolism, stress response modulation, and sleep pathway optimization - creating a multi-dimensional support system:

- Neurotransmitter Synthesis and Metabolic Support - 5-HTP + Vitamins B6, B1, B12: rebuild serotonin, GABA, and dopamine pathways.
- Neuronal Electrical Activity Modulation and Central Relaxation - Magnesium glycinate + L-Theanine: stabilize membrane potential and brainwave patterns.
- Stress Axis Buffering and Neuro-immune Modulation - Ashwagandha + Vitamin D: regulate HPA axis activity, TPH2 expression, and inflammation-linked tryptophan metabolic shunts.

This approach supports neurotransmitter availability at the biochemical source, reduces abnormal cortisol signaling and excitotoxicity, and promotes faster sleep onset with deeper restorative phases - providing scientifically grounded, gentle, and evidence-based support for individuals facing emotional instability, sleep disturbances, and neuro-fatigue.

1) Magnesium Glycinate

Magnesium glycinate is a chelated compound formed by binding magnesium with the amino acid glycine, offering high bioavailability, excellent gastrointestinal tolerance, and additional neurotransmitter-modulating properties.

It is characterized by multi-target efficacy, low side effects, and suitability for long-term supplementation in neuropsychiatric health interventions.

A. Core Roles of Magnesium in Neuro-regulation

Magnesium is the second most abundant intracellular cation, participating in more than 300 enzymatic reactions. Within the nervous system, it exerts key inhibitory and stabilizing effects on neuronal excitability and electrical activity.

- NMDA Receptor Blockade - At resting membrane potential, magnesium ions act as voltage-dependent blockers within the NMDA (N-Methyl-D-Aspartate) receptor channel pore, preventing abnormal calcium (Ca^{2+}) influx. This reduces glutamate-mediated excitotoxicity and calcium overload - pathophysiological processes closely associated with anxiety, depression, insomnia, and neuro-inflammation. Magnesium's stabilizing effect helps maintain membrane potential and synaptic plasticity.
- HPA Axis Modulation - Magnesium deficiency can trigger overactivation of the hypothalamic-pituitary-adrenal (HPA) axis, elevating adrenocorticotropic hormone (ACTH) and cortisol levels. This "low-magnesium–high-cortisol" feedback loop worsens chronic stress states. Magnesium supplementation suppresses

corticotropin-releasing hormone (CRH) secretion, attenuating HPA axis hyperactivity and improving stress resilience.

B. Synergistic Role of Glycine in the Nervous System

Glycine is a primary inhibitory neurotransmitter in the spinal cord, brainstem, and retina. By activating glycine receptors (GlyR), it increases chloride ion permeability, inducing neuronal hyperpolarization and inhibiting impulse transmission - producing sedative, antispasmodic, and muscle-relaxing effects.

In the cerebral cortex, glycine also functions as an NMDA receptor co-agonist. Its modulatory effects vary by concentration and receptor subtype, and in the presence of magnesium, it supports balanced NMDA activity, preventing excitatory fluctuations.

C. Dual-Mechanism Synergy and GABA System Support

Magnesium and glycine complement each other structurally and functionally: magnesium reduces excitatory glutamatergic input, while glycine enhances inhibitory signaling output. This combination markedly strengthens GABAergic modulation.

Studies show that magnesium enhances GABA_A receptor affinity for GABA and increases chloride channel opening frequency - helping to reduce anxiety, lower neuronal hyperexcitability, and shorten sleep onset latency.

D. Clinical Evidence for Magnesium Glycinate

a) Reduction of Anxiety Symptoms

Boyle, N. B., Lawton, C., & Dye, L. (2017). Nutrients, 9(5), 429 - Systematic review of 18 human studies (including 4 RCTs) found significant reductions in anxiety scores among individuals with mild-to-moderate anxiety, premenstrual anxiety, and high-stress occupations.

Magnesium glycinate was consistently ranked as one of the most bioavailable and best-tolerated forms.

b) Improvement in Insomnia with Anxiety Features

Abbasi, B., et al. (2012). Journal of Research in Medical Sciences, 17(12), 1161-1169- RCT involving 46 elderly primary insomnia patients supplemented with 500 mg magnesium (including glycine) daily for 8 weeks.

The magnesium group showed improved sleep latency, total sleep time, and reduced early morning awakenings, along with increased serum melatonin and decreased cortisol - indicating HPA axis involvement.

c) Suppression of Cortical Hyperexcitability

Wienecke, T., et al. (2016). Cephalalgia, 36(7), 585-593 - Human cortical stimulation studies demonstrated magnesium’s ability to suppress cortical excitability via NMDA receptor inhibition and GABA neuron potential modulation.

Magnesium glycinate showed enhanced brain penetration and stabilization of cortical discharges.

d) Bioavailability and Tolerability Advantage

Walker, A. F., et al. (2003). Magnesium Research, 16(4), 239-246 - Magnesium glycinate had superior absorption and serum magnesium elevation compared to inorganic salts, with significantly lower gastrointestinal discomfort, making it ideal for sensitive individuals and chronic use.

e) Epidemiological Association with Mood Disorders

Jacka, F. N., et al. (2009). American Journal of Psychiatry, 167(3), 305–311 - Lowest quartile magnesium intake was associated with significantly higher anxiety and depression scores, particularly in populations with high-sugar, refined diets - highlighting magnesium deficiency as a risk factor for anxiety and sleep disorders.

Summary of Evidence-Based Properties for Magnesium Glycinate

Functional Target	Clinical Support Area	Evidence Level
NMDA receptor antagonism	Reduced excitotoxicity, stabilized neuronal firing	A
GABA pathway modulation	Anxiolytic effects, sleep induction	A
HPA axis downregulation	Lower perceived stress, reduced physiological arousal	B

Functional Target	Clinical Support Area	Evidence Level
Sleep architecture	Shorter sleep latency, deeper slow-wave sleep	A
High bioavailability	Better absorption and tolerance vs. other magnesium salts	A

E. Bioavailability and Safety

Unlike inorganic forms such as magnesium oxide or carbonate, magnesium glycinate is absorbed in the small intestine via active amino acid transporters, independent of gastric acidity. This provides higher bioavailability and lower gastrointestinal irritation, making it suitable for individuals with sensitive digestion or long-term supplementation needs. Clinical data indicate that 120-200 mg/day elemental magnesium is effective for anxiety reduction, sleep initiation improvement, and stress recovery without sedative side effects.

F. Applicable Conditions and Populations

- Emotional fluctuations and sleep initiation difficulties due to high workload or chronic stress
- Persistent sympathetic hyperactivity (e.g., rapid heart rate, muscle tension, inability to “switch off” thoughts)
- Individuals with high neuro-sensitivity or baseline anxiety
- Those with concurrent muscle soreness, spasms, or daytime fatigue

✓ *Boyle, N. B., Lawton, C., & Dye, L. (2017) – The effects of magnesium supplementation on subjective anxiety and stress—a systematic review – Nutrients, 9(5), 429.*

- Systematic review: Magnesium supplementation can relieve anxiety and stress, related to NMDA inhibition mechanisms.

✓ *Kirkland, A. E., Sarlo, G. L., & Holton, K. F. (2018) – The role of magnesium in neurological disorders – Nutrients, 10(6), 730.*

- Role of magnesium in the nervous system: includes inhibiting NMDA overactivation and supporting the GABA system.

2) L-Theanine

L-Theanine is a non-protein, naturally occurring L-α-amino acid predominantly found in the young leaves of the tea plant, contributing to the characteristic “umami” and “fresh aroma” of tea infusions. Owing to its unique neuro-modulatory mechanisms, it has gained recognition in recent years as a “neuro-homeostatic nutrient” within functional nutrition research.

A. Blood–Brain Barrier Penetration

L-Theanine crosses the blood-brain barrier via the large neutral amino acid transport system, with high bioavailability. Peak brain activity occurs within 30-60 minutes after ingestion, making it a fast-acting yet gentle modulator for emotional regulation.

B. α-Wave Enhancement - Relaxed but Alert

Its most notable neuro-electrophysiological effect is the marked enhancement of α-wave (8-13 Hz) activity, which is linked to a state of “relaxed alertness,” characterized by mental clarity and muscular relaxation.

EEG studies consistently show significant increases in α-wave activity in the occipital and parietal cortices within 45 minutes of ingestion, lasting approximately 60-90 minutes. Unlike sedatives, L-Theanine does not suppress β-waves or induce δ-waves, thereby avoiding daytime drowsiness and supporting a “non-sedative anxiolytic” profile.

C. Multi-Neurotransmitter Pathway Modulation - GABA–5HT–DA Axis

L-Theanine positively modulates multiple central neurotransmitter systems through distinct mechanisms:

- GABA elevation - Enhances inhibitory neural signaling, reduces cortical neuron firing frequency, and alleviates hyper-activation of the nervous system.
- 5-hydroxytryptamine (5-HT) increase - Inhibits reuptake and upregulates synthesis in the brainstem and limbic system.
- Dopamine (DA) enhancement - Promotes synthesis and release in the striatum and hippocampus, improving positive mood and motivational states.

This “non-specific multi-transmitter modulation” forms the basis for its effects in emotional stabilization, sustained attention, and relaxation - particularly relevant for individuals experiencing high stress with coexisting cognitive overload.

D. Glutamate System Antagonism - Reducing Excitotoxicity

Structurally similar to glutamate, L-Theanine can competitively bind to certain glutamate receptor subtypes, thereby reducing glutamate-induced calcium influx and excitotoxicity. Additionally, it modulates the glutamine–glutamate cycle, indirectly enhancing GABA synthesis, providing an intrinsic “braking mechanism” for overactive neurons.

E. Synergy with Magnesium Glycinate

L-Theanine primarily acts on neurotransmitter pathways, while magnesium glycinate stabilizes membrane potential and inhibits NMDA receptor over-activity.
Their complementary mechanisms provide anxiolytic effects, optimize sleep readiness, and increase deep-sleep proportions without causing daytime sedation - making them particularly suitable for individuals intolerant to sedatives who need to maintain cognitive clarity.

F. Clinical Evidence

- Higashiyama, A., et al. (2011) - A randomized, double-blind trial demonstrated that daily intake of 200 mg L-Theanine for 4 weeks significantly reduced State-Trait Anxiety Inventory (STAI) scores in adults.
- Other RCTs have shown that L-Theanine shortens sleep onset latency and improves subjective sleep satisfaction, particularly in mild insomnia with high cognitive arousal.

- In school-aged children, supplementation improved sustained attention and inhibitory control, supporting its dual action on cognition and emotion.

G. Applicable Conditions and Populations

- Daytime mental tension, stress-induced tachycardia, or distractibility
- High nighttime cognitive arousal, difficulty initiating sleep without excessive sedation
- Irritable, restless, anxiety-prone states
- Situational anxiety regulation (e.g., students in preparation phase, public speaking, examinations, competitive events)

✓ *Nobre, A. C., Rao, A., & Owen, G. N. (2008) – L-theanine, a natural constituent in tea, and its effect on mental state – Asia Pacific Journal of Clinical Nutrition, 17(S1), 167–168.*

- EEG experiments confirmed L-theanine significantly increases α-wave activity, associated with a "relaxed but alert" state.

✓ *Unno, K., et al. (2013) – Anti-stress effect of theanine on students during pharmacy practice: positive correlation among salivary α-amylase activity, trait anxiety and subjective stress – Pharmacology Biochemistry and Behavior, 111, 128–135.*

- Observational study: L-theanine improved both physiological and psychological stress indicators during cognitive strain.

3) Ashwagandha

Ashwagandha (Withania Somnifera) is a medicinal plant whose primary active constituents are Withanolides.

It exerts multiple neuroendocrine effects through regulation of the hypothalamic-pituitary-adrenal (HPA) axis, reduction of stress hormone levels, enhancement of neuroplasticity, and anti-inflammatory activity.

These combined mechanisms make it well-suited for neuro-functional support in states of chronic stress, anxiety, fatigue, and disrupted sleep architecture.

A. Regulation of HPA Axis Activity - Breaking the "High-Stress-High-Cortisol" Cycle

The HPA axis is the body's central stress-response system. Dysregulation is characterized by disrupted diurnal cortisol rhythms, elevated baseline levels, or impaired feedback inhibition, all of which can contribute to anxiety, low mood, and frequent awakenings.

Withanolides in Ashwagandha modulate the hypothalamic CRH-pituitary ACTH-adrenal cortisol pathway at multiple points, significantly reducing morning/evening cortisol in chronic stress while restoring rhythmic fluctuation and enhancing resilience to acute stressors.

- In a randomized, double-blind trial using standardized KSM-66 extract (≥5% Withanolides), 60 days of supplementation reduced salivary cortisol by up to 27.9%, alongside significant improvements in Hamilton Anxiety Rating Scale (HAMA) and Perceived Stress Scale (PSS) scores.

B. Relief of Chronic Stress-Induced Anxiety, Cognitive Fatigue, and Sleep Disturbance

Chronic HPA axis hyper-activation and heightened sympathetic tone can destabilize prefrontal-limbic system function, manifesting as:

- Irritability and emotional dysregulation
- Reduced attention span and “brain fog”
- Shallow sleep, vivid dreams, or early-morning awakenings

Ashwagandha has been shown to significantly alleviate these stress-related neuropsychological sub-health states.

- Multiple clinical studies demonstrate reduced scores in generalized anxiety disorder (GAD) and superior improvements over placebo in sleep onset latency, nocturnal awakenings, and subjective restorative sleep ratings - particularly in “anxious insomnia” and “mental fatigue-linked mood fluctuation” phenotypes.

C. Support of Neuroplasticity - BDNF Upregulation and Cognitive Flexibility

Chronic stress suppresses hippocampal brain-derived neurotrophic factor (BDNF) expression, impairing synaptic connectivity and emotional resilience.
Ashwagandha upregulates BDNF via the ERK/CREB signaling pathway, promoting neuronal plasticity and regeneration.

- Human trials have reported enhanced learning and memory metrics, as well as improved cognitive flexibility, attentional shifting, and emotional recovery after stress, supporting its role in sustaining cognitive–emotional balance in prolonged high-pressure states.

D. Anti-Inflammatory Effects and IDO Pathway Inhibition

Psychological stress can activate the indole-amine 2,3-dioxygenase (IDO) pathway through pro-inflammatory cytokines such as TNF-α and IL-6, diverting tryptophan metabolism toward kynurenine and neurotoxic derivatives (e.g., 3-HK, QUIN), thereby reducing serotonin synthesis and promoting mood disorders.

Ashwagandha suppresses IL-6 and TNF-α, blocks stress-induced tryptophan diversion, and indirectly increases serotonin availability - creating a dual-pathway intervention model for mood regulation and immune homeostasis.

E. Clinical Evidence

a) High-Concentration Standardized Extract Reduces Stress and Anxiety

Chandrasekhar et al., 2012 - 60-day RCT in adults with stress-related anxiety showed a 27.9% cortisol reduction, significant improvements in GHQ-28, PSS, and HADS scores, and excellent safety profile for KSM-66.

b) Multidimensional Stress Recovery (HPA Axis, Biochemical, Psychological Metrics)

Lopresti et al., 2019 - 8-week RCT in high-stress but otherwise healthy adults improved perceived stress, sleep quality, reaction time, and heart rate variability; serum cortisol decreased significantly with no adverse events.

c) Improved Sleep Quality in Insomnia

Langade et al., 2019 - 12-week RCT in older adults (>65 years) showed shorter sleep latency, fewer awakenings, higher vitality scores, and improved PSQI scores over placebo; also reduced anxiety.

d) Anxiety Symptom Relief in GAD

Cooley et al., 2009 - RCT in mild-to-moderate GAD patients found 56.5% average reduction in HAM-A scores, with concurrent improvements in sleep and quality of life; superior to standard counseling.

e) Systematic Review and Meta-Analysis Confirmation

Pratte et al., 2014 - Review of five human trials confirmed consistent improvements in anxiety, sleep, and cortisol regulation, with no serious adverse events.

Summary: High-Quality Clinical Evidence on Ashwagandha

Functional Target	Clinical Effect	Reference	Evidence Grade
HPA Axis Regulation	Reduces cortisol levels,	Chandrasekhar	A

Functional Target	Clinical Effect	Reference	Evidence Grade
	enhances stress resilience	(2012)	
Anxiety Reduction	Significant decrease in anxiety scores, alleviates mental tension	Lopresti (2019)	A
Sleep Quality Improvement	Shortens sleep onset latency, increases deep sleep proportion	Langade (2019)	A
Multi-System Stress Relief	Improves psychological, sleep, and heart rate variability indicators	Lopresti (2019)	A
Consistent Evidence Across Reviews	Systematic reviews confirm efficacy and safety	Pratte (2014)	A

This table consolidates key findings from randomized controlled trials and systematic reviews, highlighting Ashwagandha's robust evidence base for modulating stress physiology, improving anxiety symptoms, enhancing sleep architecture, and delivering broad psychophysiological benefits with excellent safety.

F. Dosage Form, Dose, and Safety

Keyora MoodFlow 8 in 1 contains 200 mg/day standardized Ashwagandha root extract (≥10% Withanolides). This dosage and form have demonstrated efficacy and safety in multiple clinical trials lasting 8-12 weeks.

G. Applicable Conditions and Populations

- Individuals under sustained high expectations and self-imposed pressure (e.g., executives, exam candidates)
- Early awakening, restless, or dream-rich insomnia
- Stress-induced anxiety/irritability with mental fatigue and concentration difficulties
- Immune vulnerability with mood sensitivity

✓ *Chandrasekhar, K., Kapoor, J., & Anishetty, S. (2012) – A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha root in reducing stress and anxiety – Indian Journal of Psychological Medicine, 34(3), 255–262.*

- Using KSM-66 extract, 60 days of supplementation significantly reduced cortisol and anxiety scores.

✓ *Lopresti, A. L., Smith, S. J., Malvi, H., & Kodgule, R. (2019) – An investigation into the stress-relieving and pharmacological actions of an ashwagandha (Withania somnifera) extract: A randomized, double-blind, placebo-controlled study – Medicine, 98(37), e17186.*

- Further supports its triple-axis mechanism in stress relief, anxiolysis, and sleep improvement.

4) 5-HTP (5-Hydroxytryptophan)

5-HTP is the direct biochemical precursor of serotonin (5-HT) in humans, formed as an intermediate metabolite after the hydroxylation of tryptophan.

Compared with dietary tryptophan supplementation, 5-HTP bypasses competitive transport limitations in the gut and across the blood–brain barrier, allowing rapid entry into the central nervous system (CNS) and efficient conversion to serotonin in the presence of vitamin B6.

This makes it one of the most well-characterized and clinically validated natural interventions for “low serotonin state”–related mood disorders and circadian rhythm disturbances.

A. Bypassing Tryptophan Transport Competition - Directly Increasing Brain Serotonin Precursors

Tryptophan, the traditional substrate for 5-HT synthesis, crosses the blood–brain barrier via the LAT1 transporter, competing with other large neutral amino acids (e.g., leucine, phenylalanine, and valine). Even with sufficient dietary intake, this competition limits its CNS delivery.

5-HTP, as a hydroxylated intermediate, is a non-competitive transport substrate and enters the brain more efficiently, where it is rapidly converted to serotonin by aromatic L-amino acid decarboxylase (AADC).

B. B6-Dependent Conversion - Ensuring 5-HT Synthesis Efficiency

The 5-HTP → 5-HT conversion requires pyridoxal-5′-phosphate (PLP), the active form of vitamin B6, as an AADC coenzyme.

- Low B6 status can cause premature peripheral conversion of 5-HTP, reducing CNS serotonin availability.
- Co-supplementation with B6 optimizes conversion efficiency and central bioavailability, forming a closed-loop mechanism within the formula.

Serotonin modulates:

- Limbic system (amygdala, hippocampus) - emotional reactivity
- Raphe nuclei - HPA axis negative feedback
- Hypothalamus - melatonin synthesis and sleep-wake rhythm

Together, this builds an “emotion-stress-sleep” regulatory circuit.

C. Core Role in Mood Disorders

Low serotonin is a well-established neurochemical basis for depression, anxiety, obsessive-compulsive disorder, and stress-related disorders.

5-HTP supplementation can:

- Suppress hyper-reactivity of the amygdala, reducing fear and hypervigilance
- Enhance prefrontal cortex control, improving impulse regulation and emotional balance
- Attenuate HPA axis overactivation, reducing physiological stress perception
- Promote positive affect and social motivation

D. Melatonin Synthesis Support - Restoring Circadian Rhythm and Sleep Architecture

Serotonin is the sole substrate for pineal melatonin synthesis, which occurs at night through hydroxylation and methylation steps. 5-HTP supplementation:

- Improves daytime mood stability
- Enhances nighttime melatonin production, promoting sleep readiness, shortening sleep latency, and increasing deep sleep proportion
- Particularly beneficial for sleep-onset insomnia and delayed sleep phase disorder, especially when comorbid with anxiety or depression
- Functions as a bidirectional regulator - daytime mood stabilization and nighttime sleep repair

E. Clinical Evidence

a) Depression and Low Mood

- Shaw et al., 2002 (Cochrane review) - Found significant improvements in mild-to-moderate depressive symptoms, with relatively fast onset and minimal side effects.
- Poldinger et al., 1991- Showed efficacy comparable to SSRIs in mood improvement, but with better tolerability, making it suitable for individuals intolerant to medication or with functional mood disturbances.

b) Anxiety Support

- 5-HTP increases CNS serotonin levels, reducing anxiety, tension, and irritability.

- Co-administration with vitamin B6 further improves stability and conversion efficiency (Birdsall, 1998).

c) Sleep Rhythm and Onset Improvement

- As a melatonin precursor, 5-HTP improves sleep onset in mood - or stress-related insomnia.
- Hartmann, 1982 - Demonstrated shorter sleep latency and longer deep sleep duration with 5-HTP supplementation.

F. Dosage, Tolerability, and Safety

Typical dosage: 100-200 mg/day in 1-2 divided doses.

In **Keyora MoodFlow 8 in 1** formula, 5-HTP is paired with B6 at the lower end of the clinical range to minimize mild side effects (e.g., transient gastrointestinal discomfort, vivid dreams) while maintaining long-term efficacy and safety.

Compared with conventional antidepressants, onset is gentler, dependence risk is lower, and withdrawal effects are minimal - making it suitable for mild-to-moderate symptoms or long-term maintenance in recovery.

G. Applicable Conditions and Populations

- Persistent low mood, emotional suppression, loss of motivation, or anhedonia
- Chronic anxiety or tension with unstable daytime mood plus nighttime insomnia

- Maintenance and adjunctive recovery in MDD, PMDD, SAD remission
- Sleep disorders from impaired melatonin synthesis (e.g., elderly, shift workers, circadian misalignment)

✓ *Shaw, K., Turner, J., & Del Mar, C. (2002) – Tryptophan and 5-hydroxytryptophan for depression – Cochrane Database of Systematic Reviews, (1).*

- Cochrane systematic review: 5-HTP shows positive effects in mild-to-moderate depression.

✓ *Birdsall, T. C. (1998) – 5-Hydroxytryptophan: a clinically-effective serotonin precursor – Alternative Medicine Review, 3(4), 271–280.*

- Review article: 5-HTP is an effective serotonin precursor with clear mechanisms; effect enhanced when combined with B6.

5) Vitamin B1 (Thiamine)

Vitamin B1 is a water-soluble vitamin that functions as an essential coenzyme in the nervous system. Its primary role is to sustain neuronal mitochondrial energy metabolism, neurotransmitter synthesis, and myelin integrity - thereby preventing “brain energy deficit”– induced symptoms such as poor concentration, slowed thinking, mood instability, and neuronal hyperexcitability. It is a fundamental factor for building an “energy-stable cognitive-emotional foundation.”

A. Mitochondrial Energy Metabolism - Supporting Neuronal Function

Thiamine pyrophosphate (TPP) serves as a required coenzyme for multiple key enzymes in the tricarboxylic acid (TCA) cycle:

- Pyruvate dehydrogenase (PDH): Links glycolysis to the TCA cycle by converting pyruvate to acetyl-CoA
- α-Ketoglutarate dehydrogenase (α-KGDH): Generates high-energy intermediates for ATP synthesis
- Transketolase: Participates in the pentose phosphate pathway, producing NADPH and nucleotides

These enzymes are highly expressed in neurons to maintain membrane potential, synaptic transmission, and calcium efflux-processes with high energy demand.
B1 deficiency can cause localized “energy starvation,” especially affecting the prefrontal cortex (cognition) and limbic system (emotion), leading to reduced attention span, impaired decision-making, fatigue, and brain fog.

B. Preventing Energy-Deficit–Induced Mood Dysregulation

Reduced ATP synthesis in the brain impairs neurotransmitter reuptake and vesicular release efficiency, destabilizing GABA, 5-HT, and dopamine levels.
This fluctuation can lead to mood instability, irritability, and heightened arousal.
As a metabolic “starter cofactor,” B1 can improve energy-deficit–related low mood in its early stages and enhance emotional resilience.

C. Cognitive and Anti-Fatigue Support

Clinical evidence suggests that B1 supplementation improves executive function, processing speed, and attentional control - particularly in individuals with high cognitive load (e.g., students, programmers, and executives) or in suboptimal recovery states.

- A randomized, double-blind trial showed that daily 50 mg thiamine for two months reduced error rates in sustained attention tasks, lowered subjective fatigue scores, and increased “positive mood” subscale scores.

D. Reducing Neuro-excitotoxicity and Oxidative Stress

Within the brain, TPP can help limit glutamate accumulation, promote lactate clearance, and enhance NADPH regeneration - thus reducing excitotoxicity and halting oxidative chain reactions.

- In mild-to-moderate thiamine deficiency (especially in individuals with marginal dietary intake), these protective functions are compromised, manifesting as neuronal hyperexcitability, difficulty maintaining sleep, and reduced cognitive load tolerance. This underscores its long-term importance for maintaining “baseline neural tone stability.”

E. Deficiency Risks and Susceptible Populations

B1 is water-soluble and not stored in the body, with a high turnover rate. Risk factors for deficiency include:

- High-carbohydrate diets (increased demand due to glycolytic load)
- Chronic psychological stress and elevated adrenaline (increased metabolic clearance)
- High cognitive workload or prolonged attention demand
- Frequent alcohol use or impaired gastrointestinal absorption (reducing B1 uptake and activation)

F. Role and Synergy in the Formula

In **Keyora MoodFlow 8 in 1**, B1 acts as the “neuronal energy foundation,” working with:

- **B6** for neurotransmitter synthesis
- **B12** for myelin integrity and methylation processes

This synergy aims to:

- Provide the energetic background needed for 5-HTP-driven neurotransmitter synthesis
- Prevent secondary mood fluctuations triggered by mental fatigue
- Support stable neural tone in the cognitive-to-sleep transition period

✓ *Benton, D., Donohoe, R. T., & Sillance, B. (1995) – The influence of the vitamin B1 on mood – Neuropsychobiology, 32(2), 98–105.*

- RCT: Thiamine supplementation improved cognitive performance and subjective mood state.

✓ *Zhang, Z., et al. (2021) – The importance of thiamine (vitamin B1) in energy metabolism – Nutrients, 13(11), 1–17.*

- Review: B1 participates in energy metabolism and stabilizes brain energy status, with significant impact on mental symptoms.

6) Vitamin B6 (Pyridoxine)

Vitamin B6 is an essential water-soluble vitamin that, once converted into its active form - pyridoxal-5'-phosphate (PLP) - participates in over 100 biochemical reactions. It is a required coenzyme for the synthesis of several key neurotransmitters in the nervous system and is considered one of the rate-limiting factors in neurotransmitter metabolism. B6 plays a central role in pathways regulating mood, stress adaptation, and sleep maintenance.

A. A Key Coenzyme in Neurotransmitter Synthesis

PLP serves as a cofactor in multiple decarboxylation and transamination reactions, directly contributing to the biosynthesis of:

- 5-HTP → Serotonin (5-HT) via aromatic L-amino acid decarboxylase (AADC)
- Glutamate → γ-aminobutyric acid (GABA) via glutamate decarboxylase (GAD)

- L-Dopa → Dopamine → Norepinephrine via dopamine β-hydroxylase pathways

B6 deficiency directly reduces the efficiency of these pathways, leading to decreased inhibitory neurotransmitters (GABA, 5-HT) and dysregulation of sympathetic monoamines, manifesting as anxiety, insomnia, irritability, and poor concentration.

B. An Essential Cofactor in the 5-HTP Conversion Pathway

5-HTP in the formula requires AADC to convert into serotonin, and this enzymatic activity is strongly dependent on adequate PLP levels. In B6 deficiency, 5-HTP is prone to premature peripheral conversion, lowering central serotonin elevation and potentially causing mild gastrointestinal discomfort (e.g., nausea).

Sufficient B6 intake is thus the “foundational safeguard” for 5-HTP’s efficacy. Combined supplementation of B6 and 5-HTP has been adopted in multiple clinical studies to accelerate and stabilize anti-anxiety and antidepressant effects.

C. Modulating the GABA Pathway for Anxiety Relief

GABA is the primary inhibitory neurotransmitter in the CNS, and its synthesis requires PLP activation of GAD. When B6 is insufficient, GABA levels fall, resulting in:

- Increased neuronal excitability and reduced α-wave activity
- Longer sleep onset latency and more nighttime awakenings
- Reduced emotional inhibition, manifesting as irritability, agitation, and hypervigilance

Studies indicate that B6 supplementation can significantly raise GABA levels, easing anxiety and sleep initiation problems - particularly in “cognitive hyperarousal” insomnia.

D. Balancing Monoamine Neurotransmitters to Support Positive Mood

B6 is involved in the conversion of L-Dopa to dopamine (DA) and DA to norepinephrine (NE). Adequate intake helps maintain stable DA levels in the limbic system, supporting motivation and reducing anhedonia or low mood - especially relevant in “motivation-depletion” depression induced by chronic stress.

Additionally, B6 contributes to one-carbon metabolism, indirectly maintaining S-adenosylmethionine (SAM) synthesis and neurotransmitter methylation capacity, positively influencing the stability of long-chain neurotransmitters and brain methylation status.

E. Secondary Mechanism: Inhibiting the IDO Pathway and Tryptophan Diversion

B6 participates in multiple transamination reactions in the kynurenine pathway, playing a key role in regulating tryptophan’s metabolic direction. Adequate supplementation can inhibit tryptophan shunting toward neurotoxic metabolites such as quinolinic acid (QUIN), thereby indirectly supporting central serotonin synthesis and slowing the progression of inflammation-induced mood disorders.

F. At-Risk Groups and Applicable Conditions

- Diets high in refined carbohydrates or plant-based patterns with low B6 intake
- Individuals under chronic stress with elevated cortisol (accelerated PLP metabolism)
- Users of oral contraceptives, antiepileptic drugs, or alcohol (which interfere with B6 activation and absorption)
- Those with mood fluctuations, sleep disturbances, or high cognitive workload

In **Keyora MoodFlow 8 in 1**, B6 is included at a synergistic dosage (typically 1.3-2 mg/day or higher) to ensure stable operation of neurotransmitter synthesis pathways, forming the foundation for the formula's **mood-cognition-sleep tri-axis modulation**.

✓ *Merete, C., Falcon, L. M., & Tucker, K. L. (2008) – Vitamin B6 is associated with depressive symptomatology in Massachusetts elders – Journal of the American College of Nutrition, 27(3), 421–427.*

- B6 deficiency is significantly associated with depressive states in older adults.

✓ *Dakshinamurti, K. (2005) – Vitamin B6 in metabolism and nervous system function – In Subcellular Biochemistry (Vol. 35, pp. 289–316). Springer.*

- Mechanism details: B6 supports the synthesis of GABA, 5-HT, dopamine, and other neurotransmitters.

7) Vitamin B12 (Cobalamin)

Vitamin B12 is a cobalt-containing water-soluble vitamin found primarily in animal-derived foods. Once activated in the body, it participates in myelin sheath synthesis, one-carbon

metabolism, neurotransmitter methylation, and homocysteine clearance - serving as a core factor for maintaining nervous system function, protecting cognitive performance, and suppressing neuro-inflammation.

Deficiency can lead to multi-level neuropsychiatric impairment, with markedly elevated risk among vegetarians, older adults, and individuals with impaired gastrointestinal function.

A. Supporting Myelin Sheath Synthesis and Axonal Conduction

B12 functions as a coenzyme for methylmalonyl-CoA mutase (MCM) and methionine synthase (MTR), facilitating the generation of myelin components (e.g., phospholipids) from fatty acid metabolism, and supplying nucleotides for DNA and myelin synthesis. Deficiency results in incomplete or degenerating myelin structures and slowed conduction velocity, manifesting clinically as limb numbness, paresthesia, memory decline, irritability, or depressive symptoms - often classified as “subclinical neuropathy.”

- B12 is the only nutrient capable of reversing early symptoms of subacute combined degeneration (SCD) and is used in functional nutrition interventions to preserve myelin integrity and stable nerve conduction.

B. Supporting S-Adenosylmethionine (SAM) Synthesis and Neurotransmitter Methylation

In the MTR-catalyzed reaction, B12 facilitates the remethylation of homocysteine (Hcy) to methionine (Met), which subsequently generates SAMe - a universal methyl donor in the nervous system. SAM supports:

- Methylation activation of neurotransmitters such as norepinephrine (NE) and dopamine (DA)
- Phospholipid synthesis and membrane stability
- Epigenetic DNA regulation and maintenance of synaptic plasticity

B12 deficiency reduces SAM levels, impairing stable neurotransmitter release and inter-regional brain communication, leading to cognitive inflexibility and diminished emotional regulation capacity.

C. Reducing Homocysteine Accumulation to Alleviate Neuro-inflammation and Vascular Toxicity

B12 is one of the essential vitamin-dependent cofactors in the Hcy → Met pathway. Elevated Hcy is neurotoxic and vasculotoxic, capable of activating NMDA receptors, triggering excitotoxicity, increasing blood-brain barrier permeability, and promoting inflammatory cytokines such as IL-6 and TNF-α.

- Plasma Hcy ≥10 μmol/L is positively correlated with depression, Alzheimer's disease, and post-stroke cognitive decline.

- B12 supplementation lowers Hcy levels, and its effect is enhanced when combined with folate and B6, making it suitable for individuals at risk of inflammation-related mood disorders or cognitive decline.

D. At-Risk Populations and Clinical Manifestations

B12 deficiency is most common in:

- Vegetarians - B12 is exclusively found in animal-derived foods; long-term vegan diets carry a high deficiency risk
- Older adults - Reduced gastric acid secretion limits B12 release and absorption, leading to “functional deficiency”
- Long-term users of acid-suppressing drugs or metformin - Both interfere with intestinal B12 absorption
- Individuals with malabsorption - e.g., atrophic gastritis, small intestine disorders, or post-surgical states

Early deficiency symptoms are nonspecific, including memory decline, difficulty concentrating, mood fluctuations, mild depression, and slowed reaction time. Without correction, these may progress to peripheral neuropathy or cognitive impairment.

E. Role in the Formula and Synergistic Value

In **Keyora MoodFlow 8 in 1**, B12 functions as a structural-support neuro-nutrient, forming a multi-dimensional support network with B1 (energy metabolism), B6 (neurotransmitter synthesis), and 5-HTP (neurotransmitter precursor) to sustain neurotransmitter pathways, myelin synthesis, and metabolic stability. Key synergies include:

- Enhancing SAMe availability to stabilize dopamine and norepinephrine pathways
- Mitigating Hcy-induced neuro-inflammatory activation to protect cerebrovascular function
- Supporting long-term cognitive and emotional stability strategies for older adults or vegetarians

✓ *Reynolds, E. (2006) – Vitamin B12, folic acid, and the nervous system – The Lancet Neurology, 5(11), 949–960.*

- B12 deficiency impacts the central nervous system via myelin, homocysteine, and SAMe pathways.

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

- Systematic review: Multiple relationships between B12, cognition, mood, myelin, and inflammation.

8) Vitamin D (Cholecalciferol)

Vitamin D is not merely a vitamin for calcium-phosphorus metabolism in the traditional sense; it is a steroid hormone precursor with extensive biological regulatory functions.

Its active form, vitamin D_3, directly modulates neurotransmitter metabolism, neuro-inflammation, circadian rhythm, and neurodevelopment in multiple brain regions.
It plays a pivotal role in regulating serotonin (5-HT) synthesis, maintaining sleep architecture, and mediating mood-immune system interactions.

A. Regulating Tryptophan Hydroxylase 2 (TPH2) Expression to Enhance Central 5-HT Synthesis

Central serotonin synthesis depends on TPH2 activity. VD_3 can activate the VDR → transcription factor pathway, upregulating TPH2 gene expression, increasing the rate of tryptophan-to-5-HT conversion, and improving serotonin availability in the brain.

- In parallel, vitamin D downregulates peripheral TPH1 expression, reducing tryptophan's diversion into gut-immune system catabolic pathways (e.g., the kynurenine pathway), creating a "central priority" substrate allocation.
  This bidirectional regulation has significant intervention potential for individuals with "low-serotonin" anxiety, depression, and circadian rhythm disorders.

B. Supporting Melatonin Synthesis and Stabilizing Sleep Rhythms

5-HT is the direct precursor to melatonin, and vitamin D can modulate the expression of AANAT and HIOMT in the pineal gland to sustain melatonin synthesis pathway activity.
Melatonin is essential for initiating nighttime sleep signals, maintaining deep sleep stages, and synchronizing circadian rhythms.

- Clinical studies have linked vitamin D status to subjective sleep quality, sleep latency, and nighttime awakenings. Long-term deficiency reduces pineal melatonin output at night, predisposing individuals to “sleep-onset insomnia” and “circadian misalignment” insomnia.

C. Modulating Neuro-inflammation and Immune Activation

VDRs are widely expressed in the hippocampus, hypothalamus, and prefrontal cortex. VD_3 modulates glial cell function, decreases pro-inflammatory cytokines such as IL-6 and TNF-α, and suppresses COX-2 expression, thereby reducing neurotransmitter fluctuations under pro-inflammatory conditions.

- Chronic low-grade neuro-inflammation is a key underlying mechanism in depression, anxiety, and sleep disturbances. Vitamin D deficiency compromises neuro-immune axis regulation, amplifying the risk of inflammation-induced tryptophan depletion (via IDO activation) and GABA/5-HT dysfunction.

D. Evidence Linking Vitamin D to Mood Disorders, Anxiety, and Sleep Disturbance

- Multiple cohort studies have shown that serum vitamin D levels below 50 nmol/L are significantly associated with higher incidence of depression and generalized anxiety disorder, particularly among older adults, women, and those with chronic illness.
- Randomized, double-blind trials have demonstrated that daily supplementation with 800-2000 IU vitamin D_3 for 8-12 weeks can improve mild-to-moderate depression

scores, enhance subjective well-being, and improve sleep continuity, with effects comparable to standard psychological interventions.

E. Target Populations and High-Risk Profiles

- Insufficient sunlight exposure - high-latitude residents, winter seasons, indoor workers
- Dark-skinned individuals - reduced cutaneous synthesis efficiency
- Older adults - diminished skin synthesis and hepatic/renal activation capacity
- Anxiety or sleep disorders with chronic inflammation or autoimmune background
- Individuals with obesity or high BMI - vitamin D is sequestered in adipose tissue, reducing circulating bioavailability

F. Dosage and Safety Parameters

In **Keyora MoodFlow 8 in 1**, vitamin D_3 (cholecalciferol) is used for its high bioactivity and stability. The long-term recommended dosage is 400-1000 IU/day.

✓ *Patrick, R. P., & Ames, B. N. (2014) – Vitamin D hormone regulates serotonin synthesis. Part 1: relevance for autism – FASEB Journal, 28(6), 2398–2413.*

- Detailed mechanism paper: Vitamin D upregulates TPH2 and regulates central serotonin synthesis.

✓ *Muscogiuri, G., et al. (2017) – Vitamin D and sleep regulation: Is there a role for vitamin D? – Current Pharmaceutical Design, 23(32), 2490–2494.*

- Review: Relationship between vitamin D, circadian rhythm regulation, and insomnia.

II Core Efficacy and Mechanisms of Action

Keyora MoodFlow 8 in 1 is specifically designed for multi-axis neuro-regulatory modulation, targeting the three core functional systems of *emotion–sleep–cognition*.

It modulates the homeostasis of key neurotransmitters such as serotonin (5-HT), GABA, and dopamine, while synergistically intervening in underlying mechanisms including HPA axis hyper-activation, circadian rhythm disruption, and imbalances in neuronal electrical activity. In addition, it supports myelin metabolism, neuroplasticity, and cerebral energy homeostasis.

This makes it suitable for complex states in modern high-stress environments, such as mood instability, sleep-onset difficulties, and reduced attentional capacity.

1) Emotion Stabilization Mechanisms:

Triple-Pathway Intervention in Stress-Induced Neurotransmitter Dysregulation

A. Enhancing Serotonin Synthesis and Transmission

- Core Mechanism - Provides 5-HTP to bypass the competitive transport bottleneck of tryptophan across the blood–brain barrier. With vitamin B6 as a cofactor, 5-HTP is

rapidly converted to 5-HT in the central nervous system, strengthening emotional regulation and reducing sensitivity to negative stimuli.

- Synergistic Factors - Vitamin D enhances TPH2 expression, increasing the initiation rate of 5-HT synthesis; vitamin B12 supports SAMe production, maintaining neurotransmitter methylation activation.
- Applicable Population - Individuals with low mood, stress hypersensitivity, and fatigue-prone emotional disorders.
- Literature Support - Shaw et al., 2002 (Cochrane) - Patrick & Ames, 2014.

Serotonin Synthesis Pathway (5-HTP / B6 / B12 / Vit D)

✓ *Shaw, K., Turner, J., & Del Mar, C. (2002). Tryptophan and 5-hydroxytryptophan for depression. Cochrane Database of Systematic Reviews.*

- Cochrane systematic review supporting the efficacy of 5-HTP in improving mild to moderate depression.

✓ *Birdsall, T. C. (1998). 5-Hydroxytryptophan: a clinically-effective serotonin precursor. Alternative Medicine Review, 3(4), 271–280.*

- Review detailing the physiological conversion pathway of 5-HTP and highlighting its regulatory role in the 5-HT pathway in synergy with B6.

✓ *Patrick, R. P., & Ames, B. N. (2014). Vitamin D and the omega-3 fatty acids control serotonin synthesis and action, part 1: relevance for the pathogenesis of depression. FASEB Journal, 28(2),*

761–781.

- Demonstrates vitamin D's upregulation of TPH2 expression and its importance in 5-HT regulation.

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

- Discusses B12's role in SAMe production, methylation, and neurotransmitter synthesis.

B. Downregulating Chronic HPA Axis Activation to Buffer High-Cortisol States

- Core Mechanism - Ashwagandha has been validated in RCTs to significantly lower cortisol levels under chronic stress, improving impaired HPA axis negative feedback and enhancing physiological stress resilience.
- Systemic Interaction - GABA and cortisol exhibit reciprocal inhibitory regulation; GABA-supporting components (magnesium glycinate, L-Theanine) further lower the stress-response threshold.
- Applicable Population - Individuals in long-term high-pressure environments presenting with anxiety, elevated heart rate, irritability, and insomnia.
- Literature Support - Chandrasekhar et al., 2012 - Lopresti et al., 2019.

HPA Axis Regulation / Cortisol Reduction (Ashwagandha)

✓ *Chandrasekhar, K., Kapoor, J., & Anishetty, S. (2012). A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha root in reducing stress and anxiety in adults. Indian Journal of Psychological*

Medicine, 34(3), 255–262.

- Ashwagandha significantly reduces cortisol levels and improves psychological coping capacity.

✓ *Lopresti, A. L., Smith, S. J., Malvi, H., & Kodgule, R. (2019). An investigation into the stress-relieving and pharmacological actions of an ashwagandha (Withania somnifera) extract: a randomized, double-blind, placebo-controlled study. Medicine, 98(37), e17186.*

- Clinical evidence for Ashwagandha's dual effects on HPA axis modulation and BDNF enhancement.

C. Strengthening GABA Pathway Inhibition to Relieve Neuronal Over-Excitation

- Core Mechanism - Magnesium glycinate exerts dual actions: magnesium ions antagonize NMDA receptor overactivation, reducing glutamate-induced excitotoxicity, while glycine directly activates inhibitory neurons to enhance GABA efficacy.
- Supplementary Support - L-Theanine promotes GABA and dopamine release in the brain, increases alpha-wave activity, and induces a relaxed-yet-alert state. Vitamin B6 acts as a cofactor for the rate-limiting enzyme in GABA synthesis.
- Applicable Population - Individuals with nervous tension, anxiety-prone personalities, daytime over-arousal, or nighttime racing thoughts.
- Literature Support - Boyle et al., 2017 - Nobre et al., 2008.

GABA / Glutamate / NMDA Regulation (Mg / Glycine / L-Theanine)

✓ *Boyle, N. B., Lawton, C., & Dye, L. (2017). The effects of magnesium supplementation on subjective anxiety and stress—a systematic review. Nutrients, 9(5), 429.*

- Systematic review on the effects of magnesium supplementation in anxiety and stress, supporting enhancement of the GABAergic pathway.

✓ *Unno, K., et al. (2013). Theanine intake improves the shortened sleep latency and nocturnal awakening induced by caffeine in rats and humans. Journal of Physiological Anthropology, 32(1).*

- Human and animal studies supporting L-theanine's role in GABA/DA modulation and alpha-wave enhancement.

✓ *Nobre, A. C., Rao, A., & Owen, G. N. (2008). L-theanine, a natural constituent in tea, and its effect on mental state. Asia Pacific Journal of Clinical Nutrition, 17(S1), 167–168.*

- EEG study demonstrating L-theanine's alpha-wave enhancement and improvement of the relaxed–alert state.

2) Sleep Rhythm Mechanisms:

Multi-Point Intervention via Precursor Supply, Neurotransmitter Modulation, and Rhythm Reconstruction

A. Enhancing the Melatonin Pathway to Restore Sleep Onset and Circadian Synchrony

- Core Mechanism - 5-HTP serves as the direct precursor for melatonin, which - assisted by vitamin B6 and vitamin D - is converted via AANAT and HIOMT into melatonin. This pathway is particularly crucial for "emotion-related insomnia" and "delayed sleep phase-type insomnia."

- Synergistic Pathways - Ashwagandha lowers nocturnal cortisol activation, preventing its inhibitory effect on melatonin synthesis; vitamin D also attenuates immune-activation-related wakefulness.
- Applicable Population - Individuals with insomnia triggered by mood fluctuations, irregular sleep schedules, or frequent time-zone shifts.
- Literature Support - Hartmann, 1982 - Muscogiuri et al., 2017 - Langade et al., 2019.

B. Shortening Sleep Latency and Improving Deep-Sleep Efficiency

- Core Mechanism - Strengthening the GABAergic pathway is central to initiating sleep. Magnesium glycinate reduces neuronal excitability and enhances inhibitory neural activity; L-Theanine raises GABA/5-HT levels, inducing a natural “relaxed but not sedated” sleep onset.
- Clinical Observations - Magnesium glycinate shortens sleep latency and improves subjective sleep scores; L-Theanine increases deep-sleep proportion and reduces nocturnal awakenings.
- Applicable Population - Individuals with prolonged sleep onset, overactive nighttime cognition, or frequent nocturnal awakenings.
- Literature Support - Abbasi et al., 2012 - Unno et al., 2013.

C. Repairing Nocturnal Neuro - Endocrine Activation Peaks to Reduce Early-Morning Awakening

- Core Mechanism - Ashwagandha helps correct “circadian rhythm” dysregulation of the HPA axis, re-establishing the night-suppressed, morning-activated dynamic pattern, thus reducing early awakening and shallow-sleep episodes.
- Interactive Pathway - Supports nocturnal synaptic restoration via BDNF, enhancing the brain’s nighttime repair capacity.
- Applicable Population - Individuals experiencing middle-of-the-night awakenings, early-morning waking, or poor restorative sleep.
- Literature Support - Lopresti et al., 2019 - Langade et al., 2019.

✓ *Hartmann, E. (1982). Effects of L-tryptophan and 5-hydroxytryptophan on sleep in humans. Advances in Biochemical Psychopharmacology, 34, 187–198.*

- Early research showing 5-HTP’s ability to shorten sleep latency and increase deep-sleep proportion.

✓ *Langade, D., et al. (2019). Clinical evaluation of the safety and efficacy of Ashwagandha root extract in insomnia and anxiety: A double-blind, randomized, placebo-controlled study. Cureus, 11(9), e5797.*

- Ashwagandha improves both subjective and objective sleep quality and reduces nocturnal awakenings.

✓ *Muscogiuri, G., et al. (2017). Vitamin D and sleep regulation: Is there a role for vitamin D? Current Pharmaceutical Design, 23(32), 2490–2494.*

- Review study on vitamin D’s role in sleep rhythm regulation and its relationship to insomnia.

3) Cognitive Support Mechanisms:

Tri-Pathway Restoration of Brain Performance via Signal Transmission, Metabolism, and Plasticity

A. Promoting Alpha-Wave Generation to Improve Attentional Stability and Working Memory

- Core Mechanism - L-Theanine has been shown via EEG to significantly increase alpha-wave activity (8–13 Hz), fostering a simultaneous state of relaxation and focus, which supports attentional engagement and cognitive load management.
- Neurofunctional Significance - Elevated alpha-wave activity is considered a prerequisite neural condition for achieving optimal attention and memory performance.
- Applicable Population - Individuals with distractibility, mental drift, or difficulty initiating focused work/study.
- Literature Support - Nobre et al., 2008 - Unno et al., 2013.

B. Maintaining Myelin Structure and Stability of Neural Signal Transmission

- Core Mechanism - Vitamin B12 is essential for myelin synthesis, while vitamin B1 acts as a coenzyme in key glucose-metabolism enzymes, together ensuring stable axonal signal conduction and rapid neural responsiveness.

- Risk Groups - Vegetarians, older adults, and high mental workload populations frequently present with suboptimal B-vitamin metabolism or bioavailability.
- Applicable Population - Individuals experiencing brain fog, slowed reaction time, or significant fatigue during prolonged concentration.
- Literature Support - Reynolds, 2006 - Benton et al., 1995.

C. Enhancing Neuroplasticity and Learning Pathway Adaptation

- Core Mechanism - Ashwagandha elevates brain-derived neurotrophic factor (BDNF), promoting synaptic remodeling and memory-pathway reorganization, aiding cognitive recovery and long-term memory consolidation.
- Synergistic Support - Vitamin B12 contributes to SAMe synthesis, boosting neurotransmitter methylation activity and enhancing synaptic responsiveness.
- Applicable Population - Individuals with low learning efficiency, reduced cognitive flexibility, or stress-related learning impairments.
- Literature Support - Lopresti et al., 2019 - O'Leary & Samman, 2010.

✓ *Benton, D., Griffiths, R., & Haller, J. (1995). Thiamine supplementation mood and cognitive functioning. Psychopharmacology, 117(3), 313–320.*

- Thiamine supplementation improves attentional stability and recovery from mental fatigue.

✓ *Reynolds, E. (2006). Vitamin B12, folic acid, and the nervous system. The Lancet Neurology, 5(11), 949–960.*

- Explores the effects of B12 deficiency on cognition, mood, and neural transmission.

III Keyora MoodFlow 8 in 1 and Depression Intervention

Intervening through the "Neuro-Endocrine-Rhythm" tri-axis to restore the biological foundation of emotional stability

Depressive states are not solely the result of a single neurotransmitter deficiency; rather, they represent a complex neuro-regulatory disorder involving multiple dimensions: insufficient serotonin synthesis, impaired excitatory-inhibitory balance in the CNS, chronic stress-driven endocrine activation, and compromised neuroplasticity.

Keyora MoodFlow 8 in 1 targets five key pathological pathways in depression, delivering multi-nutrient, evidence-based support through its eight active components.

1) Targeting 5-HT Pathway Dysfunction

- Bypassing the Tryptophan Bottleneck to Enhance Central Serotonin Activity

Core Formula: 5-HTP + Vitamin B6 + Vitamin D

- In depression, the tryptophan-to-serotonin conversion pathway is often compromised, especially under high-cortisol states where competitive transport across the blood–brain barrier limits tryptophan entry into the CNS.
- 5-HTP directly crosses the blood–brain barrier independent of competitive transport mechanisms, providing an immediate precursor for central serotonin synthesis.

- Vitamin B6 is the essential coenzyme for aromatic L-amino acid decarboxylase, which converts 5-HTP to 5-HT; deficiency leads to precursor accumulation with reduced functional output.
- Vitamin D upregulates TPH2 expression, enhancing the CNS's capacity to synthesize 5-HT, while also mitigating risk for seasonal affective depression associated with low sunlight exposure.

Applicable Symptoms: Low mood, anhedonia, morning symptom worsening, blunted emotional reactivity.

2) **Attenuating Chronic Stress Drive**

- Suppressing HPA Axis Overactivation and Cortisol-Related Symptoms

Core Formula: Ashwagandha + Magnesium Glycinate

- Chronic activation of the HPA axis underlies many depressive phenotypes, including early-morning awakening, irritability, weight loss, and decreased libido.
- Ashwagandha is one of the most extensively studied botanical adaptogens. Standardized extracts have been shown in multiple double-blind RCTs to reduce baseline cortisol by 22-30% and to alleviate anxiety, mood instability, and stress-related symptoms.
- Magnesium glycinate contributes from a neuro-electrical modulation angle: Mg^{2+} antagonizes NMDA receptors, reducing glutamate-induced excitotoxicity, while

glycine acts as an inhibitory neurotransmitter within the GABA pathway, strengthening stress-buffering capacity.

Applicable Symptoms: Anxiety with depression, sleep initiation difficulty, irritability, HPA axis dysregulation.

3) Restoring Neurotransmitter Balance

- Enhancing GABA and Dopamine Activity to Reduce Irritability and Fatigue

Core Formula: L-Theanine + Magnesium Glycinate + Vitamin B6

- Depressive states often feature diminished GABA and dopamine system activity, leading to tension, irritability, attentional deficits, and fatigue.
- L-Theanine crosses the blood–brain barrier and significantly increases alpha-wave activity (as shown in EEG studies), while promoting the release of GABA, dopamine, and serotonin, creating a relaxed-yet-alert mental state.
- Vitamin B6 is an essential cofactor for rate-limiting enzymes in GABA (GAD) and dopamine (DDC) synthesis, determining neurotransmitter functional activity.
- Magnesium glycinate complements this effect by modulating inhibitory–excitatory balance, reinforcing overall neurotransmitter homeostasis.

Applicable Symptoms: Nervous sensitivity, restlessness, inability to sustain attention, brain fog.

4) Supporting Neuroplasticity and Myelin Repair

- Improving Cognitive Slowing and Emotional Recovery

Core Formula: Ashwagandha + Vitamin B12 Metabolic Support

- Depression is often associated with reduced neuroplasticity and inadequate BDNF expression, impairing the brain's capacity for emotional adaptation.
- Ashwagandha has been shown to increase BDNF expression, promoting synaptic plasticity recovery and long-term memory consolidation, as well as improving learning-emotion adaptability.
- Vitamin B12 is central to SAMe synthesis, enabling neurotransmitter methylation (e.g., 5-HT, DA) and myelin repair, preventing conduction delays that lead to suboptimal cognitive function.
- Particularly beneficial for cognitive-decline-related depression or fatigue-dominant phenotypes.

Applicable Symptoms: Slowed thinking, delayed responses, poor learning efficiency, cognitive impairment, mild brain fog.

5) Synchronizing Sleep-Mood Rhythms

- Addressing Mood-Sensitive Insomnia and Circadian Disruption

Core Formula: 5-HTP + Vitamin B6 + Ashwagandha + Vitamin D

- Depression and insomnia often have a bidirectional relationship. In cases characterized by sleep initiation difficulty or early-morning awakening, disruptions in hormonal rhythms (5-HT-melatonin pathway) and nocturnal cortisol elevation are common contributors.
- 5-HTP supplementation provides substrate for melatonin synthesis; B6 optimizes the conversion; Vitamin D modulates circadian-related enzymes (TPH2, AANAT).
- Ashwagandha helps blunt nocturnal cortisol surges, reducing early awakenings and "rhythm-type mood disturbances."

Applicable Symptoms: Difficulty falling asleep, early-morning awakening, morning mood deterioration.

6) Clinical Consensus

- Nutritional Psychiatry Perspectives on Depression Management

Recent clinical consensus in functional medicine and nutritional psychiatry emphasizes that depression is a multi-axis imbalance involving the neuro-endocrine-immune-circadian-metabolic systems.

While pharmacological therapy can relieve symptoms, in mild-to-moderate functional depression, cases of drug intolerance, cognitive-predominant depression, or suboptimal mood regulation, multi-nutrient interventions are considered a safer and more sustainable approach.

Key insights:

- **5-HTP + B6** is among the most direct strategies to bypass tryptophan metabolic bottlenecks and raise serotonin levels, particularly effective in morning-worsening and slow-reacting depression.
- Ashwagandha is the most well-documented non-pharmaceutical HPA axis modulator, suitable for stress-induced or anxiety–depression mixed types.
- Magnesium glycinate + L-Theanine synergy is increasingly applied to regulate central electrical activity and GABA-glutamate balance, benefiting high cognitive-load and tension-prone depression.
- B12, B6, and Vitamin D combination is viewed in functional medicine as a triple-support strategy for neurotransmitter metabolism, neuro-repair, and inflammation control - especially useful in cognitive-type or circadian-disrupted depression.

Keyora MoodFlow 8 in 1 *integrates all five of these strategies, covering neurotransmitter metabolism, cortisol regulation, circadian restoration, neuro-electrical stability, and neuroplasticity rebuilding.*

A. Pathophysiological Consensus on Depression:

The Tri-Axial Dysregulation of Neurotransmission, Endocrine, and Circadian Systems

Contemporary research in psychiatry and functional medicine has reached a consensus that depression is not merely a result of serotonin deficiency, but rather a multifaceted neuro-regulatory disorder involving dysregulation across three major axes:

- Neurotransmitter metabolic imbalance - Disrupted synthesis, conversion, or signal transmission of serotonin (5-HT), dopamine (DA), norepinephrine (NE), and GABA.
- Chronic HPA axis hyper-activation - Persistent cortisol elevation under chronic stress impairs central emotional regulation and destabilizes neurotransmitter homeostasis.
- Neuroplasticity impairment - Reduced expression of BDNF compromises synaptic connectivity and hampers emotional resilience and adaptability.
- Circadian rhythm disruption - Interactions between dysregulated diurnal rhythms and 5-HT–melatonin signaling pathways result in symptom patterns such as “morning worst” or “nocturnal awakenings.”
- Neuro-inflammation and metabolic interference - Elevated homocysteine levels and brain energy deficits further impair neural function.

This multi-dimensional model forms the current clinical consensus on the etiology of depression and highlights the necessity for integrative nutritional support beyond pharmacological treatment.

B. Nutritional Psychiatry Consensus:

Five Non-Pharmacological Intervention Strategies

a) **5-HTP + B6 + Vitamin D** as the “Golden Pathway” for Enhancing Central Serotonin

- Cochrane reviews identify 5-HTP as an effective adjunct in mild-to-moderate depression.
- Vitamin B6 is the rate-limiting cofactor for 5-HTP decarboxylation into active 5-HT.
- Vitamin D enhances TPH2 expression, promoting central 5-HT synthesis - especially valuable in seasonal and sunlight-deficient depression.

This tri-nutrient approach is among the most recognized strategies in nutritional neurotransmitter interventions.

b) **Ashwagandha:** The Most Clinically Validated Adaptogen for HPA Axis Regulation

- Multiple RCTs confirm its ability to lower baseline cortisol levels by 20-30% and alleviate stress-induced mood disturbances.
- Its mechanism is non-sedative and suitable for co-administration with pharmaceuticals.

Particularly beneficial for stress-induced, mixed anxiety-depression presentations or SSRI non-responders.

c) **Non-Sedative Modulation of GABA and NMDA Pathways**

- Magnesium is a natural NMDA receptor antagonist that attenuates glutamate-induced excitotoxicity.

- L-Theanine enhances alpha-wave activity and promotes GABA and DA release, supporting a “relaxed yet alert” mental state.

This pathway is well-suited to neuro-sensitive or mentally fatigued individuals with depressive tendencies.

d) **B12 and SAMe Support** as Key Interventions for Cognitive-Type Depression

- B12 deficiency - prevalent among vegetarians and older adults - impairs neurotransmitter methylation.
- B12 is essential for SAMe synthesis, which maintains dopaminergic/noradrenergic activation and myelin integrity.

Clinical guidelines recommend B12 supplementation in cognition-dominant or brain-fog depression.

e) **Neurotransmitter-Circadian Dual-Pathway Modulation as a Treatment Trend**

- Depression coexists with sleep disturbances in up to 70% of cases, making rhythm regulation a critical target.
- 5-HTP serves as the precursor to melatonin; B6 and D facilitate its rhythmic conversion.
- Ashwagandha mitigates nocturnal cortisol spikes, addressing early waking and night-time arousals.

The integrated modulation of "5-HT + Melatonin + HPA" is regarded as a central model for circadian-type depression recovery.

C. Positioning and Recommended Target Populations for Keyora MoodFlow 8 in 1

Keyora MoodFlow 8 in 1 embodies the five major non-pharmacological strategies outlined above, delivering a structurally complete nutritional system from ingredient pairing to mechanistic targeting:

- Provides a full 3-factor serotonin synthesis triad (5-HTP + B6 + Vitamin D).
- Includes RCT-backed HPA suppressor - Ashwagandha.
- Combines dual-action neurotransmitter modulation agents (magnesium glycinate + L-Theanine).
- Reinforces the B12-SAMe-myelin repair axis for cognitive support.
- Constructs a closed-loop sleep–mood–circadian regulation system for functional rhythm recovery.

Recommended Target Populations:

- Individuals with mild to moderate depression, mood swings, or subclinical emotional instability.
- Patients undergoing psychotropic tapering or medication discontinuation.
- Individuals experiencing comorbid sleep disturbances and mood symptoms.

- High cognitive demand individuals, students, or those with anxiety-prone temperaments.
- Vegetarians and elderly populations requiring neurotransmitter support.

7) Summary Table - Keyora MoodFlow 8 in 1 in Depression Intervention

Intervention Pathway	Core Nutrient Combination	Applicable Depression Subtype
5-HT Deficiency Supplementation	5-HTP + B6 + Vitamin D	Low-mood type, post-medication tapering
HPA Axis Cortisol Reduction	Ashwagandha + Magnesium Glycinate	Stress-induced, anxiety-associated
GABA-Dopamine Stabilization	L-Theanine + Magnesium + B6	Tension-prone, fatigue/brain-fog type
Neuroplasticity & Myelin Repair	Ashwagandha + B12	Cognitive-decline type, elderly depression
Mood–Sleep Rhythm Synergy	5-HTP + B6 + Vitamin D + Ashwagandha	Circadian-disrupted, morning-worsening

✓ *Shaw, K., Turner, J., & Del Mar, C. (2002). Tryptophan and 5-hydroxytryptophan for depression. Cochrane Database of Systematic Reviews.*

- Cochrane systematic review – supports the efficacy of 5-HTP in improving mild to moderate depression.

✓ *Patrick, R. P., & Ames, B. N. (2014). Vitamin D and the omega-3 fatty acids control serotonin synthesis and action, part 1: relevance for the pathogenesis of depression. FASEB Journal, 28(2), 761–781.*

- Demonstrates that vitamin D enhances central 5-HT synthesis by upregulating TPH2 expression.

✓ *Birdsall, T. C. (1998). 5-Hydroxytryptophan: a clinically-effective serotonin precursor. Alternative Medicine Review, 3(4), 271–280.*

- Reviews the physiological conversion pathway of 5-HTP and emphasizes the importance of its synergy with B6 in improving depression.

✓ *Chandrasekhar, K., Kapoor, J., & Anishetty, S. (2012). A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha root in reducing stress and anxiety in adults. Indian Journal of Psychological Medicine, 34(3), 255–262.*

- Clinical study shows Ashwagandha significantly reduces cortisol and alleviates anxiety.

✓ *Boyle, N. B., Lawton, C., & Dye, L. (2017). The effects of magnesium supplementation on subjective anxiety and stress—a systematic review. Nutrients, 9(5), 429.*

- Systematic review confirms magnesium supplementation relieves anxiety and stress-related symptoms.

✓ *Nobre, A. C., Rao, A., & Owen, G. N. (2008). L-theanine, a natural constituent in tea, and its effect on mental state. Asia Pacific Journal of Clinical Nutrition, 17(S1), 167–168.*

- EEG studies show L-theanine enhances alpha wave activity and promotes a relaxed yet alert state.

✓ *Reynolds, E. (2006). Vitamin B12, folic acid, and the nervous system. The Lancet Neurology, 5(11), 949–960.*

- Explores the impact of vitamin B12 deficiency on cognitive and emotional function, highlighting its neuro-supportive role.

IV Keyora MoodFlow 8 in 1 and Anxiety Intervention

Targeting the "Excitation-Inhibition-Stress" Axis to Alleviate Tension and Neuro-Overactivation

The neurobiological underpinnings of anxiety often involve imbalances in the GABAergic system, elevated cortisol levels, overactivation of central norepinephrine (NE) and glutamate (Glu) pathways, and dysregulated neurotransmitter conversion.

Keyora MoodFlow 8 in 1 formulates eight synergistic nutrients to address the core neural circuits of anxiety - establishing a balance between central excitation and inhibition, dampening both acute and chronic stress responses, and optimizing neurotransmitter turnover efficiency.

1) Enhancing GABAergic Activity and Inhibitory Neurotransmission

Goal: Stabilize Hyperactive Neural States

Core Ingredients: Magnesium Glycinate + L-Theanine + Vitamin B6

- Anxiety is commonly accompanied by impaired GABA function, manifesting as lowered neural excitation thresholds, distractibility, and persistent mental agitation.
- Magnesium glycinate suppresses NMDA receptor activity via Mg^{2+}, mitigating glutamate-induced excitotoxicity, while glycine itself acts as an inhibitory neurotransmitter supporting GABA signaling.
- L-Theanine, as demonstrated by EEG studies, increases alpha wave activity—promoting a relaxed yet alert neural state—while modulating central GABA and dopamine levels to relieve tension.
- Vitamin B6 functions as a coenzyme for glutamate decarboxylase (GAD), essential for GABA synthesis; its deficiency may increase anxiety susceptibility.

Applicable Symptoms: Irritability, inability to relax, difficulty initiating sleep, mental restlessness, exaggerated psychological reactivity.

2) Buffering HPA Axis Hyperactivity

Goal: Reduce Cortisol Peaks and Stress-Driven Anxiety

Core Ingredients: Ashwagandha + Magnesium Glycinate

- Individuals with chronic anxiety often exhibit HPA axis dysregulation, including elevated cortisol and disrupted circadian patterns, manifesting as morning palpitations, agitation, and hypervigilance.

- Ashwagandha, a clinically validated adaptogen, has been shown in multiple RCTs to significantly reduce cortisol levels, improve stress resilience, and alleviate generalized anxiety symptoms.
- Magnesium glycinate complements this effect by modulating ion channel activity to blunt sympathetic overactivation, thereby dampening physiologic hyperarousal.

Applicable Symptoms: Morning anxiety, persistent inner tension, mood lability, social anxiety, emotional collapse under chronic stress.

3) Improving Neurotransmitter Synthesis and Conversion

Goal: Support Balanced 5-HT and NE Activity

Core Ingredients: 5-HTP + Vitamin B6 + Vitamin D

- Symptoms such as chronic worry and anticipatory anxiety are often linked to central serotonin (5-HT) deficiency.
- 5-HTP bypasses peripheral tryptophan competition, directly contributing to brain 5-HT synthesis.
- Vitamin B6 is a coenzyme not only for 5-HTP → 5-HT but also for dopamine → norepinephrine conversion, playing a dual role in emotional regulation and sympathetic tone.
- Vitamin D upregulates TPH2 expression, enhancing endogenous serotonin production and mitigating neuro-inflammation-driven anxiety.

Applicable Symptoms: Chronic emotional tension, excessive worry, overthinking before sleep, sympathetic-dominant insomnia.

4) Correcting Anxiety-Associated Sleep Dysregulation

Goal: Integrate Neural Relaxation with Hormonal Rhythm Restoration

Core Ingredients: 5-HTP + Ashwagandha + Magnesium Glycinate

- Anxiety is frequently accompanied by difficulty falling asleep, fragmented sleep, and shallow sleep, largely due to nocturnal cortisol spikes and disrupted melatonin synthesis.
- 5-HTP serves as a direct precursor to melatonin, and with B6 cofactor support, promotes circadian regulation and nighttime relaxation.
- Ashwagandha has demonstrated in RCTs the ability to improve both subjective and objective sleep parameters by alleviating stress-induced arousals.
- Magnesium glycinate stabilizes neuronal excitability and supports GABA signaling, thereby reducing sleep latency.

Applicable Symptoms: Delayed sleep onset, frequent nocturnal awakenings, vivid dreaming, early morning anxiety with tachycardia.

5) Clinical Consensus:

Keyora MoodFlow 8 in 1 as a Systemic Nutritional Strategy for Anxiety

A. Pathophysiological Consensus:

The GABA-HPA-Neurotransmitter Tri-Axis Dysfunction Model

Current evidence in functional medicine and nutritional psychiatry recognizes anxiety not as a mere psychological stress response but as a chronic neuro-functional disorder involving systemic interplay. The key pathophysiological axes include:

- GABA and Glutamate Imbalance: Impaired inhibitory control leads to excessive cortical excitability, reflected in hypervigilance, sleep-onset issues, and cognitive overstimulation.
- Chronic HPA Axis Activation: Persistent sympathetic tension disrupts cortisol circadian rhythms, contributing to mood swings, morning anxiety, and irritability.
- Deficits in Neurotransmitter Synthesis and Conversion: Insufficient 5-HT, NE, and DA availability or impaired turnover compromises emotional stability and stress adaptability.

Additional features often include reduced alpha wave activity, unstable EEG profiles, impaired neuroplasticity, and diminished attentional control. These highlight the need for anxiety interventions to target the inhibition-excitation-stress axis, while simultaneously restoring neurotransmitter balance and circadian rhythm.

B. B. Nutritional Psychiatry Consensus:

Five Core Mechanisms for Nutritional Intervention in Anxiety

a) Enhancing GABA Function for Inhibitory-Excitatory Balance

- GABA downregulation and glutamate upregulation are key drivers of neural hyperexcitability in anxiety.
- Magnesium Glycinate offers a dual mechanism: NMDA antagonism via Mg^{2+} and glycine-mediated GABA potentiation.
- L-Theanine enhances alpha wave activity, promoting relaxation without sedation.
- Vitamin B6 ensures sustained GABA biosynthesis.

→ Recommended for: "inability to relax," "sensory-overload type anxiety"

b) Modulating the HPA Axis to Buffer Chronic Stress Load

- Conditions such as GAD, social anxiety, and nighttime palpitations are linked to cortisol rhythm disruption.
- Ashwagandha reduces cortisol without sedation and restores circadian balance.
- Magnesium Glycinate stabilizes neuronal reactivity under sympathetic activation.

→ Especially useful for: "morning anxiety," "stress reactivity amplification," "tension-type GI symptoms"

c) Optimizing Neurotransmitter Synthesis for Emotional Resilience

- Traditional tryptophan metabolism may falter under high cortisol; 5-HTP bypasses this limitation.

- Vitamin B6 also supports DA→NE conversion, modulating sympathetic output.
- Vitamin D enhances TPH2-mediated 5-HT biosynthesis.

→ Beneficial for: "anxiety with depressive traits," "drug-sensitive anxious individuals"

d) Addressing Anxiety-Linked Sleep and Circadian Disturbances

- Symptoms include delayed sleep onset, fragmented sleep, and excessive dreaming.
- 5-HTP + B6 reinforce melatonin biosynthesis and circadian regulation.
- Ashwagandha + Magnesium reduce nighttime cortisol and hyperarousal.

→ Enables a full "pre-sleep relaxation circuit," a non-pharmacological cornerstone of rhythm stabilization.

e) Supporting Cognitive Function and Stress Regulation

- Chronic anxiety impairs attention, decision-making, and mental processing speed.
- Vitamin B12 supports myelin repair, neurotransmission, and SAMe synthesis for dopaminergic methylation.
- L-Theanine improves focus and cognitive flexibility under pressure.

→ Recommended for: "anxiety with mental fatigue," "neurocognitive-deficit–type anxiety"

C. Targeted Positioning of Keyora MoodFlow 8 in 1 in Anxiety Management

With its precisely calibrated blend of eight neuro-supportive nutrients, **Keyora MoodFlow 8 in 1** effectively addresses all five core pathophysiological domains of anxiety:

- Non-sedative GABA pathway modulation for safe use during daytime hours
- Full-spectrum neurotransmitter support, balancing inhibition and excitation alongside NE/5-HT regulation
- Clinically validated adaptogen (Ashwagandha) for long-term stress response modulation
- Sleep-emotion-circadian axis integration, interrupting the "insomnia-anxiety-fatigue" cycle
- Non-dependent, gentle formula, suitable during medication tapering, emotional sub-health, and daily neuro-care

D. Recommended Target Populations

- Individuals with persistent mental tension or high cognitive workload
- Morning anxiety or social performance anxiety subtypes
- Rumination and excessive worry before bedtime
- Patients undergoing psychiatric medication reduction or discontinuation
- Individuals with irritability, attention deficits, and sympathetic overactivation
- Women experiencing Perimenopausal fluctuations in anxiety, sleep, and neural regulation

6) Summary Table: Keyora MoodFlow 8 in 1 in Anxiety Intervention

Intervention Axis	Core Ingredients	Applicable Anxiety Subtypes
GABA Enhancement / NMDA Inhibition	Magnesium Glycinate + L-Theanine + B6	Neuro-irritable, attention-distractible types
HPA Axis Modulation / Anti-Stress Support	Ashwagandha + Magnesium Glycinate	Chronic stress, morning-anxiety subtypes
Serotonin-Norepinephrine Regulation	5-HTP + B6 + Vitamin D	Generalized anxiety, ruminative insomnia
Circadian-Sleep-Anxiety Axis Support	5-HTP + Ashwagandha + Magnesium Glycinate	Nocturnal anxiety, sleep-fragmentation profiles

- ✓ *Chandrasekhar, K., Kapoor, J., & Anishetty, S. (2012) A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha root in reducing stress and anxiety in adults. Indian Journal of Psychological Medicine, 34(3), 255–262*

  - RCT double-blind trial — Demonstrated that Ashwagandha (Withania somnifera) significantly reduced cortisol levels and alleviated anxiety scores.

- ✓ *Liao, J., et al. (2022) The anxiolytic effects of L-theanine on clinical anxiety and stress: A systematic review and meta-analysis. Nutrients, 14(7), 1526*

- Systematic review and meta-analysis — Confirmed the significant anxiolytic effects of L-theanine, particularly beneficial for individuals under psychological stress and high-pressure conditions.

✓ *Boyle, N. B., Lawton, C., & Dye, L. (2017) The effects of magnesium supplementation on subjective anxiety and stress: A systematic review. Nutrients, 9(5), 429*

- Systematic review — Found that magnesium supplementation effectively reduced subjective anxiety, tension, and physiological stress responses.

✓ *Birdsall, T. C. (1998) 5-Hydroxytryptophan: a clinically-effective serotonin precursor. Alternative Medicine Review, 3(4), 271–280*

- Overview study — Summarized the mechanisms and foundational rationale for using 5-HTP in anxiety management, emphasizing its role in rapidly replenishing serotonin.

✓ *Hidese, S., et al. (2019) Effects of chronic L-theanine administration in patients with major depressive disorder: An open-label study. Acta Neuropsychiatrica, 31(2), 72–79*

- Clinical trial — Demonstrated that L-theanine improved both anxiety and cognitive impairment, as evidenced by enhanced attention and increased alpha wave activity.

✓ *Rao, T. S., Asha, M. R., Ramesh, B. N., & Jagannatha Rao, K. S. (2008) Understanding nutrition, depression and mental illnesses. Indian Journal of Psychiatry, 50(2), 77–82*

- Review on nutritional psychiatry — Discussed the integrative roles of B-vitamins, magnesium, and 5-HTP in the regulation of anxiety and mood states.

✓ *Morris, G., & Maes, M. (2014) A neuro-immune model of depression and its subtypes: implications for immune-nutritional interventions. Current Opinion in Psychiatry, 27(5), 289–296*

- Proposed the neuro–immune–neurotransmitter axis model — Highlighted the combined

importance of HPA axis modulation and nutritional interventions in managing anxiety and depression comorbidity.

V Keyora MoodFlow 8 in 1 and Insomnia Intervention

A non-pharmacological sleep restoration system targeting the tri-axis of neuro-transmitters-circadian rhythm-stress

Insomnia is no longer regarded as an isolated sleep disorder, but rather a complex state involving disruptions in neurotransmitter homeostasis, circadian rhythm dysregulation, elevated cortisol levels, sustained cognitive hyperarousal, and imbalanced neuro-electrical activity.

In the context of anxiety, depression, stress overload, and heightened neural excitability, symptoms such as sleep-onset difficulties, frequent nighttime awakenings, and early-morning arousals often co-occur, forming a self-perpetuating loop of “sleep-emotion-cognition axis dysregulation.”

Keyora MoodFlow 8 in 1 addresses five biological pathways that underlie the onset and maintenance of insomnia through a multi-targeted approach.

It offers a scientifically formulated nutritional system that synergistically supports neurotransmitter activation, HPA axis modulation, GABA balance, melatonin precursor supplementation, and stabilization of neuro-electrical activity - ensuring efficacy, safety, and reliability.

1) **Activating the Melatonin Synthesis Pathway:**

Enhancing the circadian conversion of 5-HTP into melatonin

Core formulation: 5-HTP + Vitamin B6 + Vitamin D

- The melatonin pathway follows the sequence: tryptophan → 5-HT → N-acetyl-5-HT → melatonin, with 5-HTP being the most efficient precursor for central synthesis.
- In states of depression or high cortisol, tryptophan is shunted toward the kynurenine pathway via IDO, reducing 5-HTP availability.
- 5-HTP crosses the blood–brain barrier without competing for tryptophan transport, entering directly into the central synthesis route.
- Vitamin B6 serves as a coenzyme for aromatic L-amino acid decarboxylase, a rate-limiting enzyme for 5-HTP → 5-HT conversion.
- Vitamin D upregulates TPH2 and AANAT, enhancing both serotonin and melatonin synthesis at key enzymatic steps.

This forms the "5-HTP–B6–VD axis" for circadian sleep initiation.

Applicable symptoms: sleep-onset difficulties, nighttime awakenings, circadian misalignment, emotionally agitated nocturnal insomnia.

2) **Stabilizing Neuro-electrical Activity:**

Mitigating excessive neural excitability

Core formulation: Magnesium Glycinate + L-Theanine

- EEG studies show insomniacs often exhibit altered alpha–delta wave ratios and hyperactive brainwave activity.
- Magnesium glycinate acts as a dual-function NMDA antagonist and GABA activator:
- Magnesium antagonizes NMDA receptors, reducing glutamate-induced excitotoxicity.
- Glycine serves as an inhibitory neurotransmitter, supporting GABA-A receptor activation and neural calmness.
- L-Theanine increases alpha-wave activity (relaxed wakefulness) and enhances GABA and serotonin co-release.

This non-sedative combination supports neuro-electrical balance and is ideal for hypersensitive neural types.

Applicable symptoms: pre-sleep mental overactivation, difficulty relaxing, heightened sensory reactivity (e.g., racing heart, muscle tension).

3) **Regulating HPA Axis Activation Rhythms:**

Reducing nighttime cortisol surges that cause early awakenings

Core formulation: Ashwagandha + Magnesium Glycinate

- Early-morning awakenings and difficulty returning to sleep are often due to nocturnal cortisol surges.

- Ashwagandha is the only adapt-ogenic plant validated in multiple RCTs to reduce nighttime cortisol peaks.
- Particularly effective for “anxious nocturnal insomnia” and “morning agitation upon awakening.”
- Magnesium glycinate further reduces sympathetic arousal thresholds, enhancing nocturnal inhibitory tone.

This constructs a regulatory loop for the “nighttime-cortisol-GABA axis.”

Applicable symptoms: early awakenings, fragmented sleep, vivid dreams, accompanied by morning anxiety or mood instability.

4) **Maintaining Circadian Synchrony:**

Supporting natural melatonin production and hormonal transitions

Core formulation: 5-HTP + Vitamin D + Ashwagandha

- Vitamin D enhances expression of circadian clock genes in the SCN (suprachiasmatic nucleus), increasing light sensitivity.
- It also regulates TPH2 and AANAT expression, facilitating synchronized serotonin–melatonin biosynthesis.
- Ashwagandha supports circadian rhythm genes (e.g., Clock, BMAL) and coordinates neuroendocrine rhythm alignment.

This reconstructs the "5-HT–melatonin–cortisol" circadian transition mechanism.

Applicable symptoms: circadian reversal, sleep–wake misalignment, post-travel or night-shift rhythm disruption.

5) **Alleviating Emotion-Driven Insomnia:**

Enhancing mood stabilization and sleep restorative quality

Core formulation: 5-HTP + B6 + Vitamin D + Ashwagandha

- Emotional insomnia typically presents as "pre-sleep emotional intensification" and ruminative recall–worry cycles.
- 5-HTP enhances emotional stability by increasing serotonin availability, reducing nighttime negative rumination.
- Vitamin D modulates neuro-inflammation and immune rhythms, improving sleep quality under emotional burden.
- Ashwagandha provides axis-wide support (mood–rhythm–stress), ideal for emotion-related sleep disturbances.

This builds an integrated "emotion–neural–sleep" axis for long-term regulation.

Applicable symptoms: emotionally activated pre-sleep states, morning-worsened insomnia, and mood-triggered night awakenings.

6) Clinical Consensus: The Systemic Nutritional Approach of Keyora MoodFlow 8 in 1 for Insomnia

A. Modern Medical Consensus:

Insomnia as a Multi-Axial Neurological Dysregulation

Sleep medicine, nutritional psychiatry, and functional medicine now converge on a shared understanding:

Insomnia is not merely “difficulty falling asleep” or “light sleep” but a chronic dysfunction involving neuroendocrine and circadian desynchrony. Key pathological pathways include:

- Impaired melatonin synthesis: due to 5-HTP and B6 deficiency or reduced TPH2/AANAT expression, weakening circadian sleep signals.
- Neurotransmitter imbalances: low GABA and excessive glutamatergic activity keep the brain in a hyper-alert state.
- Nocturnal HPA axis overactivation: leads to early waking, fragmented sleep, and dream proliferation.
- Clock gene dysregulation: results in circadian desynchronization via the SCN–melatonin–cortisol axis.
- Persistent emotional arousal: under anxiety/depression, keeps the "cognitive–alertness" circuit active at night.

This explains the paradigm shift from sedative-focused to multi-axis modulation strategies and underscores the need for integrative nutritional designs targeting the neurotransmitter-circadian-stress triad.

B. Nutritional Intervention Consensus:

Building a non-dependent, low-side-effect, circadian-synergistic support system

While pharmacological agents (e.g., benzodiazepines, antidepressants) offer short-term relief, long-term side effects and dependency risks have fueled a clinical shift toward nutrient-based, non-pharmacological interventions.

Widely recognized mechanisms include:

a) Melatonin precursor synthesis (5-HTP + B6 + VD) for initiating sleep and circadian alignment.

b) Non-sedative GABA enhancement (Magnesium Glycinate + L-Theanine) to calm hypersensitive neural activation.

c) Nocturnal cortisol reduction (Ashwagandha) to restore low-stress nighttime windows.

d) Clock gene and SCN activity support (via Vitamin D) to synchronize light perception with hormonal rhythms.

e) Emotion-linked insomnia pathway modulation through the 5-HTP–mood–rhythm axis to ease cognitive-emotional overactivation.

This integrated approach has been validated in functional medicine, CBT-I (Cognitive Behavioral Therapy for Insomnia), and chronic fatigue syndrome protocols.

C. Systemic Nutritional Positioning and Advantages of Keyora MoodFlow 8 in 1

Keyora MoodFlow 8 in 1 is anchored in tri-axis intervention (rhythm-neurotransmitter-stress), using high-bioavailability, clinically validated neuro-regulatory nutrients. It offers:

- A three-step melatonin synthesis scaffold: precursor (5-HTP) + coenzyme (B6) + gene expression support (VD)
- A non-sedative neuro-relaxation strategy via electrophysiology and neurotransmitter co-modulation
- Inclusion of Ashwagandha, the most validated adaptogen for HPA regulation and stress-induced insomnia
- Full coverage for emotion-driven chronic sleep issues, especially in anxiety or depression backgrounds
- High safety profile, non-habit forming, suitable for drug tapering, long-term neuro-regulatory care, and daily support

D. Recommended Target Populations

- Individuals with circadian-type insomnia: sleep-onset difficulties, early-morning awakenings, vivid dreams
- Those under chronic stress with nighttime cortisol dysregulation

- High-sensitivity types with pre-sleep mental activation and neural excitability
- Menopausal, high-cognitive-load, or student populations with emotion-sleep disruptions
- People with sleep impairments due to anxiety, depression, or emotional disorders
- Those seeking non-pharmacological, long-term support for sleep without sedative dependence

7) Conclusion: Summary of Keyora MoodFlow 8 in 1's Multi-Path Insomnia Support Strategy

Intervention Pathway	Core Nutrient Combination	Target Insomnia Subtype
Melatonin synthesis activation	5-HTP + B6 + VD	Sleep-onset difficulties, circadian rhythm disruption
Neural excitability modulation	Magnesium Glycinate + L-Theanine	Pre-sleep arousal, hyperactive neural states
Nighttime cortisol reduction	Ashwagandha + Magnesium	Early-morning awakenings, vivid dreams
Circadian rhythm reconstruction	5-HTP + VD + Ashwagandha	Circadian misalignment, post-shift/travel
Emotion–sleep axis support	5-HTP + B6 + VD + Ashwagandha	Emotion-driven insomnia, anxiety-linked onset difficulties

- ✓ *Muscogiuri, G., et al. (2017). Vitamin D and sleep regulation: Is there a role for vitamin D? Current Pharmaceutical Design, 23(32), 2490–2494.*

  - Review study – Investigated the regulatory role of vitamin D on TPH2 and AANAT expression, supporting its involvement in sleep and circadian rhythm modulation.

- ✓ *Chandrasekhar, K., et al. (2012). A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha root in reducing stress and anxiety in adults. Indian Journal of Psychological Medicine, 34(3), 255–262.*

  - RCT clinical study – Demonstrated that Ashwagandha significantly reduces cortisol levels and improves stress-related nighttime awakenings and sleep disruptions.

- ✓ *Birdsall, T. C. (1998). 5-Hydroxytryptophan: a clinically-effective serotonin precursor. Alternative Medicine Review, 3(4), 271–280.*

  - Mechanism review – Highlighted the ability of 5-HTP to cross the blood–brain barrier and promote melatonin synthesis, offering significant support for sleep-onset and circadian-type insomnia.

- ✓ *Rao, T. S., et al. (2008). Understanding nutrition, depression and mental illnesses. Indian Journal of Psychiatry, 50(2), 77–82.*

  - Review article – Discussed the synergistic roles of nutrients such as B6, B12, magnesium, and 5-HTP in the co-regulation of mood and sleep.

- ✓ *Liao, J., et al. (2022). The anxiolytic effects of L-theanine on clinical anxiety and stress: A systematic review and meta-analysis. Nutrients, 14(7), 1526.*

  - Systematic review and meta-analysis – Showed that L-theanine enhances alpha wave activity, promotes relaxation and sleep initiation, and does so without sedative side effects.

✓ *Boyle, N. B., et al. (2017). The effects of magnesium supplementation on subjective anxiety and stress: A systematic review. Nutrients, 9(5), 429.*

- Systematic review – Indicated that magnesium supplementation improves sleep disorders linked to neural hyperexcitability, including difficulties with sleep initiation and nighttime awakenings.

✓ *Zhao, Y., et al. (2019). The role of melatonin in sleep disorders: Review and meta-analysis. Frontiers in Neuroendocrinology, 55, 100819.*

- Literature review – Emphasized the key role of the 5-HTP–melatonin pathway in improving multiple types of insomnia through enhanced endogenous melatonin production.

VI Intervention Strategy of Keyora MoodFlow 8 in 1 for Emotion-Cognition-Sleep Dysregulation under High Cognitive Load and Occupational Stress

Targeting the Integrated Axis of Neuro-Metabolic Imbalance, Emotional Tension, and Circadian Disruption

In contexts of prolonged cognitive overload and sustained psychological stress, individuals often present with overlapping disturbances across mood, sleep, and neurocognitive function.

Populations such as **students, intensive knowledge workers, and small business owners** typically experience a dynamic interplay of *task pressure, dysregulated routines, and chronic mental strain*, manifested as:

- Difficulty concentrating and cognitive sluggishness
- Emotional instability, alternating between anxiety and depressive states
- Insomnia, early morning awakening, and daytime fatigue
- Brain fog, delayed response, reduced learning efficiency
- Chronic neuro-metabolic exhaustion with both physical and mental fatigue

Keyora MoodFlow 8 in 1 addresses the functional triad of *"cognitive overload + emotional tension + circadian dysregulation"* through five synergistic mechanisms that restore neurotransmitter pathways, stabilize stress responses, and resynchronize biological rhythms - offering a sustained, non-pharmaceutical support strategy tailored to high-stress, cognitively demanding populations.

1) Rapid Restoration of Neurotransmitter Metabolism to Enhance Cognitive Stability and Stress Resilience

Core Formula: 5-HTP + Vitamin B6 + Vitamin B12

- Chronic cognitive demand coupled with emotional strain depletes central neurotransmitter pools, leading to mood swings and attentional deficits
- 5-HTP provides a direct precursor to serotonin (5-HT), enhancing emotional resilience and reducing irritability and stress-induced breakdown
- Vitamin B6 acts as a rate-limiting coenzyme for the synthesis of dopamine, GABA, and norepinephrine, supporting neurochemical stability

- Vitamin B12 promotes SAMe synthesis and supports neurotransmitter methylation and myelin sheath integrity, enhancing neural conduction

***Synergistic Pathway**: "5-HT + DA + GABA + NE" multi-transmitter co-regulation*

Applicable Symptoms: Irritability, agitation, poor concentration, mental fatigue, slow responses, brain fog

2) **Modulation of Stress-Induced Autonomic Dysregulation to Improve Neuro-flexibility**

Core Formula: Ashwagandha + Magnesium Glycinate

- Chronic task pressure, exam preparation, and business risks activate the HPA axis persistently, manifesting as tension, palpitations, and anxiety-related insomnia
- Ashwagandha is the most clinically studied adaptogen, shown to reduce cortisol levels by 20–30% and restore autonomic balance
- Magnesium Glycinate modulates NMDA receptor excitotoxicity and stabilizes neuro-electrical activity to prevent stress-related neural exhaustion

***Best suited for** individuals with "high daytime tension - difficulty unwinding at night"*

Applicable Symptoms: Nervousness, palpitations, inability to relax, alternating hypo- and hyper-reactivity, daytime inefficiency

3) **Regulation of Cognitive-Anxiety-Emotional Hyperarousal Loop to Improve Learning and Work Performance**

Core Formula: L-Theanine + Magnesium Glycinate + Vitamin B6

- Students and knowledge workers often experience “thought overflow - cognitive lock - attention fragmentation,” creating a state of *“chronic wakefulness - cognitive tension”*
- L-Theanine enhances alpha wave activity, promoting a “relaxed yet focused” brain state (similar to EEG patterns observed in meditation)
- Vitamin B6 supports the balance of dopamine, norepinephrine, and GABA, mitigating excitatory overload and cognitive fatigue
- Magnesium stabilizes neural excitability and enhances GABAergic tone, improving the rhythmicity of neurotransmission

Best suited for *individuals with “daytime attention collapse – nighttime insomnia – anxiety-induced focus deficit”*

Applicable Symptoms: Pre-exam anxiety, distractibility, low work efficiency, cognitive overload

4) **Restoration of Circadian Rhythm Synchronization:** Breaking the Loop of Day-Night Reversal, Sleep Disruption, and Emotional Dysregulation

Core Formula: 5-HTP + Vitamin D + Ashwagandha

- High-intensity cognitive work is often accompanied by circadian misalignment: *daytime fatigue*, *nocturnal mental hyperactivity*, and *difficulty returning to sleep after early awakening*
- The 5-HTP → 5-HT → Melatonin pathway provides essential substrate support for circadian hormone rhythms
- Vitamin D modulates the expression of circadian genes (Clock, BMAL), enhancing light-sensitive entrainment and day-night transition capacity
- Ashwagandha further supports nocturnal cortisol rhythm regulation, improving natural sleep onset and morning wakefulness

***Tripartite restoration across**: hormonal regulation, neurotransmitter rhythms, and electrophysiological stability*

Applicable Symptoms: Daytime drowsiness, nocturnal arousal, early morning awakening, rhythm inversion

5) Prevention of Cognitive Resource Depletion and Neuro-energetic Imbalance: Enhancing Neural Endurance

Core Formula: Vitamin B1 + Vitamin B12 + Magnesium Glycinate

- Vitamin B1 is a key coenzyme for neuronal glucose metabolism; deficiency leads to brain energy deficit, mental fatigue, and cognitive dullness
- Vitamin B12 supports myelin synthesis and repair, maintaining high-speed neural transmission - commonly deficient under high cognitive workloads
- Magnesium plays a central role in neural energy metabolism, ATP synthesis, NMDA receptor inhibition, and calcium homeostasis

***Functional Network**: B1–B12–Mg axis for neuro-energetic stability and cognitive stamina*

Applicable Symptoms: Slow cognitive recovery, memory lapses, persistent fatigue, neurasthenic presentations

6) **Clinical Consensus:** Systemic Nutritional Intervention for Stress-Related Cognitive and Emotional Dysregulation

A. **Functional Medicine Perspective:** The “Cognition-Emotion-Rhythm” Tri-Axis Dysregulation as Core Pathophysiology in High-Load Populations

In clinical contexts, high-cognition groups such as students, knowledge workers, and entrepreneurs do not simply exhibit anxiety or attentional disorders in isolation. Instead, they frequently display functional neuro-systemic imbalances driven by the disruption of three tightly coupled axes:

- Neurotransmitter depletion: Chronic cognitive demand accelerates consumption of serotonin (5-HT), dopamine (DA), and GABA. Without adequate precursors and cofactors, symptoms manifest as inattention, agitation, and cognitive fatigue
- HPA axis hyper-activation: Persistent stress skews autonomic dominance toward sympathetic overdrive, elevating cortisol and resulting in emotional instability, shallow sleep, and impaired energy metabolism
- Circadian disruption: Imbalanced study/work schedules and stress-induced rhythm misalignment downregulate expression of melatonin-related enzymes (TPH2, AANAT) and SCN genes, causing *daytime lethargy–nighttime hyperactivity* and clock dysfunction

These dysregulated axes reinforce one another, forming a pathological feedback loop of "low daytime efficiency - nocturnal hyperarousal - chronic non-recovery," which often progresses into comorbid cognitive, mood, and sleep disorders.

B. **Nutritional Psychiatry Consensus:** Multi-Axis Intervention Targeting Transmitters, Rhythm, and Stress

Research in nutritional psychiatry and brain health nutrition identifies five key non-pharmaceutical mechanisms with high relevance to this population:

a) Neurotransmitter activation: Providing precursors (5-HTP), enzymatic cofactors (B6, B12), and methyl donors to restore synthesis of 5-HT, DA, GABA, and NE

b) Stress axis modulation: Using adapt-ogenic botanicals such as Ashwagandha to rebalance HPA activity and reduce chronic cortisol burden

c) Neural relaxation: Enhancing alpha wave activity and GABA function through L-Theanine and magnesium without sedative side effects

d) Circadian gene regulation: Upregulating SCN rhythm genes (Clock/BMAL) via Vitamin D to enhance environmental light response and hormonal entrainment

e) Neuro-energetic support: Ensuring availability of coenzymes (B1, B12) and magnesium for ATP synthesis, myelin repair, and cognitive endurance

This framework has been widely applied in practice - including exam anxiety programs, office stress management, and executive cognitive-sleep interventions - and is now embedded in consensus guidelines for nutritional cognitive fatigue protocols.

C. **Keyora MoodFlow 8 in 1:** Systemic Advantage in Supporting High-Cognition, High-Stress Individuals

As a synergistic neuro-nutritional formulation designed for the *neurotransmitter–circadian-emotional axis*, **Keyora MoodFlow 8 in 1** demonstrates the following advantages:

- Clinically validated, high-bioavailability actives: including standardized Ashwagandha, 5-HTP, and L-Theanine

- Full-pathway support: from raw material (e.g., 5-HTP) → enzymatic cofactor (B6, B12) → gene regulation (VD), ensuring comprehensive axis restoration
- Multimodal effects: building an integrated "relaxation-focus-sleep-mood" network to break the loop of *chronic stress - low performance - poor sleep*

Versatile application scenarios: usable as medication tapering support, exam-period brain support, daily neuro-nutrient management, or non-pharmaceutical intervention

D. Recommended Target Populations

Population Type	Description	Primary Intervention Goals
Students	Prolonged learning, exam stress, mental exhaustion	Mood stabilization, attention enhancement, sleep quality
Knowledge workers	High-frequency decisions, cognitive fatigue, sensitivity	Cognition–rhythm co-regulation, pressure buffering
Entrepreneurs	Operational stress, anxiety-depression cycles, rhythm shifts	Neuro-stamina support, rhythm repair, mood fluctuation control

7) **Summary:** Systemic Support Strategy of **Keyora MoodFlow 8 in 1** for Cognitive-Stress Overload States

Intervention Pathway	Core Formula	Targeted Subtypes/Populations
Multi-Transmitter	5-HTP + B6 + B12	Mood swings, inattention, brain fog

Intervention Pathway	Core Formula	Targeted Subtypes/Populations
Activation		
Stress Axis Modulation	Ashwagandha + Magnesium Glycinate	Entrepreneurs, high-load professionals
Alpha Wave Enhancement + GABA	L-Theanine + Magnesium + B6	Anxious students, cognitively overloaded individuals
Circadian Synchronization	5-HTP + Vitamin D + Ashwagandha	Daytime fatigue, nocturnal arousal, rhythm disruption
Neuro-energetic Support	B1 + B12 + Magnesium	Chronic brain fatigue, memory loss, learning decline

- ✓ *Chandrasekhar, K., Kapoor, J., & Anishetty, S. (2012) A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha root in reducing stress and anxiety in adults. Indian Journal of Psychological Medicine, 34(3), 255–262*

  - Double-blind RCT study – Ashwagandha significantly reduced cortisol levels and alleviated emotional tension and fatigue under high-stress conditions.

- ✓ *Liao, J., et al. (2022) The anxiolytic effects of L-theanine on clinical anxiety and stress: A systematic review and meta-analysis. Nutrients, 14(7), 1526*

  - Systematic review and meta-analysis – L-theanine increased alpha wave activity and improved cognitive anxiety, attention dysregulation, and mental tension.

- ✓ *Boyle, N. B., Lawton, C., & Dye, L. (2017) The effects of magnesium supplementation on subjective anxiety and stress: A systematic review. Nutrients, 9(5), 429*

  - Systematic review – Magnesium supplementation reduced subjective stress perception and neural sensitivity, particularly relevant for individuals with high cognitive workload.

- ✓ *Birdsall, T. C. (1998) 5-Hydroxytryptophan: a clinically-effective serotonin precursor. Alternative Medicine Review, 3(4), 271–280*

  - Overview study – 5-HTP serves as a key supplement for serotonin synthesis under cognitive overload, supporting emotional stability and circadian rhythm recovery.

- ✓ *Rao, T. S., Asha, M. R., Ramesh, B. N., & Jagannatha Rao, K. S. (2008) Understanding nutrition, depression and mental illnesses. Indian Journal of Psychiatry, 50(2), 77–82*

  - Narrative review – Highlights the integrative application of B vitamins, magnesium, and 5-HTP in combined cognitive–emotional interventions.

- ✓ *Muscogiuri, G., et al. (2017) Vitamin D and sleep regulation: Is there a role for vitamin D? Current Pharmaceutical Design, 23(32), 2490–2494*

  - Circadian nutrition review – Vitamin D regulates TPH2 and circadian gene expression, enhancing synchronization of brain cognitive–sleep systems.

- ✓ *Kennedy, D. O. (2016) B vitamins and the brain: Mechanisms, dose and efficacy—A review. Nutrients, 8(2), 68*

  - Comprehensive review of B vitamins – Describes the role of B1, B6, and B12 in supporting brain energy metabolism, neurotransmitter synthesis, and cognitive function.

VII Keyora MoodFlow 8 in 1 in the Nutritional Intervention for Menopausal Symptoms

Targeting the Neuro-Endocrine-Circadian Tri-Axis to Alleviate Emotional Instability, Sleep Disorders, and Cognitive Decline

During the menopausal transition, women experience complex physiological and psychological changes.

The core disturbance is not merely hormonal deficiency, but rather a multi-axis dysfunction syndrome involving neurotransmitter imbalance, HPA axis hyperactivity, and circadian rhythm disruption - all driven by ovarian decline.

Typical manifestations include:

- Emotional lability with alternating irritability, anxiety, and depressive moods
- Decreased sleep quality with coexisting difficulty falling asleep and nocturnal awakenings
- A sense of cognitive “slowness,” memory decline, and brain fog
- Heightened mental tension and significantly reduced stress resilience
- Worsening of symptoms in the early morning and pronounced circadian misalignment

Keyora MoodFlow 8 in 1 targets the underlying neurobiological imbalances associated with the menopausal stage and establishes five core regulatory pathways that support

the coordinated recovery of emotional regulation, sleep quality, and cognitive performance.

1) **Neurotransmitter Balance:**

Mitigating Menopausal Anxiety, Irritability, and Depressive Symptoms

Core ingredients: 5-HTP + Vitamin B6 + Vitamin D

- Declining ovarian function and estrogen levels impair central serotonin (5-HT) activity - a key driver of mood instability.
- 5-HTP bypasses tryptophan transport competition and directly supplies substrate for brain serotonin synthesis.
- Vitamin B6 is an essential coenzyme for the conversion of 5-HTP to 5-HT. Without it, precursor accumulation yields low functional output.
- Vitamin D upregulates TPH2 expression, enhances 5-HT synthesis efficiency, and alleviates seasonal affective symptoms due to low light exposure.

This pathway builds the biochemical foundation for emotional stabilization.

Applicable symptoms: mood swings, tearfulness, irritability, morning-worsening depressive insomnia

2) **HPA Axis Modulation and Cortisol Rhythm Correction:**

Enhancing Stress Resilience

Core ingredients: Ashwagandha + Magnesium Glycinate

- Menopausal women often exhibit compensatory HPA axis hyper-activation, resulting in anxiety, nocturnal arousal, and heightened reactivity.
- Ashwagandha has been clinically shown to lower baseline cortisol levels by 20–30%, restoring the stress–relaxation balance and improving anxiety and nighttime awakenings.
- Magnesium glycinate inhibits excitotoxic glutamate activity and overactive neural firing, enhancing nighttime GABAergic tone.

Especially effective for stress-related insomnia.

Applicable symptoms: nervous tension, palpitations, easy arousal, heavy stress burden, fragmented sleep

3) **Restoring Coupled Rhythm of Sleep and Emotion:**

Breaking the “Insomnia-Depression” Cycle

Core ingredients: 5-HTP + B6 + VD + Ashwagandha

- Melatonin and serotonin secretion decline during menopause, while nocturnal cortisol rises—creating a “hyper-aroused at night” circadian disruption.
- 5-HTP + B6 provides the necessary substrate for melatonin synthesis; vitamin D regulates expression of core circadian genes.

- Ashwagandha reduces nighttime stress reactivity and prevents premature early-morning arousals.

Together, these form a regulatory triangle: 5-HT - Melatonin - Cortisol, enhancing circadian coherence.

Applicable symptoms: difficulty initiating sleep, early morning awakenings, daytime fatigue, nighttime emotional activation, circadian reversal

4) **Supporting Neuroplasticity and Cognitive Function:**

Addressing “Brain Fog” and Attention Deficits

Core ingredients: Vitamin B12 + Ashwagandha

- Estrogen decline downregulates BDNF expression, impairs synaptic plasticity, and contributes to memory loss and cognitive sluggishness.
- Ashwagandha has shown potential in clinical populations to enhance BDNF expression and support cognitive recovery.
- Vitamin B12 promotes SAMe synthesis, facilitates neurotransmitter methylation, supports myelin regeneration, and prevents neurodegenerative risk.

A nutritional strategy targeting memory and cognitive regression in menopause.

Applicable symptoms: memory blunting, slowed response, poor attention, reduced academic or work efficiency

5) **Buffering Neuro-Metabolic Depletion:**

Preventing Energy-Mood Collapse Cycles

Core ingredients: Vitamin B1 + B6 + Magnesium Glycinate

- Mood instability during menopause is often exacerbated by low energy states: fatigue → irritability → insomnia → more fatigue.
- Vitamin B1 participates in cerebral glucose metabolism and lactate clearance, improving neuronal energy efficiency.
- B6 and magnesium jointly regulate neurotransmitter synthesis, membrane potential, and stress buffering systems.

This dual-layer support - energy + neurotransmitters - stabilizes mood and restores daytime vitality.

Applicable symptoms: fatigue, mental fog, emotional instability tied to low energy, feelings of collapse

6) **Clinical Consensus:**

Systemic Nutritional Strategies of **Keyora MoodFlow 8 in 1** for Menopausal Syndromes

A. Menopausal Dysregulation Involves Multi-Axis Dysfunction

Beyond hormone replacement or symptomatic treatment for anxiety and depression, the modern clinical view emphasizes the regulation of three major axes - neurotransmitters, endocrine response, and circadian rhythms - through targeted nutritional support.
This approach promotes neural homeostasis, stress buffering, and hormonal rhythm restoration as the foundation of systemic recovery.

B. Non-Pharmacological Nutritional Interventions Offer Safety and Adherence Advantages

Compared to hormone therapy, compound nutritional formulations are well-suited for individuals sensitive to drugs, concerned about side effects, or seeking daily and long-term support.
They are especially appropriate for women in the Perimenopausal phase up to around age 60, as either a first-line intervention or as complementary support to HRT.

C. Keyora MoodFlow 8 in 1 Delivers Multi-Mechanism, System-Level Support

All eight ingredients in the formula have demonstrated clinical pathways closely associated with key menopausal symptoms - including insomnia, anxiety, and cognitive decline:

- A preventive nutritional strategy for early menopausal functional decline

- A supportive adjunct to hormonal therapy
- A daily integrative tool for managing emotional, sleep, and cognitive symptoms

7) **Summary:** Support Strategy of Keyora MoodFlow 8 in 1 Across the "Emotion-Sleep-Cognition" Tri-Axis in Menopause

Intervention Pathway	Core Ingredient Combination	Applicable Menopausal States
5-HT Enhancement and Emotional Stability	5-HTP + B6 + VD	Mood swings, alternating anxiety-depression states
Stress Axis Modulation	Ashwagandha + Magnesium Glycinate	Tension, palpitations, difficulty initiating sleep
Circadian Hormonal Regulation	5-HTP + B6 + VD + Ashwagandha	Morning symptom worsening, circadian disruption
Cognitive Function Recovery	Ashwagandha + B12	Brain fog, slow processing, memory decline
Neural Energy Support	B1 + B6 + Magnesium	Emotional collapse, low mental performance, persistent fatigue

✓ *Chandrasekhar, K., Kapoor, J., & Anishetty, S. (2012)* – A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha root in reducing stress and anxiety in adults – Indian Journal of Psychological Medicine*, 34(3), 255–262*

– Double-blind RCT – Ashwagandha significantly reduces cortisol levels and improves anxiety and insomnia symptoms, applicable to stress-induced activation states in menopause

- ✓ ***Birdsall, T. C.*** *(1998)* – 5-Hydroxytryptophan: a clinically-effective serotonin precursor – Alternative Medicine Review*, 3(4), 271–280*

  – Overview study – 5-HTP effectively replenishes central 5-HT, supporting neurotransmitter regulation in menopausal anxiety, depression, and sleep disorders

- ✓ ***Muscogiuri, G., et al.*** *(2017)* – Vitamin D and sleep regulation: Is there a role for vitamin D – Current Pharmaceutical Design*, 23(32), 2490–2494*

  – Review study – Vitamin D modulates melatonin circadian rhythms, alleviating common sleep rhythm disturbances in menopausal women

- ✓ ***Liao, J., et al.*** *(2022)* – The anxiolytic effects of L-theanine on clinical anxiety and stress: A systematic review and meta-analysis – Nutrients*, 14(7), 1526*

  – Meta-analysis – L-theanine significantly improves anxiety and enhances alpha wave activity, applicable to menopausal cognitive tension and sleep-onset difficulties

- ✓ ***Kennedy, D. O.*** *(2016)* – B vitamins and the brain: Mechanisms, dose and efficacy—A review – Nutrients*, 8(2), 68*

  – Review – Vitamins B1, B6, and B12 provide essential support for neuro-metabolism, cognitive function, and emotional stability, suitable for interventions in menopausal brain fatigue and brain fog

- ✓ ***Miller, A. H., & Raison, C. L.*** *(2016)* – The role of inflammation in depression: From evolutionary imperative to modern treatment target – Nature Reviews Immunology*, 16(1), 22–34*

– Highlights the link between menopausal mood disorders and chronic low-grade inflammation – VD and B vitamins may serve as auxiliary anti-inflammatory and emotional regulatory nutrients

- ✓ ***Kuszewski, J. C., et al.*** *(2020)* – The effect of ashwagandha (Withania somnifera) on sleep: A systematic review – PLOS One*, 15(11), e0241799*

– Systematic review – Ashwagandha improves subjective sleep quality and reduces nighttime awakenings, applicable to menopausal nocturnal sleep fragmentation

VIII Summary of the Synergistic Mechanisms of the Eight Nutrients in Keyora MoodFlow 8 in 1

A comprehensive regulatory system centered on the neuro-endocrine-circadian tri-axis

Keyora MoodFlow 8 in 1 features a synergistic formulation of eight nutrients with well-documented neuro-regulatory functions. It is designed to support five fundamental dimensions of brain health: neurochemical balance, neuro-electrical activity, endocrine stress response, circadian synchronization, and neuroplasticity, forming a tightly integrated regulatory loop.

1) Serotonin Pathway Support (5-HT Synthesis Axis)

Key ingredients: 5-HTP + Vitamin B6 + Vitamin D

- 5-HTP bypasses the competitive transport limitation of tryptophan and directly supplies the substrate for central serotonin synthesis.
- Vitamin B6 serves as a coenzyme for aromatic L-amino acid decarboxylase (AADC), facilitating 5-HTP → 5-HT conversion.
- Vitamin D upregulates TPH2 expression, enhancing transcriptional capacity of the serotonin pathway.

Functional benefits*: Improves emotional stability, alleviates anxiety and depression, and provides biochemical support for melatonin synthesis.*

2) GABA/Glutamate Neuro-electrical Balance

Key ingredients: Magnesium Glycinate + L-Theanine + Vitamin B6

- Glycine acts as an inhibitory neurotransmitter, while magnesium antagonizes NMDA receptors, mitigating glutamate-induced excitotoxicity.
- L-Theanine promotes alpha wave activity and facilitates spontaneous release of GABA, dopamine, and serotonin.
- Vitamin B6 is an essential cofactor for GAD and DDC, involved in the synthesis of GABA and dopamine.

Functional benefits*: Relieves neuronal hyperactivity, stress-induced insomnia, and attention dysregulation.*

3) Chronic Stress Response and HPA Axis Modulation (Stress–Cortisol Axis)

Key ingredients: Ashwagandha + Magnesium Glycinate

- Ashwagandha reduces baseline cortisol levels, improving stress reactivity and emotional irritability.
- Magnesium buffers neuroendocrine overload, enhancing neural resilience under prolonged stress.

Applicability*: Ideal for individuals with chronic high stress or alternating anxiety–depression symptoms.*

4) Circadian Rhythm and Sleep Architecture Synchronization

Key ingredients: 5-HTP + Vitamin B6 + Vitamin D + Ashwagandha

- 5-HTP and B6 facilitate melatonin synthesis.
- Vitamin D modulates TPH2 and AANAT expression, influencing activity in the master clock (SCN).
- Ashwagandha reduces nighttime cortisol rebound, restoring hormonal rhythm coupling.

Functional benefits*: Improves early awakening, circadian misalignment, and rhythm-based insomnia.*

5) Neuroplasticity and Cognitive Support

Key ingredients: Ashwagandha + Vitamin B12

- Ashwagandha enhances BDNF expression, promoting synaptic plasticity and stress adaptability.
- Vitamin B12 supports SAMe synthesis, ensuring myelin integrity and neural signal transmission efficiency.

***Functional benefits**: Alleviates brain fog, cognitive slowing, attention deficits, and emotional-cognitive coupling delays.*

6) Neuro-energetics and Brain Fatigue Resilience

Key ingredients: Vitamin B1 + Vitamin B6 + Magnesium

- Vitamin B1 participates in essential enzymatic complexes (PDH, α-KGDH) for cerebral energy metabolism.
- Vitamin B6 modulates neurotransmitter and hormone synthesis, buffering mitochondrial metabolic stress.
- Magnesium supports ATP synthesis and facilitates post-neuronal activity recovery.

***Functional benefits**: Breaks the "high cognitive load - mental exhaustion - emotional collapse" loop and enhances daytime neural recovery.*

7) Summary Table: Eight Nutrients, Six Synergistic Mechanisms

Functional Dimension	Ingredient Combination	Primary Function	Applicable Symptoms
5-HT Pathway	**5-HTP + B6 + VD**	Emotional stabilization, anti-depressant effect	Low mood, worse in mornings
GABA/Glutamate Balance	**Magnesium Glycinate + L-Theanine + B6**	Neuro-tension relief, sleep initiation support	Tension-related anxiety, difficulty falling asleep
HPA Axis Buffering	**Ashwagandha + Magnesium Glycinate**	Stress resilience, emotional buffering	Irritability, palpitations, early awakening
Circadian Regulation	**5-HTP + B6 + VD + Ashwagandha**	Restoring circadian rhythm	Morning awakening, circadian disruption
Neuroplasticity	**Ashwagandha + B12**	Cognitive enhancement, neuroprotection	Brain fog, slow reactions, memory decline
Brain Energy Support	**B1 + B6 + Magnesium**	Fatigue relief, anti-burnout effect	Cognitive slowing, low energy, emotional exhaustion

✓ *Birdsall, T. C. (1998)* – 5-Hydroxytryptophan: a clinically-effective serotonin precursor – Alternative Medicine Review, 3(4), 271–280

– Describes how 5-HTP bypasses the competitive transport limitation of tryptophan, enhances central serotonin activity, and improves mood and circadian-related functions.

- ✓ ***Muscogiuri, G., et al. (2017)*** – Vitamin D and sleep regulation: Is there a role for vitamin D – Current Pharmaceutical Design, 23(32), 2490–2494

  – A review indicating that vitamin D upregulates TPH2 and AANAT, participates in 5-HT and melatonin synthesis, and modulates circadian rhythm and mood stabilization.

- ✓ ***Shan, A., & Rahman, M. M. (2021)*** – Role of Vitamin B6 in neurotransmitter synthesis and functions – Biomedical Research and Therapy, 8(5), 4315–4321

  – Demonstrates that vitamin B6 is an essential coenzyme in the synthesis of several neurotransmitters (5-HT, GABA, dopamine, norepinephrine), acting as a rate-limiting factor in neurotransmitter metabolism.

- ✓ ***Boyle, N. B., Lawton, C., & Dye, L. (2017)*** – The effects of magnesium supplementation on subjective anxiety and stress: A systematic review – Nutrients, 9(5), 429

  – A systematic review confirming magnesium's role in stabilizing neuronal discharge, buffering glutamate excitotoxicity, and reducing stress-induced anxiety symptoms.

- ✓ ***Liao, J., et al. (2022)*** – The anxiolytic effects of L-theanine on clinical anxiety and stress: A systematic review and meta-analysis – Nutrients, 14(7), 1526

  – L-theanine significantly promotes alpha wave activity, enhances GABA, dopamine, and serotonin levels, and alleviates anxiety and attention deficits.

- ✓ ***Chandrasekhar, K., Kapoor, J., & Anishetty, S. (2012)*** – A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha root in reducing stress and anxiety in adults – Indian Journal of Psychological Medicine, 34(3), 255–262

– A standardized Ashwagandha extract significantly reduces cortisol levels and improves stress-related anxiety, cognitive impairment, and sleep disruptions.

- ✓ ***Kennedy, D. O. (2016)*** – B vitamins and the brain: Mechanisms, dose and efficacy—A review – Nutrients, 8(2), 68

  – Details the critical roles of vitamins B1, B6, and B12 in brain energy metabolism, myelin maintenance, and neurotransmitter synthesis, supporting interventions for brain fatigue and neurohomeostasis.

- ✓ ***Owecki, M., et al. (2018)*** – Homocysteine and vitamin B12 status in depression and cognitive decline – Journal of Neural Transmission, 125(1), 159–165

  – Identifies B12 deficiency as a contributor to cognitive decline and depression, highlighting its neuroprotective role in myelin repair and neurotransmitter methylation.

- ✓ ***Kuszewski, J. C., et al. (2020)*** – The effect of ashwagandha (Withania somnifera) on sleep: A systematic review – PLOS One, 15(11), e0241799

  – A systematic review showing that Ashwagandha improves sleep efficiency and reduces nighttime awakenings, applicable to circadian-linked emotional and sleep disorders.