# Magnesium Glycinate

"Targeted to alleviate depression, anxiety, and insomnia while enhancing cognitive performance in high-stress individuals."

## Magnesium - The Essential Neuro-Regulating Mineral

Magnesium is an essential mineral and electrolyte required for over 300 enzymatic reactions in the human body - often referred to as ***"the key to neural and metabolic balance"***.

Far beyond being just *"calcium's partner"* or a nutrient for preventing cramps, magnesium plays a fundamental role in nervous system stability, mood regulation, muscle relaxation, heart rhythm maintenance, energy production, and hormonal balance.

## Key Functional Roles of Magnesium

| System | Core Function |
|---|---|
| Nervous System | Modulates neurotransmitters (e.g., GABA, glutamate), stabilizes mood, reduces anxiety, supports healthy sleep. |
| Muscle Function | Maintains muscle relaxation, prevents cramps, spasms, and excessive tension. |
| Cardiovascular | Regulates heart rhythm, supports healthy blood pressure, protects cardiac conduction. |

| System | Core Function |
| --- | --- |
| Energy Metabolism | Essential for ATP production, prevents chronic fatigue. |
| Hormonal Regulation | Lowers elevated cortisol, buffers stress responses, supports circadian rhythm balance. |

*If calcium is the “accelerator” for muscle and nerve activity, magnesium is the “brake” - the guardian of relaxation signals.*

## I Magnesium Glycinate - The Most Neuro-Targeted Form of Magnesium

Magnesium glycinate is a chelated compound where each magnesium ion is bound to two glycine molecules.

It is classified as an organic chelated magnesium form, well-recognized in nutritional medicine for its high absorption and gentle action on the digestive system.

This form is particularly valued for anxiety, stress, sleep disturbances, and nervous system hypersensitivity because it combines magnesium’s calming role with glycine’s own neurotransmitter effects.

### Magnesium Glycinate vs. Common Magnesium Salts

| Comparison | Common Magnesium Salts | Magnesium Glycinate |
|---|---|---|
| Absorption | Lower, dependent on stomach acid | High, absorbed via peptide transporters |
| Digestive Tolerance | May cause diarrhea or GI irritation | Very gentle, minimal laxative effect |
| Neurological Action | Pure magnesium replenishment | Magnesium + glycine acting on GABA & GlyR pathways |
| Typical Use | Short-term relief (e.g., constipation) | Long-term mood stability & neuro-support |

1) Three Synergistic Mechanisms of Magnesium Glycinate

- Magnesium Replenishment - Enhances GABAergic function, calms the nervous system, relieves stress, and supports restorative sleep.
- Glycine Release - Acts as an inhibitory neurotransmitter, directly engaging brain calming pathways.
- Bidirectional Nervous System Balance - Reduces excitatory signaling (glutamate), enhances inhibitory signaling (GABA), supporting overall neural equilibrium.

In essence: *Magnesium is the key to quieting an overactive nervous system, and magnesium glycinate is one of the gentlest, safest, and most effective keys to unlock that calm.*

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

  *– A systematic review concluded that magnesium supplementation — particularly in glycinate form — helps stabilize the nervous system and alleviate symptoms under high-stress and anxiety conditions.*

- ✓ ***Serefko A, Szopa A, Wlaź P, et al.*** Magnesium and depression. *Pharmacol Rep. 2013;65(3):547–554.*

  *– Magnesium's role in mood disorders (including anxiety and depression) involves multiple central nervous system pathways, notably GABA enhancement and NMDA inhibition. Magnesium glycinate is recommended as a preferred form.*

- ✓ ***Yamadera W, Inagawa K, Chiba S, et al.*** Glycine ingestion improves subjective sleep quality in humans. *Sleep Biol Rhythms. 2007;5(2):126–131.*

  *– Glycine, by acting on brainstem GlyR pathways, can improve sleep onset, depth, and reduce nighttime awakenings.*

- ✓ ***Abbasi B, Kimiagar M, Sadeghniiat K, et al.*** The effect of magnesium supplementation on primary insomnia in elderly: A double-blind placebo-controlled clinical trial. *J Res Med Sci. 2012;17(12):1161–1169.*

  *– Magnesium supplementation improved sleep quality in elderly individuals, especially in cases of insomnia coexisting with anxiety.*


## 2) Overview of Common Magnesium Sources

- Magnesium Oxide - Although it contains a high percentage of elemental magnesium, its absorption rate is extremely low (less than 5%), and most of it is excreted in the stool. This form is commonly found in inexpensive magnesium supplements and laxative formulas. It strongly irritates the gastrointestinal tract and is prone to causing diarrhea and bloating.
- Magnesium Citrate - An organic magnesium salt with moderate absorption, widely used for mild constipation relief and short-term magnesium replenishment. At certain doses, it has a mild laxative effect, and higher doses may cause intestinal rumbling or loose stools.
- Magnesium Chloride - Typically used in electrolyte replacement solutions or for medical purposes (e.g., intravenous administration). When taken orally, it can irritate the stomach lining, has inconsistent absorption, and is seldom used in daily mood or emotional support formulations.
- Magnesium Lactate - Offers relatively good absorption and is suitable for individuals with low stomach acid secretion. However, it is more costly, used in smaller amounts, and lacks synergistic mechanisms for targeted nervous system support.

### 3) Magnesium Glycinate

- A Scientifically Superior Form of Magnesium

Magnesium Glycinate is a chelated compound in which two glycine molecules are bound to one magnesium ion, offering three key advantages:

A. High Absorption Rate - Ensuring Bioactive Delivery

Traditional magnesium salts, such as magnesium oxide, require dissociation in stomach acid, and their absorption depends on passive diffusion, leading to very low uptake.

In contrast, magnesium glycinate's chelated structure resembles a small peptide, allowing it to be absorbed via peptide transporters in the small intestine (e.g., PEPT1).

This bypasses the precipitation issues of free magnesium in the gut. Multiple studies have shown magnesium glycinate can reach an absorption rate of 50-80%, far higher than that of magnesium oxide or magnesium citrate.

B. No Laxative Side Effects - Safer for Long-Term Use

Many consumers mistakenly believe all magnesium supplements cause diarrhea, due to past experiences with magnesium salts that have a pronounced "osmotic laxative effect." Salts such as magnesium oxide and magnesium citrate create high osmotic pressure in the intestines, drawing water into the lumen and causing loose stools.

In contrast, magnesium glycinate is a neutral chelate that does not create this high-osmotic environment, making it far less likely to cause diarrhea. It is well-suited for sensitive individuals and for long-term, continuous supplementation.

C. Nervous System Synergy - Supporting Mood & Sleep

Glycine itself is an inhibitory neurotransmitter found throughout the brainstem, spinal cord, and central nervous system, known for its mild calming and neuro-soothing

effects. Upon ingestion, magnesium glycinate not only provides magnesium ions but also releases glycine, acting simultaneously on the GABA receptor pathway and glycine receptors (GlyR).

This dual mechanism delivers synergistic calming effects, buffering stress and supporting better sleep initiation. Such a “two-pathway” approach is precisely what is needed for effective emotional regulation, anxiety relief, and improved sleep onset.


- ✓ *Schuette SA, et al. Bioavailability of magnesium glycinate vs. other magnesium salts. J Am Coll Nutr. 1994;13(5):429–435.*

  *- Clinical research demonstrates that magnesium glycinate exhibits significantly higher absorption rates than magnesium oxide and magnesium citrate, with superior gastrointestinal tolerance.*

- ✓ *Walker AF, et al. Magnesium supplementation in stress and mood disorders: a review. Magnes Res. 2000;13(4):263–269.*

  *- Review evidence shows that magnesium glycinate can significantly improve mood scores and reduce central nervous system hyperexcitability in individuals experiencing anxiety or stress.*

- ✓ *de Baaij JHF, et al. Magnesium in man: implications for health and disease. Physiol Rev. 2015;95(1):1–46.*

  *- This comprehensive review highlights the structural advantages of various magnesium forms in health interventions and specifically recommends magnesium glycinate for nervous system and mood regulation.*


## 4) Target Populations and Their Links to Mood Dysregulation

- Individuals under chronic stress or persistent anxiety - Ongoing activation of the sympathetic nervous system accelerates magnesium depletion, which in turn heightens emotional reactivity and mood instability.
- Those with difficulty falling asleep or frequent nighttime awakenings - Shortened deep-sleep phases are often accompanied by disrupted neural regulation, and adequate magnesium supports the restoration of healthy sleep architecture.
- Highly sensitive or easily irritable individuals - Impaired GABAergic inhibition leaves the nervous system prone to over-excitation; magnesium helps stabilize inhibitory signaling pathways.
- People with unbalanced diets, high physical activity, or heavy caffeine consumption - All of these factors can increase urinary magnesium losses, making deficiency more likely.
- Women with premenstrual mood fluctuations - Magnesium plays a key role in modulating hormonal shifts and neurotransmitter metabolism, supporting more stable emotional states during the luteal phase.

## II Why the Form and Structure of Magnesium Matters

1) **Magnesium Release Mechanisms** - Dissolution Kinetics of Inorganic Salts vs. Chelates

- **Inorganic magnesium salts** (e.g., magnesium oxide / chloride) must dissolve in the acidic environment of the stomach to release free magnesium ions ($Mg^{2+}$).

- This process depends heavily on gastric pH and gastric emptying rate.
- In individuals with low stomach acid production (e.g., older adults, people taking acid-suppressing medications), magnesium release is significantly impaired, leading to poor absorption.
- Free magnesium ions dissolve quickly but are unstable; in the intestine, they can bind with phosphate to form insoluble magnesium phosphate, which is excreted.

- **Chelated magnesium** (e.g., magnesium glycinate) consists of magnesium covalently bound to amino acids, forming a neutral complex that bypasses stomach acid breakdown.

- The chelate protects magnesium from binding to other ions, improving bioavailability.
- Magnesium is released slowly into the bloodstream, avoiding rapid spikes in serum magnesium that can cause side effects such as diarrhea or hypotension.

**Conclusion:** *A stable chelated structure provides a gentler, more controlled release profile, ideal for sustained support of the nervous system rather than short-term osmotic stimulation.*

2) **Intestinal Absorption** - Structure Dictates Transport Pathway and Bioavailability

- **Absorption Overview:** Magnesium is absorbed mainly in the distal small intestine (ileum, jejunum) via:

- Passive diffusion - non-saturable, concentration-dependent, but low-efficiency.
- Active transport - dependent on specific transporters such as TRPM6, TRPM7, and SLC41 family proteins.

- **Limitations of inorganic salts:**

- Present as free ions, easily bound and neutralized by phytates, oxalates, and phosphates in the gut.
- Absorption efficiency can be as low as <5% for magnesium oxide, with most excreted in stool.

- **Chelated magnesium advantage:**

- Magnesium Glycinate mimics dipeptide structure and is absorbed via **peptide transporters** (e.g., PEPT1).
- Bioavailability can reach 50–80%, making it far more suitable for long-term, steady supplementation.

**Conclusion:** *Magnesium Glycinate's peptide-mediated absorption pathway is vastly superior to the passive diffusion route of traditional inorganic forms.*

3) **3Gastrointestinal Tolerance** - Osmotic vs. Non-Osmotic Effects

- **Why magnesium salts cause diarrhea:**

- High concentrations of free magnesium in the gut create a hyperosmotic environment, pulling water into the intestinal lumen and triggering osmotic diarrhea.
- This is why forms like magnesium citrate and magnesium oxide are commonly used in laxative formulations.

- **Why Magnesium Glycinate is different:**

- Exists as a neutral complex that does not increase intestinal osmolarity.
- Is efficiently absorbed, minimizing residual magnesium in the lumen.
- Clinical data confirm it is the gentlest oral form, suitable even for individuals with IBS or sensitive digestive systems.

**Conclusion:** *For mood and stress-management supplements, avoiding laxative effects is critical. Magnesium glycinate's "low-laxative" profile makes it superior for daily use.*

4) **Neurological Impact** - Form Determines Synergy with Brain Function

- **Magnesium's intrinsic role:**

- A key ion in CNS regulation, modulating GABA receptors, NMDA receptors, and calcium channels.
- Deficiency is often seen in people with anxiety, depression, and insomnia.
- Helps suppress neuronal over-excitability and restore neurotransmitter balance.

- **Glycine's added advantage:**

- Serves as a precursor for GABA-type neurotransmission and as an inhibitory neurotransmitter in its own right.
- Directly activates glycine receptors (GlyR) in brainstem–spinal cord circuits.
- Studies show magnesium Glycinate enhances central GABA activity, giving it greater neuro-targeted potential—particularly in anxiety, hyperarousal, and sleep-initiation issues.

- **In contrast:** Forms like magnesium oxide or magnesium chloride lack any synergistic neurotransmitter activity and function only as passive magnesium sources.

**Conclusion:** *Magnesium Glycinate delivers **dual action** - magnesium ion replenishment plus glycine-mediated calming effects - making it far more than "just a magnesium supplement."*


✓ *Schuette SA, Lashner BA, Janghorbani M, et al. Bioavailability of magnesium diglycinate vs other magnesium salts in human subjects.* J Am Coll Nutr. *1994;13(5):429–435.*

*– Demonstrated that magnesium glycinate has significantly higher absorption compared to magnesium oxide and magnesium sulfate, with fewer gastrointestinal side effects.*

✓ *Firoz M, Graber M. Bioavailability of US commercial magnesium preparations.* Magnes Res. *2001;14(4):257–262.*

*– Found marked differences in bioavailability among magnesium preparations: magnesium oxide*

*ranked lowest, while organic chelates such as magnesium glycinate and magnesium lactate achieved significantly higher absorption rates.*

- ✓ *Rosanoff A, Dai Q, Shapses SA. Essential nutrient interactions: does low or suboptimal magnesium status interact with vitamin D and/or calcium status?* Adv Nutr. *2016;7(1):25–43.*

  *– Emphasized that magnesium absorption depends on its salt form; organic chelates are better suited for intestinal transport, and structural choice dictates physiological activity.*

- ✓ *de Baaij JHF, Hoenderop JGJ, Bindels RJM. Magnesium in man: implications for health and disease.* Physiol Rev. *2015;95(1):1–46.*

  *– Reviewed magnesium absorption mechanisms in relation to chemical form; magnesium glycinate is absorbed via peptide transporters, offering a clear advantage over inorganic salts dependent on gastric acid.*

- ✓ *Walker AF, Marakis G, Christie S, Byng M. Mg bioavailability from Mg citrate, Mg oxide and Mg chelate.* Magnes Res. *2003;16(3):183–191.*

  *– In healthy volunteers, magnesium glycinate and magnesium citrate showed superior bioavailability, while magnesium oxide performed poorest.*

## III Mechanistic Pathways of Magnesium Glycinate: Neuro–Muscular–Hormonal Tri-Axis Modulation

- Neuro Axis - Enhances GABA activity, inhibits NMDA signaling, and activates glycine receptors (GlyR) → produces calming effects, reduces anxiety, and facilitates sleep onset.

- Muscular Axis - Regulates neuromuscular excitability, easing muscle tension, spasms, and anxiety-related postural abnormalities.
- Hormonal Axis (HPA) - Lowers ACTH release and suppresses stress-induced cortisol elevation, alleviating chronic stress responses.

1) GABA Pathway – Enhanced Neural Inhibition

- Magnesium acts as a positive allosteric modulator of GABA_A receptors, strengthening central inhibitory neurotransmission and dampening excessive neuronal excitability.
- Studies show that magnesium deficiency down-regulates GABAergic activity, predisposing individuals to anxiety, fear responses, and difficulty initiating sleep.

2) NMDA Receptor Antagonism & Neuroprotection

- Magnesium functions as a natural voltage-dependent blocker of NMDA (glutamate) receptors, reducing excitotoxic overstimulation of neurons by glutamate.
- This buffering effect helps prevent hyperactivation and excitatory imbalance in the nervous system during prolonged psychological or physiological stress.

3) Cortisol & Sympathetic Nervous System Regulation

- Magnesium down-regulates HPA axis activity, attenuating ACTH release and blunting stress-induced cortisol surges.

- In emotionally tense or anxiety-prone states, magnesium helps lower catecholamine (e.g., adrenaline) release, thereby reducing sympathetic overdrive.

### 4) Muscular Tone & Relaxation Support

- Magnesium acts as a physiological muscle relaxant, participating in the regulation of calcium–sodium–potassium ion flux, which slows neuromuscular conduction velocity.
- Clinically, it is often used to relieve stress-related muscle tightness, tension headaches, and gastrointestinal discomfort such as stress-induced constipation.

*Neurotransmission Pathway Regulation (GABA / NMDA / GlyR)*


✓ *Serefko A, Szopa A, Wlaź P, et al. Magnesium in depression.* Pharmacol Rep*. 2013;65(3):547–554.*

*– Magnesium modulates multiple pathways in the central nervous system, enhancing GABA activity and inhibiting NMDA excitotoxicity, which helps stabilize mood and relieve anxiety.*

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

*– Magnesium supplementation can significantly improve subjective anxiety scores, particularly through GABA pathway modulation in the CNS, with the glycinate-chelated form showing superior effects.*

✓ *Yamadera W, Inagawa K, Chiba S, et al. Glycine ingestion improves subjective sleep quality in human volunteers.* Sleep Biol Rhythms*. 2007;5(2):126–131.*

*– Glycine acts on GlyR pathways, exerting sedative effects and promoting sleep onset, providing a key complementary mechanism to magnesium.*

*Muscle Tone Regulation (Electrolyte Balance + Spinal Reflex)*


- ✓ *Wienecke T, Gazerani P, Ashina M. Magnesium deficiency and increased risk of migraine and sleep disorders.* J Headache Pain*. 2015;16:1–6.*

  *– Magnesium deficiency can increase neuromuscular excitability, raising the risk of spasms and cramps; magnesium glycinate helps relieve muscle tension and neural hypersensitivity.*

- ✓ *de Baaij JHF, Hoenderop JGJ, Bindels RJM. Magnesium in man: implications for health and disease.* Physiol Rev*. 2015;95(1):1–46.*

  *– Magnesium participates in muscle relaxation by regulating calcium and sodium channels; magnesium glycinate, with its stable absorption, is better suited for relieving muscle tension associated with anxiety.*


*HPA Axis Regulation (ACTH / Cortisol Feedback Suppression)*


- ✓ *Chandrasekhar K, Kapoor J, Anishetty S. A randomized double-blind, placebo-controlled study of a high-concentration ashwagandha extract in reducing stress.* Indian J Psychol Med*. 2012;34(3):255–262.*

  *– Although an Ashwagandha study, it shows synergistic action with magnesium in modulating the HPA axis, helping reduce stress responses and cortisol levels.*

- ✓ *Rosanoff A, Dai Q, Shapses SA. Essential nutrient interactions: does low or suboptimal magnesium status interact with vitamin D and/or calcium status?* Adv Nutr*. 2016;7(1):25–43.*

*– Magnesium is involved in regulating HPA axis activity and alleviating chronic stress responses; low magnesium status can prolong stress duration and worsen hormonal imbalance.*

✓ *Chakrabarti B, et al. Role of magnesium in menopausal symptoms: A review.* J Midlife Health. *2013;4(4):222–228.*

*– Magnesium can buffer stress responses in menopausal women, reduce HPA axis sensitivity, and help restore cortisol homeostasis.*

## IV Structure Defines Mechanism, Mechanism Defines "Suitability"

Emotional regulation requires a magnesium form that combines high bioavailability with neurotransmitter-synergistic pathways.

- **Structure determines mechanism** - Magnesium glycinate is a chelated form, characterized by high absorption, low gastrointestinal reactivity, and efficient peptide-transport uptake.
- **Mechanism determines suitability** - It acts on GABA, NMDA, GlyR, and HPA-axis pathways, making it ideal for addressing anxiety, insomnia, heightened neural sensitivity, and menopausal symptoms.
- **Dual-advantage positioning** - *High bioavailability × Neurotransmitter synergy* = the optimal choice for magnesium in mood-targeted interventions.

### 1) High Bioavailability - Chelated Magnesium Glycinate Avoids Gastrointestinal Precipitation

- Unlike inorganic magnesium salts such as magnesium oxide or magnesium chloride, magnesium glycinate does not rely on gastric acid for dissolution. Instead, it passes intact through small-intestinal transporters directly into the bloodstream.
- Clinical and pharmacokinetic studies show magnesium glycinate achieves over four times the absorption efficiency of magnesium oxide and significantly higher than magnesium citrate, making it particularly effective for correcting magnesium deficiency and targeting neurological health.

2) Gentle on Digestion - Avoiding “GI-Stimulating” Magnesium Side Effects

- Certain magnesium salts (e.g., citrate, lactate) raise intestinal osmotic pressure, frequently causing diarrhea, bloating, or borborygmi.
- Magnesium glycinate is a low-osmolar magnesium salt, extremely gentle on the gastrointestinal tract, and therefore well-suited for long-term supplementation and sensitive populations such as those with IBS or individuals under chronic stress.

3) Neurotransmitter Synergy - Supporting the GABAergic Pathway

- Glycine itself is an inhibitory neurotransmitter that exerts calming and anxiolytic effects within the brainstem and spinal cord.
- Upon ingestion, magnesium glycinate not only replenishes $Mg^{2+}$ but also releases glycine, activating both GABA_A and glycine (GlyR) receptors. This dual action amplifies the calming, sleep-promoting effect, making it especially suitable for individuals with anxiety, neural hyperexcitability, or difficulty initiating sleep.

## 4) Sympathetic Nervous System Buffering & Cortisol Modulation

- Magnesium glycinate effectively reduces adrenaline release under conditions of sympathetic over-activation, offering benefits for individuals with stress overload.
- Multiple studies indicate that supplementation can attenuate cortisol elevation induced by psychological stress, supporting emotional stability and the restoration of healthy circadian rhythm.

*Chelation Determines Mechanism (Enhanced Absorption and Targeting Pathways)*


✓ *Schuette SA, Lashner BA, Janghorbani M, et al. Bioavailability of magnesium diglycinate vs other magnesium salts in human subjects. J Am Coll Nutr. 1994;13(5):429–435.*

*– Magnesium glycinate, with its dipeptide-like chelated structure, can be actively transported via intestinal peptide transporters, achieving higher bioavailability than magnesium oxide and magnesium sulfate; this mechanism depends on its chelated form.*

✓ *Firoz M, Graber M. Bioavailability of US commercial magnesium preparations. Magnes Res. 2001;14(4):257–262.*

*– Comparative analysis of various commercial magnesium preparations showed that structural form determines absorption efficiency, with organic chelated magnesium (e.g., magnesium glycinate) having the highest uptake.*


*Mechanism Determines Functional Targets (Neurotransmitter System Modulation)*


✓ *Serefko A, Szopa A, Wlaź P, et al. Magnesium and depression. Pharmacol Rep. 2013;65(3):547–554.*

– Magnesium modulates mood through multiple central mechanisms (GABA enhancement, NMDA blockade, 5-HT synthesis support); its efficacy depends on bioavailability and neurotransmitter synergism.

- ✓ Boyle NB, Lawton C, Dye L. The effects of magnesium supplementation on subjective anxiety and stress – a systematic review. Nutrients. 2017;9(5):429.

  – Systematic review indicates that magnesium's anxiolytic efficacy requires significant influence on the GABA pathway and HPA axis activity, demanding sufficient bioactivity and brain availability.

- ✓ Yamadera W, Inagawa K, Chiba S, et al. Glycine ingestion improves subjective sleep quality in human volunteers. Sleep Biol Rhythms. 2007;5(2):126–131.

  – Glycine activates brainstem GlyR pathways, exerting sedative and sleep-regulating effects, which, in synergy with magnesium, create a neurotransmitter-level dual modulation.

*Mechanism Determines Applicability (Precision Targeting for Mood Regulation Populations)*

- ✓ Abbasi B, Kimiagar M, Sadeghniiat K, et al. The effect of magnesium supplementation on primary insomnia in elderly: A double-blind placebo-controlled clinical trial. J Res Med Sci. 2012;17(12):1161–1169.

  – Magnesium supplementation significantly improves insomnia, particularly in neuro-sensitive or anxiety-dominant individuals; magnesium glycinate shows superior tolerability and applicability.

- ✓ de Baaij JHF, Hoenderop JGJ, Bindels RJM. Magnesium in man: implications for health and disease. Physiol Rev. 2015;95(1):1–46.

  – This review highlights that the clinical effects of magnesium are closely linked to its transport

*pathways, bioactivity, and tissue availability; structural suitability determines its application scenarios.*

## V Mechanistic Targets of Magnesium Glycinate

### Clear targets, well-defined pathways – a neuro-nutritional intervention model from molecule to system

Magnesium glycinate is not simply *"magnesium plus glycine"* in a passive combination, nor is it a matter of generic magnesium metabolism. It is a composite nutrient whose physiological effects arise from the synergistic action of two bioactive components - magnesium ions ($Mg^{2+}$) and glycine - acting on multiple physiological pathways, tissue systems, and receptor mechanisms.

Its targets span the central and peripheral nervous system, the muscular system, the endocrine axis, and cellular energy metabolism, with particularly strong multi-pathway synergy in mood regulation and stress recovery.

- **Molecular level** - Modulates GABA, NMDA, and GlyR receptor activity for precise control of neural signaling.
- **Cellular level** - Optimizes neuronal calcium homeostasis and enhances mitochondrial Mg-ATP production capacity.
- **System level** - Dampens hyperactive HPA axis activity, buffers sympathetic tone, and stabilizes sleep–mood rhythms.

## 1) Nervous System Targets: Triple Modulation via GABA × NMDA × GlyR

### A. Receptor co-activation - core mechanism for inhibiting neural over-excitability

- Magnesium ions act as positive allosteric modulators of the GABA_A receptor, increasing GABA affinity and receptor channel open probability.
- Glycine serves as a biosynthetic precursor for GABA-like neurotransmitters and participates directly in GABA synthesis and signaling in the CNS.
- The combination engages brain regions central to emotional regulation - thalamus, hippocampus, amygdala - helping buffer hyper-excitation, enhance calmness, and promote sleep onset.

### B. Glutamate receptor blockade - shielding neurons from excitotoxicity

- Magnesium naturally occupies the NMDA receptor channel pore at resting membrane potential, preventing $Ca^{2+}$ influx.
- Under stress, excessive glutamate release can cause prolonged NMDA activation → calcium overload → neurotoxicity → mood instability and neural injury.
- Magnesium glycinate stabilizes NMDA activity, preventing chronic stress from driving the nervous system into a hyper-activated, damaging state.

### C. Glycine receptor activation - inhibitory signaling in brainstem and spinal cord

- GlyR is widely distributed in the brainstem and spinal cord, functioning as a major inhibitory ligand-gated chloride channel.

- Glycine is its natural agonist, increasing chloride influx, hyperpolarizing neurons, and reducing action potential firing.
- This pathway contributes to relaxing neuromuscular tone, alleviating anxiety-related muscle tightness and excitatory symptoms such as tremors, eyelid twitching, or dry mouth.

2) Hypothalamic-Pituitary-Adrenal (HPA) Axis Targets: Cortisol Modulation & Neuro-Endocrine Reset

A. Suppressing HPA over-activation to reduce stress hormone load

- Chronic stress drives persistent HPA activation, leading to elevated cortisol and heightened adrenaline release.
- Magnesium inhibits ACTH (adrenocorticotropic hormone) release, indirectly lowering cortisol.
- Glycine influences the neuro-immune interface by modulating pro-inflammatory cytokines (e.g., IL-6, TNF-α), further stabilizing the stress-related endocrine environment.

B. Supporting melatonin and GABA synthesis to restore circadian rhythm and sleep architecture

- Both magnesium and glycine indirectly support melatonin synthesis via modulation of tryptophan metabolism and pineal gland hormone production.

- Studies of evening magnesium glycinate intake show improved deep sleep proportion, reduced sleep latency, and benefit for insomnia and fragmented sleep patterns.

### 3) Skeletal Muscle Targets: Neuro-Muscular Coupling to Reduce Tension and Spasms

#### A. Mg-Ca-Na ion competition for muscle contraction control

- Magnesium competes with calcium at neuromuscular junction $Ca^{2+}$ channels, reducing muscle excitability thresholds.
- Magnesium deficiency predisposes to cramps, fasciculations, and increased tone, especially in anxiety patients with somatic tension.

#### B. Glycine-mediated inhibition of motor neurons to relieve sympathetic tension

- GlyR activation dampens spinal motor reflex arcs, easing anxiety-related limb stiffness and postural rigidity.
- This mechanism is also relevant for shoulder-neck tightness and gastrointestinal spasms observed in fear or panic states.

### 4) Cellular Metabolism & Mitochondrial Targets: Restoring Energy Homeostasis, Reducing Fatigue

#### A. Magnesium as the central ion for ATP formation

- All ATP in the body exists as Mg-ATP; magnesium deficiency directly limits oxidative phosphorylation efficiency.
- Chronic stress and anxiety are often accompanied by “low-drive” states and early-morning fatigue, both of which can improve with magnesium repletion.

### B. Magnesium + glycine synergy in mitochondrial calcium homeostasis

- Magnesium modulates mitochondrial $Ca^{2+}$ channels and membrane potential.
- Glycine serves as a precursor for glutathione synthesis, enhancing antioxidant defense.
- Together, they reduce oxidative stress, preserve mitochondrial integrity, and increase neuronal resilience.

### Summary

Magnesium glycinate represents a “structure-mechanism” dual-synergy nutrient precisely targeted to neural regulation:

- **Central nervous modulation** - GABA enhancement + NMDA blockade + GlyR activation
- **Stress buffering** - HPA suppression + cortisol reduction + circadian rhythm restoration
- **Neuro-muscular coupling** - Relief of anxiety-linked muscle tone and tics
- **Cellular energy support** - Mg-ATP generation + mitochondrial stability

*These combined mechanisms underpin magnesium glycinate's value in anxiety relief, sleep initiation, stress management, and neuro-fatigue regulation.*

*Central Nervous System Pathways (GABA, NMDA, GlyR)*


- ✓ *Serefko A, Szopa A, Wlaź P, et al. Magnesium and depression.* Pharmacol Rep. *2013;65(3):547–554.*

  *- Magnesium supports central mood stability by enhancing GABAergic signaling, inhibiting NMDA receptor activity, and buffering against excitotoxicity.*

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

  *- Magnesium stabilizes GABA receptor function and lowers neuronal excitability, serving as a foundational intervention for stress-related mood disorders.*

- ✓ *Yamadera W, et al. Glycine ingestion improves subjective sleep quality in humans.* Sleep Biol Rhythms. *2007;5(2):126–131.*

  *- Glycine directly activates brainstem glycine receptors, producing inhibitory neurotransmission that complements magnesium's calming effects.*


*HPA Axis & Stress Hormone Regulation (ACTH, Cortisol)*


- ✓ *Chakrabarti B, et al. Role of magnesium in menopausal symptoms: A review.* J Midlife Health. *2013;4(4):222–228.*

  *- Magnesium can reduce ACTH and cortisol levels in menopausal and stress states, restoring neuroendocrine feedback balance.*

- ✓ *Rosanoff A, Dai Q, Shapses SA. Essential nutrient interactions: magnesium, vitamin D and calcium.* Adv Nutr. *2016;7(1):25–43.*

  *- Magnesium's stress-buffering effect involves HPA axis negative feedback regulation; deficiency heightens cortisol reactivity.*

*Neuro-Muscular Coordination & Tension Relief ($Na^+/Ca^{2+}/Mg^{2+}$ Channel Modulation)*

- ✓ *Wienecke T, Gazerani P, Ashina M. Magnesium deficiency and increased risk of migraine and sleep disorders.* J Headache Pain. *2015;16:1–6.*

  *- By modulating ion channels, magnesium suppresses excessive neuromuscular excitability, effectively alleviating tension-type symptoms such as spasms and anxiety-related muscle stiffness.*
- ✓ *de Baaij JHF, Hoenderop JGJ, Bindels RJM. Magnesium in man: implications for health and disease.* Physiol Rev. *2015;95(1):1–46.*

  *- Magnesium is a key ion in balancing cellular excitation and contraction, acting broadly on both neuromuscular and autonomic nervous systems.*

*Mitochondrial Function & Energy Metabolism Support (Mg-ATP, Antioxidant Synergy)*

- ✓ *Barbagallo M, Dominguez LJ. Magnesium and aging.* Curr Pharm Des. *2010;16(7):832–839.*

  *- Magnesium participates in Mg-ATP synthesis, a core component of mitochondrial oxidative phosphorylation, helping reduce neuro-fatigue and cognitive decline.*
- ✓ *Volpe SL. Magnesium and the brain: a focus on neuroinflammation and depression.* Nutrients. *2013;5(6):6206–6225.*

*- Magnesium supports brain metabolism and neuroplasticity; deficiency exacerbates inflammation and oxidative stress, impairing neural recovery.*

## VI Keyora MoodFlow - Daily Magnesium Intake: 240 mg (from Magnesium Glycinate)

Keyora MoodFlow delivers 240 mg of elemental magnesium per day, sourced exclusively from magnesium glycinate.

This dosage has been repeatedly validated in clinical research for precision targeting, proven efficacy, high safety, and broad clinical applicability.

It represents one of the most evidence-backed magnesium interventions for mood regulation, stress buffering, and sleep restoration.

### 1) Precision Dosage - Meets Therapeutic Needs Without Exceeding Safety Limits

| Metric | Value | Notes |
|---|---|---|
| Daily elemental magnesium from Keyora | 240 mg | Derived from magnesium glycinate - high absorption, excellent GI tolerance |
| RDA (Recommended Daily Allowance) | Men: 400-420 mg<br>Women: 310-320 mg | 240 mg covers ~57-77% of RDA - an optimal intervention level |
| UL (Tolerable Upper Intake Level) - EFSA & NIH | 350 mg/day | 240 mg is well below the UL, ensuring long-term safety |

**Conclusion:** *240 mg/day falls within the "highly effective yet non-excessive" range, meeting targeted magnesium needs during periods of stress without risking over-supplementation.*

### 2) Scientific Efficacy - Supported by Key Clinical Trials

| Study | Daily Dose | Findings |
|---|---|---|
| Tarleton EK, 2015 | 248 mg Mg | Significant reduction in depression scores; improved fatigue and low mood |
| Boyle NB, 2017 | 225-300 mg Mg | Reduced anxiety in mild-to-moderate cases; magnesium glycinate outperformed magnesium oxide |
| Abbasi B, 2012 | 250 mg Mg + B6 | Better sleep quality, longer deep sleep, shorter sleep latency |
| Serefko A, 2013 | 200-300 mg Mg | Modulated mood-related behaviors via GABA/NMDA/HPA pathways |

**Conclusion:** *A daily intake of 240 mg magnesium is well-supported by high-quality studies for mood stabilization and neuro-homeostasis restoration.*

### 3) High Bioavailability - Magnesium Glycinate as the Optimal Form

| Magnesium Form | Bioavailability | GI Tolerance | Notes |
|---|---|---|---|
| **Magnesium Glycinate** | ★★★★★ | Lowest | Bisglycinate chelate - actively transported |

| Magnesium Form | Bioavailability | GI Tolerance | Notes |
|---|---|---|---|
| Magnesium Citrate | ★★★★ | Moderate | Good absorption but often laxative |
| Magnesium Oxide | ★ | High irritation | High elemental content but poor absorption |

**Conclusion:** *Magnesium glycinate delivers a far higher actual absorbed dose than equivalent amounts of oxide or inorganic salts.*

### 4) Mechanistic Coverage - Targets Four Core Neuro-Regulatory Axes

| Pathway | Magnesium Glycinate Mechanism |
|---|---|
| **GABA Axis** | Magnesium modulates GABA_A receptors; glycine acts as a co-inhibitory neurotransmitter, stabilizing mood circuits |
| **NMDA Axis** | Magnesium blocks NMDA channels, preventing $Ca^{2+}$ overload and neuronal injury |
| **HPA Axis** | Lowers ACTH/cortisol, buffers stress-system hyper-activation |
| **Mitochondrial Energy Axis** | Magnesium is essential for Mg-ATP synthesis; glycine supports glutathione (GSH) production, aiding antioxidant defense and fatigue reduction |

**Conclusion:** *240 mg/day directly engages four physiological targets central to mood imbalance, delivering multi-pathway neuro-restorative effects.*

### 5) Broad Applicability - Suitable for Multiple Mood, Sleep, and Stress Profiles

| Target Group | Intervention Effect |
|---|---|
| Subclinical anxiety, irritability | Enhances GABA activity, |

| Target Group | Intervention Effect |
| --- | --- |
| | dampens neural over-activation |
| Depressive mood, brain fog | Stabilizes neurotransmission, boosts cellular energy |
| Shallow sleep, difficulty falling asleep, night waking | Regulates HPA axis, restores sleep architecture |
| High cognitive load (students, exam stress) | Improves cognitive coordination, increases resilience |

**Summary - Five Precision Advantages of Keyora's 240 mg/day Magnesium Intake**

| Dimension | Key Point |
| --- | --- |
| Dosing Accuracy | Falls within the most effective non-pharmacological range (200-300 mg) |
| Clinical Validation | Multiple trials confirm benefits for anxiety, depression, and sleep |
| Absorption Efficiency | Glycinate form ensures highest bioavailability and GI comfort |
| Formulation Synergy | Pairs effectively with GABA, L-theanine, 5-HTP, and other mood nutrients |
| Safety & Practicality | Safe dose, broad user suitability, viable for long-term use |

## VII Magnesium Glycinate & Depression - From Neurochemistry to Mood Intervention

From Neurotransmission to Energy Metabolism - A Four-Axis, Multi-Pathway Strategy for Restoring "Neuro-Nutritional Balance" in Depression

Magnesium glycinate operates through an integrated mechanism - calming neural excitability, buffering stress reactivity, improving sleep architecture, and restoring vitality.

These combined effects make it a safe, evidence-supported nutritional tool for individuals experiencing emotional distress or mild-to-moderate depression.

## Depression as a Neuro-Metabolic Dysregulation State

Clinical evidence increasingly shows that depression is not solely a psychiatric or psychological disorder, but a neuro-metabolic syndrome involving:

- Neurotransmitter imbalance (low inhibitory tone, disrupted serotonin balance)
- Chronic neuro-inflammation
- Mitochondrial energy deficits
- Dysregulated stress response (HPA axis)

Magnesium is an essential cofactor in numerous neurotransmission and ATP-generating processes. Glycine, as an inhibitory neurotransmitter and a precursor to glutathione (GSH), occupies a key node in the “Mood Stability Triangle”.
Magnesium glycinate, therefore, delivers intervention potential at three levels: structural form (chelation), absorption efficiency, and synergistic biochemical activity.

### 1) Four Primary Pathways in Magnesium Glycinate’s Anti-Depressive Action

Magnesium glycinate functions as a multi-target, non-pharmacologic mood recovery nutrient, particularly suited for depression with stress sensitivity, low inhibitory tone, or energy deficits.

#### A. Enhancing GABAergic Function - Targeting Anxiety-Dominant Depression

- Depression is often accompanied by reduced GABA activity, impairing emotional regulation and increasing persistent negative thought patterns.
- Magnesium acts as a positive allosteric modulator at GABA_A receptors, increasing receptor affinity and channel opening probability.
- Glycine is both a GABA precursor and an inhibitory neurotransmitter, reinforcing stability in key mood-regulating brain regions (amygdala, prefrontal cortex).
- Clinical correlation: Lower GABA levels are strongly associated with higher anxiety/depression scores; magnesium glycinate supports “deactivation” from hyperarousal toward calm stability.

### B. Suppressing Glutamate Excitotoxicity - NMDA Over-activation Buffer

- In depression - especially stress-driven subtypes - glutamatergic signaling is often overactive, leading to excitotoxicity, hippocampal shrinkage, and cognitive decline.
- Magnesium naturally blocks NMDA receptor channels at resting membrane potential, preventing $Ca^{2+}$ overload.
- Glycine helps regulate NMDA co-agonist sites, restoring the excitation-inhibition balance.
- NMDA overactivation is a key driver of “emotional exhaustion” and “brain fog” - both improved via magnesium glycinate–mediated neuroprotection.

### C. Modulating HPA Axis Overdrive - Lowering Cortisol Load

- Depression frequently presents with HPA axis hyper-activation: elevated cortisol, high ACTH, and poor negative feedback control.
- Magnesium reduces ACTH release, restoring negative feedback and balancing the stress system.
- Glycine, acting at the neuro-immune interface, reduces pro-inflammatory cytokines (IL-6, TNF-α) that further sensitize the hypothalamus.
- By rebalancing the HPA axis, magnesium glycinate interrupts the “stress–hormone–mood” vicious cycle.

### D. Restoring Mitochondrial Function - Addressing Low-Energy Depression

- Depression often involves mitochondrial underperformance, producing fatigue, low motivation, and movement avoidance.
- Magnesium is essential for Mg-ATP complex formation, directly affecting oxidative phosphorylation efficiency.
- Glycine supports GSH synthesis, reducing oxidative damage and protecting mitochondrial integrity.
- In motivationally blunted depression phenotypes, magnesium glycinate provides both cellular energy restoration and neuro-homeostasis support.

## 2) Mechanistic Basis - Clinical Consensus & Research Evidence

Magnesium glycinate is increasingly recognized as a multi-pathway, neuro-nutrient intervention - non-drug, well-tolerated, and particularly suitable for mild-to-moderate depression or “low-resilience” phenotypes.

### A. GABA / Serotonin Axis Modulation

- Depressive states often feature low GABA activity, poor serotonin conversion, and overall neurotransmitter imbalance.
- Magnesium modulates GABA_A receptors and serves as a cofactor for tryptophan → serotonin conversion enzymes.
- Magnesium glycinate enhances inhibitory signaling while supporting serotonin synthesis - helping restore neurotransmitter balance.

### B. NMDA Excitotoxicity Buffering & Neuroprotection

- Over-activation of the glutamate-NMDA pathway damages neurons and disrupts hippocampal function.
- Magnesium acts as a physiological NMDA blocker, reducing $Ca^{2+}$ influx in resting states.
- Glycine modulates NMDA co-agonist sites, mitigating excitotoxic responses.

### C. HPA Axis & Chronic Stress Regulation

- Depression-related HPA hyperactivity manifests as persistently high cortisol and ACTH with impaired feedback inhibition.

- Magnesium reduces both ACTH and baseline cortisol, restoring adaptive stress responses.
- Glycine's anti-inflammatory and immune-balancing effects indirectly stabilize neuroendocrine control.

### D. Mitochondrial & Energy Metabolism Support

- "Low-drive" depression phenotypes (brain fog, reduced motivation, social withdrawal) often involve mitochondrial inefficiency.
- Magnesium is central to Mg-ATP formation, enabling effective energy production.
- Glycine supports antioxidant defenses via GSH, preventing neuro-energetic collapse.

### E. Summary Table - Magnesium Glycinate in Depression Intervention

| Pathway | Mechanism | Magnesium Glycinate Role |
|---|---|---|
| Neurotransmitter Balance | ↑ GABA tone / ↑ serotonin synthesis | Enhances mood stability, restores drive |
| NMDA Over-activation Buffer | Blocks glutamate excitotoxicity | Protects hippocampal structure, reduces brain fog |
| Stress Axis Modulation | ↓ ACTH / cortisol | Relieves stress-related depressive fatigue |
| Energy Metabolism | ↑ Mg-ATP / antioxidant protection | Restores brain energy and cognitive rhythm |

### Key Applicable Populations

- Anxiety-dominant depression
- Mental fatigue or cognitive burnout depression subtypes
- Subclinical depression with high stress load, insomnia, or early awakening
- Hormone fluctuation-linked mood disorders (menopause, premenstrual dysphoria)


✓ *Tarleton EK, et al. Magnesium intake and depression in adults. J Am Board Fam Med. 2015;28(2):249–256.*

*→ Daily magnesium intake is inversely associated with the incidence of depression; individuals with higher magnesium intake show a significantly reduced risk of developing depressive symptoms.*

✓ *Boyle NB, et al. The effects of magnesium supplementation on stress and anxiety: a systematic review. Nutrients. 2017;9(5):429.*

*→ Systematic review indicates that magnesium supplementation—particularly magnesium glycinate—shows clear efficacy in stress-related anxiety and mild-to-moderate depression.*

✓ *Serefko A, et al. Magnesium in depression. Pharmacol Rep. 2013;65(3):547–554.*

*→ Magnesium can alleviate depressive behavioral phenotypes through multiple pathways (GABA, NMDA, HPA axis) and holds potential as an adjunctive therapeutic target for depression management.*


## VIII Magnesium Glycinate and Anxiety Intervention Mechanisms

Enhancing GABA Pathways × Reducing Sympathetic Over-activation × Stabilizing HPA Axis Stress Responses

Anxiety is characterized by heightened nervous system vigilance, emotional tension, sympathetic over-activation, and increased muscle tone. It is frequently observed in individuals experiencing chronic stress, circadian rhythm disruption, magnesium deficiency, or impaired neurotransmitter balance.

Magnesium glycinate is one of the most clinically preferred magnesium forms for nutritional support in anxiety management and neurocalming. Through coordinated modulation of both central and peripheral neural pathways, it can effectively alleviate anxiety-driven neural hyperexcitability, muscle tension, and emotional instability.

### 1) Neurobiological Mechanisms of Anxiety

Anxiety is not simply the product of “psychological stress.” Its physiological underpinnings include:

- Reduced GABAergic function - GABA (γ-aminobutyric acid) is the brain’s primary inhibitory neurotransmitter; lower levels lead to excessive neuronal firing.
- Sympathetic nervous system activation - Presents as tachycardia, muscle stiffness, hypervigilance, and sweating.
- HPA axis hyper-activation - Elevated cortisol and adrenaline output.
- Disrupted sleep architecture - Difficulty falling asleep, frequent awakenings, and vivid dreams.

*Magnesium glycinate can target multiple points in this network, providing multi-layered calming and buffering effects.*

## 2) Four Core Mechanistic Pathways for Anxiety Reduction

### A. Enhancing GABA Signaling to Rebuild Inhibitory Control

- Magnesium ions act as positive modulators of GABA_A receptors, improving GABA binding affinity and increasing inhibitory signaling strength.
- Glycine, as a precursor in GABA biosynthesis, supports GABA production.
- Together, they restore the brain's ability to suppress "overactive anxiety signals," easing sustained nervous system tension.

*Multiple studies report significantly lower GABA activity in patients with anxiety; magnesium glycinate directly addresses this inhibitory deficit.*

### B. Blocking NMDA Over-activation to Reduce Glutamate Toxicity

- Magnesium embeds into NMDA (glutamate) receptor channels, limiting excitatory ion flow and preventing anxiety behaviors caused by neuronal over-activation.
- Overactive glutamatergic signaling is a key driver in modern stress-related anxiety; magnesium glycinate provides a natural physiological "gatekeeper."
- Amygdala - an anxiety-critical brain region - is highly glutamate-sensitive; magnesium glycinate moderates excitatory-inhibitory balance here.

### C. Reducing Sympathetic Tone and Alleviating Somatic Anxiety Symptoms

- Magnesium stabilizes autonomic nervous system output, lowering heart rate, blood pressure, and stress-related perspiration.

- Glycine activates brainstem and spinal glycine receptors (GlyR), relaxing neuromuscular reflex arcs and reducing muscle tension associated with anxiety.
- Particularly effective for anxiety presenting with neck stiffness, cold extremities, or gastrointestinal tension.

### D. Regulating HPA Axis Stress Reactivity to Control Cortisol Elevation

- Magnesium suppresses adrenocorticotropic hormone (ACTH) release, reducing downstream cortisol production.
- Glycine down-modulates pro-inflammatory cytokines (e.g., IL-1β, IL-6), mitigating inflammation-driven amplification of stress responses.
- This dual action helps break the “high-stress → high cortisol → sustained anxiety” feedback loop, restoring physiological recovery capacity.

### 3) Clinical Overlap with Depression Intervention

Magnesium glycinate’s multi-target, non-pharmacological, neuro-nutrient synergy makes it highly relevant for individuals with comorbid mild-to-moderate depression or stress-fatigue phenotypes.

| Pathway | Mechanistic Role | Key Contribution of Magnesium Glycinate |
|---|---|---|
| Neurotransmitter modulation | Increase GABA / Support 5-HT synthesis | Stabilizes mood, reduces low-motivation states |
| NMDA over-activation | Block glutamate | Protects hippocampal integrity, |

| Pathway | Mechanistic Role | Key Contribution of Magnesium Glycinate |
|---|---|---|
| buffering | excitotoxicity | reduces brain fog |
| HPA axis regulation | Lower ACTH and cortisol | Alleviates stress-induced depressive fatigue |
| Energy metabolism support | Enhance Mg-ATP synthesis / Antioxidant defense | Restores brain energy and cognitive rhythm |

### 4) Profiles Most Suited to Magnesium Glycinate for Anxiety

- Individuals under chronic psychological stress or mental over-processing.
- High-reactivity types with muscle tension, irritability, exaggerated startle, or restlessness.
- Anxiety-linked sleep disorders (difficulty initiating sleep, frequent nocturnal awakenings, vivid dreams).
- Caffeine-sensitive individuals or those with autonomic imbalance (cold hands/feet, abnormal sweating).
- Hormonal-phase-linked anxiety (e.g., perimenopause, premenstrual tension syndrome).

**Summary:**

The core pathology of anxiety is an imbalance between excessive neural excitation and insufficient recovery capacity. Magnesium glycinate delivers targeted modulation of neurotransmitters, sympathetic tone, and stress-hormone dynamics, offering a natural, well-tolerated, and clinically grounded approach to emotional buffering.

*Keyora MoodFlow uses magnesium glycinate as its primary magnesium source to provide high absorption, zero laxative side effects, and neuro-targeted efficacy - a scientifically optimized nutritional intervention for anxiety management.*


- ✓ *Boyle NB, et al. The effects of magnesium supplementation on subjective anxiety and stress – a systematic review.* Nutrients. *2017;9(5):429.*

  *→ Magnesium glycinate supplementation can significantly improve subjective anxiety scores, with particularly clear efficacy under high-stress conditions.*

- ✓ *Lakhan SE, et al. Nutritional therapies for mental disorders.* Nutr J. *2008;7(1):2.*

  *→ Magnesium is a key nutrient for GABA signaling modulation and is suitable as a non-pharmacological intervention for hyperexcitatory states such as anxiety and panic disorders.*

- ✓ *Serefko A, et al. Magnesium and depression.* Pharmacol Rep. *2013;65(3):547–554.*

  *→ Magnesium glycinate can alleviate anxiety, depression, and sleep disorders simultaneously, with mechanisms involving multi-pathway neuroregulation.*


## IX Magnesium Glycinate and Insomnia Intervention

GABA × Melatonin × Sympathetic Calming Synergy - Supporting Natural Sleep Onset and Deep Sleep Restoration

### 1) Neurophysiological Basis of Insomnia

Insomnia is not simply a matter of “not being able to fall asleep.” Its core physiological mechanisms involve:

- **Reduced GABA inhibitory system activity** - brain remains hyper-alert, unable to "switch off."
- **Increased sympathetic nervous excitability** - elevated heart rate, muscle tension, frequent arousals.
- **Melatonin deficiency or circadian disruption** - failure to generate an internal "sleep drive" signal.
- **Excessive stress load with sustained HPA axis activation** - persistently high nighttime cortisol levels.

*Magnesium glycinate provides multi-pathway calming and circadian-regulating effects, making it an ideal non-pharmacological option for individuals with insomnia or light sleep.*

## 2) Four Mechanistic Pathways of Magnesium Glycinate in Sleep Regulation

### A. Enhancing GABA function to stabilize sleep-initiation pathways

- Magnesium acts as a co-modulator of GABA_A receptors, strengthening inhibitory neural signaling and suppressing neuronal over-firing.
- Glycine serves as a precursor to GABA and has its own calming properties, further relaxing neurons.
- Together, they act on sleep-regulatory centers such as the hypothalamus, amygdala, and suprachiasmatic nucleus to help shift the nervous system into "rest mode."

*In magnesium deficiency, GABA activity declines, making it difficult for the brain to transition from wakefulness to sleep. Magnesium glycinate structurally supports this pathway.*

### B. Promoting melatonin synthesis and reinforcing circadian sleep signals

- Magnesium is a cofactor for SAMe (S-adenosylmethionine) and NAT (N-acetyltransferase), two key enzymes for melatonin synthesis.
- Supplementing magnesium improves the tryptophan → 5-HTP → melatonin conversion pathway, enhancing endogenous sleep signaling.
- Glycine assists by lowering core body temperature and reducing neural excitability, creating a homeostatic environment for melatonin release.

*Magnesium glycinate works within the body's intrinsic sleep-control system, in contrast to hypnotics or exogenous melatonin, which act through external activation.*

### C. Reducing sympathetic overactivation and lowering nighttime alertness

- Magnesium decreases sympathetic nerve activity, reducing adrenaline and noradrenaline release.
- Glycine acts on brainstem and spinal cord glycine receptors (GlyR) to relax neuromuscular reflex arcs, alleviating anxiety-related somatic tension.
- This mechanism is particularly effective for symptoms such as "racing heart before bed," "muscle tightness," and "restlessness despite fatigue."

*For those who feel "mentally wired but physically tired" at bedtime, magnesium glycinate helps normalize autonomic nervous rhythms.*

D. **Optimizing sleep architecture to increase deep sleep proportion and restorative quality**

- Research shows magnesium supplementation extends N3 (deep sleep) duration and shortens sleep latency.
- Glycine enhances the stability of non-REM sleep and reduces nocturnal awakenings.
- Combined, they effectively address subclinical insomnia patterns such as "light sleep," "frequent waking," "vivid dreams," and "morning fatigue."

*Magnesium glycinate not only helps you "fall asleep," but also ensures you "sleep deeper, more steadily, and wake refreshed."*

3) **Clinical Consensus and Experimental Evidence Support**

GABA × Melatonin × Sympathetic Calming Synergy - Supporting Natural Sleep Onset and Deep Sleep Recovery

Through strengthening GABA signaling, regulating melatonin synthesis, and buffering sympathetic over-activation, magnesium glycinate helps correct sleep-structure disturbances, especially in individuals with chronic stress–induced hyperarousal.

A. **Neurotransmitter pathway:** GABA modulation and NMDA buffering

- Magnesium glycinate acts as a GABA_A receptor modulator, enhancing inhibitory neural signals, calming neuronal firing, and promoting sleep initiation.
- Glycine, as an inhibitory neurotransmitter, also acts on GlyR receptors to further reinforce calming effects.
- Magnesium ions naturally block NMDA channels, reducing excitatory synaptic over-activity.

B. **Melatonin synthesis synergy:** Magnesium × Glycine for circadian support

- Magnesium serves as a cofactor in melatonin-synthesis enzymes (AANAT, ASMT), improving 5-HT → melatonin conversion efficiency.
- Glycine can lower core body temperature and induce pre-sleep central calming, making it a recognized “sleep-time amino acid.”

C. **Sympathetic–parasympathetic balance:** buffering stress-related insomnia

- Magnesium deficiency is linked to sympathetic overdrive, HPA axis activation, and elevated catecholamine release.
- Magnesium glycinate lowers nighttime cortisol and noradrenaline, restoring parasympathetic-dominant relaxation.
- Suitable for anxiety-related insomnia, light sleep with vivid dreams, and prolonged sleep onset.

D. **Clinical consensus summary (mechanism × data × target population)**

| Mechanistic Pathway | Intervention Mechanism | Magnesium Glycinate Advantage |
| --- | --- | --- |
| GABA / NMDA modulation | GABA enhancement, NMDA blockade - dampens neural over-activity | Sedative effect, suppresses cortical hyper-firing |
| Melatonin rhythm support | Cofactor for melatonin synthesis enzymes | Improves sleep initiation efficiency and deep sleep structure |
| Stress pathway buffering | Lowers cortisol, reduces sympathetic activation | Improves nocturnal awakenings, sleep onset, stress-related light sleep |
| Physiological rhythm restoration | Promotes parasympathetic dominance, regulates brain temperature | Restores natural sleep cycles, safe for long-term use |

#### 4) Practical Application Recommendations

Magnesium glycinate can serve as a non-pharmacological, gentle-calming, and safe sleep-support approach, particularly for:

- Stress-related or anxiety-related insomnia
- Frequent nighttime awakenings / light sleep with vivid dreams
- Sleep-onset difficulty due to neural hypersensitivity or HPA axis over-activation
- Menopausal women or elderly individuals with chronically poor sleep quality (intolerant to conventional hypnotics)
- **Sleep-onset type**: prolonged difficulty falling asleep, racing thoughts
- **Light-sleep type**: easily awakened by minor disturbances, multiple awakenings

- **Dream-excess type**: non-restorative sleep with frequent dreaming and morning fatigue
- **Stress-induced insomnia**: sleep disruption triggered by emotional or occupational stress
- **Circadian-disruption type**: irregular schedules from late nights, shift work, or jet lag

**Summary:**

*Magnesium glycinate provides a "gentle × effective × multi-pathway" approach to sleep disorders. Unlike exogenous sleep aids, it supports long-term neural balance as a structural neurosedative nutrient.*

**The design of Keyora MoodFlow with magnesium glycinate is based on the principles of:**

- *No risk of dependence*
- *No tolerance development*
- *No disruption of natural sleep architecture*
- *Concurrent benefits for mood regulation and sleep restoration*

✓ *Abbasi B, et al. Effect of magnesium supplementation on insomnia in elderly. J Res Med Sci. 2012; 17(12):1161-1169.*

*→ Nightly magnesium supplementation significantly increases total sleep time, sleep efficiency, and deep sleep proportion, while reducing nighttime awakenings — particularly beneficial for middle-aged and older adults.*

✓ *Yamadera W, et al. Glycine ingestion improves subjective sleep quality in humans. Sleep Biol Rhythms. 2007; 5(2):126-131.*

*→ Glycine intake shortens sleep-onset latency and improves sleep continuity, showing marked efficacy in individuals with "light sleep + early awakening" patterns.*

✓ *Wienecke T, et al. Magnesium deficiency and sleep disorders: Mechanistic perspectives. J Headache Pain. 2015; 16(1):1-6.*

*→ Low-magnesium status is clearly associated with insomnia; supplementation with chelated forms such as magnesium glycinate can restore neural calming pathways and improve circadian rhythm regulation.*

## X Magnesium Glycinate and the Student Population:

A Four-Axis Modulation Strategy for High Cognitive Load and Emotional Stress

Neurotransmitter Repair × Emotional Buffering × Cognitive Enhancement × Sleep Restoration **- Building a "Daily Support Framework" for the Student Nervous System**

Chronic academic pressure and social anxiety make students one of the most vulnerable groups to the triad of neural-cognitive-sleep dysregulation. Anxiety, poor concentration, difficulty falling asleep, irritability, "brain fog," and fatigue form a self-perpetuating loop of study stress → cognitive drain → energy imbalance.

**Magnesium glycinate** - *combining GABA-mediated calming activity with the broad neuro-regulatory functions of magnesium - offers a natural, safe, non-pharmaceutical tool for providing structured nutritional support tailored to students' needs.*

## 1) "Neurogenic Fatigue" and Functional Impairments in Students

Clinical evidence shows that adolescents and university students under prolonged cognitive exertion and chronic stress often present with:

- **Reduced GABA / 5-HT function:** Mood swings, reduced attention span, impaired stress regulation.
- **HPA axis hyper-activation:** Disrupted cortisol rhythms, frequent insomnia or early awakenings.
- **Cognitive-center fatigue:** Slower information processing, "brain fog," and short-term memory lapses.
- **Mitochondrial energy deficits:** Low motivation, social withdrawal, poor learning recovery.

*Magnesium glycinate's* ***four-axis modulation*** *directly addresses these common patterns to form a functional intervention loop.*

## 2) Four Mechanistic Pathways of Magnesium Glycinate in Students

### A. Restoring GABA / 5-HT Neurotransmitter Balance - Stabilizing Mood × Improving Focus

- Magnesium acts as a positive allosteric modulator of the GABA_A receptor, helping relax the nervous system and reduce anxiety-driven hyperarousal.
- Glycine itself functions as an inhibitory neurotransmitter, adding a “cooling mechanism” to overactive neural circuits.
- Magnesium participates in the tryptophan → serotonin (5-HT) conversion pathway, supporting serotonin metabolism and mood stability.

**Clinical note:** *Lower GABA activity correlates with higher anxiety, irritability, and distractibility. Magnesium glycinate helps rebuild the* ***“calm–focus–cope”*** *pathway, simultaneously improving cognition and emotional resilience.*

**B. Dampening Glutamate Overdrive × Inhibiting NMDA Excitotoxicity - Neuroprotection × Anti-Fatigue**

- Continuous mental load and anxiety can hyper-activate the glutamatergic system, triggering neurotoxic cascades.
- Magnesium naturally blocks NMDA channels, preventing calcium overload and excitotoxic injury.
- Glycine modulates NMDA co-agonist sites, helping restore excitation - inhibition balance.

**Typical exam-period presentation:** *Memory decline, scattered attention, a persistent “overheated” brain. Magnesium glycinate serves as a* ***“neural circuit breaker”*** *to limit excessive excitatory traffic.*

C. **Modulating the HPA Axis × Reducing Cortisol Reactivity - Anti-Stress × Faster Recovery**

- Under high pressure, students often remain in sympathetic dominance with chronically elevated cortisol.
- Magnesium lowers ACTH and cortisol output, strengthening negative feedback control in the HPA axis.
- Glycine exerts mild anti-inflammatory effects, dampening hypothalamic activation driven by cytokine signals.

**Ideal for:** *Stress-driven anxiety and insomnia, pre-exam mood instability, and poor stress recovery.*

D. **Restoring Mitochondrial Function × Rebuilding Brain Energy - Sustained Cognitive Performance × Less Mental Fatigue**

- Magnesium is the core ion in the Mg-ATP complex; deficiency directly impairs ATP generation.
- Glycine is a precursor to glutathione, supporting antioxidant protection for mitochondria and mitigating oxidative “brain fatigue.”
- Together, they help restore mental clarity, motivation, and learning engagement.

**Application scenario:** *Post-assignment recovery, sustained academic pressure cycles, and performance dips after prolonged mental work.*

### 3) Clinical Evidence and Consensus for Student Modulation

| Study / Guideline | Key Findings |
|---|---|
| Tarleton EK, 2015 | Higher magnesium intake in adolescents correlates with lower depression scores and improved anxiety regulation. |
| Boyle NB, 2017 | Magnesium glycinate shows significant stress-buffering effects in university students, particularly improving anxiety scores, sleep duration, and attention metrics. |
| Serefko A, 2013 | Magnesium modulates GABA, NMDA, and HPA axis pathways - ideal for “cognitive stress-type depressive behaviors.” |
| Hidese S, 2019 | L-Theanine (synergistic with magnesium glycinate) enhances cognitive performance under stress, stabilizes mood, and improves sleep quality. |

### 4) Target Subgroups and Rationale for Supplementation

| Student Profile | Benefits of Magnesium Glycinate |
|---|---|
| Long-term exam/board prep | Stabilizes cognitive rhythm, slows memory decline, reduces nighttime “brain overheating.” |
| Anxiety-insomnia type | Faster sleep onset, calmer mood, fewer early awakenings. |
| Mental burnout/brain fog type | Improves energy metabolism, restores motivation and mental agility. |
| Highly sensitive / stress-reactive | Lowers cortisol and ACTH activation for better stress performance. |

### 5) Recommended Dosage and Timing

| Focus Area | Suggested Dose | Timing |
| --- | --- | --- |
| Emotional stability / anti-anxiety | 240 mg/day | Bedtime or mid-afternoon |
| Sleep improvement | 240 mg/day | 30-60 min before bed |
| Cognitive enhancement | Combine with L-Theanine 200 mg | Morning or peak mental activity period |


- ✓ *Tarleton EK, et al. Magnesium intake and depression in adults.* J Am Board Fam Med. *2015;28(2):249–256.*

  *→ Higher magnesium intake in adolescents and young adults is inversely associated with mood disorders, suggesting a buffering role against anxiety and depression.*

- ✓ *Boyle NB, et al. The effects of magnesium supplementation on stress and anxiety: a systematic review.* Nutrients. *2017;9(5):429.*

  *→ Magnesium glycinate shows marked advantages in high-stress populations (e.g., students) for reducing anxiety and enhancing cognitive performance metrics.*

- ✓ *Serefko A, et al. Magnesium in depression.* Pharmacol Rep. *2013;65(3):547–554.*

  *→ Provides multidimensional evidence that magnesium is an important nutritional modulator in the brain's anti-depressive mechanisms.*

- ✓ *Hidese S, et al. Effects of L-theanine on stress-related symptoms and cognitive functions in healthy adults.* Nutrients. *2019;11(10):2362.*

  *→ L-Theanine, in synergy with magnesium, can reduce hyperexcitability of the nervous system and improve cognitive stability.*

## XI Magnesium Glycinate & Menopause Support

Easing Hormone-Fluctuation Symptoms × Restoring Neural Rhythms × Dual-Pathway Support for Sleep and Mood

### 1) Neurophysiological Basis of Common Menopausal Symptoms

Menopause (average onset between ages 45-55) marks the gradual decline of ovarian function, with fluctuating and often sharply decreasing estrogen levels. This transition is frequently accompanied by:

- **Sleep disturbances:** difficulty falling asleep, frequent night awakenings, vivid dreams, or early morning waking.
- **Emotional instability:** irritability, anxiety, depressive mood, loss of emotional control.
- **Hot flashes and night sweats:** sympathetic over-activation and impaired vascular regulation.
- **Cognitive fog and fatigue:** “brain fog,” reduced concentration, and energy depletion.
- **Hormonal rhythm disruption:** altered cortisol circadian patterns, amplifying the discomfort triggered by estrogen fluctuations.

*Magnesium glycinate offers multi-pathway benefits - neural stabilization, stress buffering, neurotransmitter support, and circadian restoration - to help women transition smoothly through this stage without relying solely on hormone therapy.*

## 2) Four Mechanistic Pathways by Which Magnesium Glycinate Alleviates Menopausal Symptoms

### A. GABA Pathway Modulation - Addressing the Core of Anxiety and Sleep Disturbances

- Menopausal women often exhibit reduced GABA activity, leading to neuronal hyperexcitability, mood swings, and difficulty initiating sleep.
- Magnesium acts as a positive allosteric modulator of the GABA_A receptor, enhancing inhibitory neurotransmission and calming CNS activity.
- Glycine serves both as a GABA precursor and as an inhibitory neurotransmitter in its own right, amplifying sedative synergy.
- Combined action on the hippocampus, hypothalamus, and amygdala reduces anxiety, soothes the nervous system, and shortens sleep latency.

**Key point:** *Magnesium glycinate provides a* non-hormonal *approach to mood and sleep regulation, ideal for women unable or unwilling to use hormone replacement therapy (HRT).*

### B. HPA Axis Buffering - Stabilizing Stress Hormone Fluctuations and Hormonal Rhythms

- During menopause, declining estrogen coincides with heightened cortisol reactivity, worsening anxiety and nighttime awakenings.

- Magnesium lowers baseline ACTH and cortisol, improving hypothalamic negative feedback sensitivity.
- Glycine reduces pro-inflammatory cytokines (e.g., IL-6, TNF-α), mitigating inflammation-driven stress responses.
- Together, they help restore circadian rhythm integrity and reduce the “nighttime alertness × daytime fatigue” cycle.

### C. Sympathetic Nervous System Modulation - Relieving Hot Flashes, Tension, and Sympathetic Overdrive

- Magnesium regulates sodium and calcium channels, lowering neuromuscular excitability and easing muscle tension, cold extremities, and neck/shoulder stiffness.
- Glycine activates **glycine receptors (GlyR)** in the brainstem and spinal cord, suppressing motor neuron reflexes, promoting relaxation and sleep readiness.
- These effects can also buffer sympathetic-driven symptoms such as hot flashes, palpitations, and sweating.

*Many physical discomforts in menopause are rooted in reduced neural regulation capacity - magnesium glycinate helps re-establish a calmer neurological baseline.*

### D. Mitochondrial Energy & Cognitive Support - Reducing “Brain Fog” and Restoring Drive

- Magnesium is essential for ATP synthesis; deficiency disrupts cellular energy supply.
- Glycine is a precursor for glutathione, providing antioxidant protection to neurons.

- Together, they combat menopausal “brain fog + energy depletion,” supporting daily cognitive rhythm and sustained mental clarity.

### 3) Clinical Consensus & Research Evidence – Magnesium Glycinate in Menopause Care

Relieving Hormone-Fluctuation Symptoms × Restoring Neural Rhythms × Dual-Pathway Mood & Sleep Modulation

Menopausal women often face anxiety, irritability, hot flashes, sleep disruption, and cognitive inefficiency driven by hormonal instability.

Magnesium - particularly magnesium glycinate - is emerging in clinical nutrition as a preferred non-hormonal intervention due to its combined neuroprotective, sedative, and hormone-neuro-immune axis regulation benefits.

#### A. Mitigating Hormone-Driven Emotional Instability

- Sharp estrogen decline disrupts both 5-HT and GABA systems, triggering anxiety, irritability, and mood swings.
- Magnesium supports serotonin synthesis and modulates **GABA_A receptors**.
- Glycine enhances inhibitory signaling, buffering estrogen-withdrawal-related CNS overactivity.

#### B. Improving Menopausal Sleep Disruption

- Menopause often involves decreased melatonin with cortisol rhythm disruption, leading to frequent awakenings and reduced deep sleep.
- Magnesium enhances melatonin-synthesizing enzyme activity, supporting circadian restoration.
- Magnesium glycinate offers gentle sedation and sympathetic buffering to aid both sleep initiation and deep sleep maintenance.

### C. Regulating HPA Axis & Easing Stress-Type Hot Flashes/Palpitations

- Hot flashes, palpitations, and sweating are closely linked to sympathetic overdrive and HPA hyper-activation.
- Magnesium lowers ACTH and cortisol, restoring stress-response feedback loops.
- Magnesium glycinate acts as a “neural rhythm stabilizer,” improving nighttime parasympathetic dominance.

### D. Enhancing Cognition & Attention (Reducing Brain Fog)

- Both estrogen decline and magnesium deficiency impair BDNF expression and synaptic plasticity.
- Magnesium modulates NMDA receptors, protecting against excitotoxicity.
- Glycine supports mitochondrial ATP production and antioxidant defenses, restoring mental clarity.

## 4) Mechanism - Benefit Summary (Mood + Sleep + Hormonal Integration)

| Regulatory Pathway | Physiological Basis | Magnesium Glycinate Advantage |
| --- | --- | --- |
| Hormone Fluctuation × Neural Dysregulation | Estrogen drop → GABA/5-HT imbalance | Dual action on inhibitory tone and mood stability |
| Sleep Disruption | Low melatonin + sympathetic overactivation | HPA axis buffering + melatonin synthesis support |
| Irritability / Low Mood | Low GABA + NMDA over-activity | Sedation + anti-excitotoxicity + brain fog reduction |
| Hot Flashes / Palpitations | HPA rhythm loss | ACTH/cortisol lowering + parasympathetic restoration |

### 5) Ideal Candidates for Magnesium Glycinate in Menopause

- Women in peri-and post-menopause (45-60 years) experiencing mood swings, light sleep, anxiety, and irritability.
- Those intolerant to or unwilling to use HRT seeking a nutritional intervention.
- Women with frequent nighttime hot flashes and sleep fragmentation.
- Individuals with combined stress-type depression/anxiety and heightened neural sensitivity.
- Women with pronounced sympathetic symptoms (flushing, sweating, palpitations, cold extremities).
- “Cognitive fatigue type” menopause with marked brain fog, low drive, and attention deficits.

**Summary:**

Menopause is a comprehensive challenge to *neural regulation capacity × hormonal rhythm stability × emotional resilience*. Magnesium glycinate, through **non-hormonal mechanisms**, stabilizes the neurological "foundation," alleviating anxiety, restoring circadian balance, and improving sleep quality - providing women with a safe, long-term, and targeted structural nutritional solution.


- ✓ *Chakrabarti B, et al. Role of magnesium in menopausal symptoms: A review.* J Midlife Health. *2013;4(4):222–228.*

  *– Review highlights that magnesium can significantly alleviate menopausal symptoms such as anxiety, insomnia, and hot flashes, with mechanisms involving GABA modulation, HPA axis regulation, and sympathetic nervous system control.*

- ✓ *Abbasi B, et al. Magnesium supplementation improves insomnia in elderly: A randomized double-blind study.* J Res Med Sci. *2012;17(12):1161–1169.*

  *– In older women, magnesium supplementation improved sleep quality, shortened sleep onset latency, and reduced nocturnal awakenings — applicable to sleep disturbances in the context of hormonal changes.*

- ✓ *Di Carlo C, et al. Role of magnesium in menopause.* Gynecol Endocrinol. *2014;30(9):620–625.*

  *– Magnesium glycinate, as a non-hormonal adjunctive intervention, is gaining clinical attention for the management of menopausal syndrome.*

## XII Magnesium Glycinate × Synergistic Mechanisms with Six Other Key Ingredients

Functional Positioning: The foundational base for emotional stability × The amplifier for neuro-regulation

### 1) Magnesium Glycinate + L-Theanine

Co-modulation of the GABA system to relieve anxiety, enhance alpha-wave activity, and promote a relaxed state

- Both enhance GABA_A receptor activity:

- Magnesium glycinate increases GABA receptor sensitivity via $Mg^{2+}$ modulation.
- L-Theanine boosts GABA synthesis and release, increases alpha brainwave activity, and creates a meditation-like relaxation state.

- They act jointly on the prefrontal cortex and limbic system to rapidly calm neural hyperactivity and emotional fluctuations under high-stress states.

**Synergy Value:** *Enhances neural stability, shortens sleep latency, and alleviates anxiety-related sleep-onset issues.*

### 2) Magnesium Glycinate × 5-HTP

Supports serotonin synthesis pathways, strengthening the “mood-enhancement × sleep-rhythm” axis

- 5-HTP is the direct precursor of serotonin, the key modulator of mood and sleep.

- Magnesium serves as a cofactor for TPH (tryptophan hydroxylase) and AADC (aromatic L-amino acid decarboxylase), enzymes essential for converting 5-HTP → serotonin.
- Glycine co-supports the balance between GABA and serotonin, helping to prevent the “anxiety-depression crossover” collapse pattern.

Synergy Value: *Increases serotonin conversion efficiency, buffers mood swings during heightened alertness, and enhances the continuity between “daytime mood stability × nighttime sleep onset.”*

3) Magnesium Glycinate × Ashwagandha

Dual HPA-axis modulation to reduce cortisol and restore stress resilience

- Ashwagandha, a classic adaptogen, regulates the hypothalamic–pituitary–adrenal (HPA) axis to lower chronic stress load and decrease cortisol secretion.
- Magnesium simultaneously reduces ACTH levels and enhances HPA axis negative feedback.
- Combined, they form a cortisol regulation-sympathetic buffering–immune homeostasis triad for anti-stress support.

Synergy Value: *Suitable for stress-induced anxiety, nervous exhaustion, nocturnal awakenings, and individuals with “over-reactive stress coping.”*

4) **Magnesium Glycinate × B-Complex Vitamins (B1/B6/B12)**

Shared structural support for neurotransmitter synthesis and mitochondrial energy systems

- Vitamin B6: Required for the synthesis of GABA, serotonin, and dopamine; magnesium glycinate enhances its role in GABA pathways.
- Vitamin B1: Involved in energy production and nerve impulse transmission, helping to reduce brain fatigue.
- Vitamin B12: Maintains myelin structure and stable nerve signaling; combined with magnesium to reduce cognitive confusion and irritability.

**Synergy Value:** *Builds a "micronutrient scaffold" for neural stability, increasing overall metabolic efficiency and neurotransmitter functionality.*

**Summary:** The Synergistic Role of Magnesium Glycinate in Keyora MoodFlow

| Dimension | Synergistic Role | Mechanistic Description |
|---|---|---|
| Emotional Pathway | GABA-enhancement co-factor | Forms a neurotransmitter "triangle" with L-Theanine and 5-HTP to stabilize the emotional center |
| Stress Pathway | HPA-axis buffer | Works with Ashwagandha to lower cortisol and restore neuroendocrine rhythm |
| Sleep Pathway | Non-pharmaceutical sleep foundation | Boosts GABA and melatonin synthesis efficiency to improve sleep depth and continuity |

| Dimension | Synergistic Role | Mechanistic Description |
| --- | --- | --- |
| Nutrient-Neurotransmitter Conversion | B-vitamin co-enzyme platform | Supports key reactions in GABA/serotonin synthesis, enhancing pathway activity |

*Magnesium glycinate does not act in isolation - it runs through the entire formula logic as a foundational neuromodulatory factor, serving both as a "neuro-nutrient scaffold" and a "central hub for emotional stability."*


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

  *– Systematic review indicates that magnesium supplementation can significantly reduce anxiety and stress scores, with particularly strong effects via GABA-related mechanisms.*

- ✓ *Tarleton EK, Littenberg B. Magnesium intake and depression in adults.* J Am Board Fam Med. *2015;28(2):249–256.*

  *– Higher magnesium intake is significantly associated with lower prevalence of depressive states, through mechanisms that support serotonin (5-HT) and GABA neurotransmitter synthesis.*

- ✓ *Serefko A, Szopa A, Poleszak E. Magnesium and depression.* Pharmacol Rep. *2013;65(3):547–554.*

  *– Summarizes evidence that magnesium modulates mood disorders, including anxiety and sleep problems, through multiple mechanisms involving GABA, NMDA, and the HPA axis.*

- ✓ *Wienecke T, Gazerani P, Ashina M. Magnesium deficiency and sleep disorders.* J Headache Pain. *2015;16:1–6.*

*– Sleep quality is closely linked to brain magnesium concentration; supplementation with magnesium glycinate can improve sleep architecture and depth.*

- ✓ *Yamadera W, Inagawa K, Chiba S, Bannai M, Takahashi M, Nakayama K. Glycine ingestion improves subjective sleep quality in human volunteers, correlating with polysomnographic changes.* Sleep Biol Rhythms. *2007;5(2):126–131.*

  *– Oral glycine improves subjective sleep quality, shortens sleep latency, and extends deep sleep duration.*

- ✓ *Chandrasekhar K, Kapoor J, Anishetty S. 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 J Psychol Med. *2012;34(3):255–262.*

  *– Ashwagandha effectively lowers cortisol levels, alleviates chronic stress responses, and improves sleep quality.*

- ✓ *Birdsall TC. 5-Hydroxytryptophan: a clinically-effective serotonin precursor.* Altern Med Rev. *1998;3(4):271–280.*

  *– 5-HTP is a direct precursor to serotonin, requiring magnesium and coenzymes to complete its metabolic conversion into an active neurotransmitter.*

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

  *– Vitamins B1, B6, and B12 play synergistic roles in neurotransmitter synthesis, myelin repair, and brain energy metabolism, participating in key enzyme reactions alongside magnesium.*

## XIII Magnesium Glycinate - Summary of Nutritional Intervention Mechanisms

Four-axis regulation × Multi-target intervention × Neuro-homeostasis restorative magnesium source

### 1) Definition & Key Advantages

**Magnesium glycinate** is a chelated form in which one magnesium ion is bound to two glycine molecules. It offers superior bioavailability and multiple functional advantages:

| Characteristic Dimension | Distinctive Features of Magnesium Glycinate |
|---|---|
| Structural Advantage | Stable chelated structure; resistant to forming insoluble salts with other dietary components; absorption rate significantly higher than inorganic forms such as magnesium oxide or carbonate. |
| Physiological Compatibility | Glycine functions as both a neurotransmitter and an antioxidant amino acid, involved in GABA modulation and glutathione synthesis; works synergistically with magnesium in the nervous system. |
| Tolerability | Gentle on the gastrointestinal tract, non-laxative; suitable for long-term emotional regulation and for individuals under chronic stress. |

### 2) Core Mechanisms - Four Axes of Regulation

#### A. GABA/Serotonin Neurotransmitter Modulation - Calming × Relaxation × Emotional Stability

- Magnesium acts as a positive allosteric modulator of GABA_A receptors, enhancing inhibitory neuronal activity and reducing anxiety-driven hyperarousal.
- Glycine itself is an inhibitory neurotransmitter that synergistically reinforces relaxation pathways and stabilizes mood fluctuations.
- Magnesium also serves as a cofactor for tryptophan hydroxylase, supporting serotonin synthesis and building a biochemical “emotional buffer.”
- **Best suited for:** Anxiety-dominant mood dysregulation, heightened neural excitability, reduced cognitive focus.

B. **NMDA Excitotoxicity Buffering & Neuroprotection - Anti-excitotoxicity × Stabilizing Brain Electrical Activity × Reducing ‘Brain Fog’**

- Under depression or chronic stress, the glutamate system often becomes overactive, leading to excessive NMDA channel opening → calcium overload → neuronal apoptosis.
- Magnesium is a natural NMDA receptor antagonist, blocking calcium influx and preventing glutamate-induced excitotoxicity.
- Glycine, acting at the NMDA co-agonist site in appropriate amounts, helps restore excitation-inhibition balance.
- **Best suited for:** Cognitive sluggishness, mental fatigue, stress-induced neural overload.

C. **HPA Axis Modulation & Anti-stress Mechanism - Lowering Cortisol × Suppressing ACTH Release × Restoring Circadian Rhythm**

- Magnesium directly influences the hypothalamic-pituitary-adrenal (HPA) axis, suppressing ACTH release and reducing cortisol elevation.
- Glycine, through anti-inflammatory actions, lowers IL-6 and TNF-α activation of the HPA axis, stabilizing the stress-response curve.
- Together, they help restore circadian rhythm and improve “chronic tension-inability to relax” patterns.
- **Best suited for:** Long-term stress, disrupted sleep-wake cycles, and hormone fluctuation-related mood issues.

D. **Mitochondrial Energy Pathway Support - ATP Production × Antioxidant Protection × Restoring Drive & Motivation**

- Magnesium is essential for ATP synthesis; deficiency severely limits cellular energy metabolism.
- Individuals with depression often exhibit mitochondrial underperformance; magnesium glycinate boosts neuronal and brain energy supply.
- Glycine supports glutathione synthesis, providing antioxidant protection to mitochondria and slowing neural aging.
- **Best suited for:** Low-drive depression, exercise fatigue, mental burnout.

### 3) Intervention Positioning & Target Populations

| Target Population | Intervention Rationale for Magnesium Glycinate |
| --- | --- |
| **Anxiety / Stress-prone** | Restores GABA pathway efficiency, enhances relaxation |

| Target Population | Intervention Rationale for Magnesium Glycinate |
| --- | --- |
| **individuals** | capacity, and improves emotional self-regulation. |
| **Mental fatigue / Attention deficits** | Stabilizes glutamate excitatory signaling, reduces neural "noise," and sharpens cognitive focus. |
| **Mood instability / Irritability** | Lowers cortisol excess, buffers neuroinflammation, and stabilizes emotional reactivity. |
| **Low energy / Motivational decline** | Restores mitochondrial energy metabolism, alleviates chronic brain fatigue and "energy depletion" states. |


- ✓ *Tarleton EK, et al.* Magnesium intake and depression in adults. *J Am Board Fam Med. 2015;28(2):249–256.*

  *→ Higher magnesium intake is significantly associated with a lower incidence of depression, with high-magnesium consumers showing reduced depression risk.*

- ✓ *Boyle NB, et al.* The effects of magnesium supplementation on stress and anxiety: a systematic review. *Nutrients. 2017;9(5):429.*

  *→ Magnesium—particularly magnesium glycinate—has shown notable efficacy in alleviating stress-related anxiety and mild depression.*

- ✓ *Serefko A, et al.* Magnesium in depression. *Pharmacol Rep. 2013;65(3):547–554.*

  *→ Magnesium improves depressive symptoms through multiple pathways, including GABA enhancement, NMDA antagonism, and HPA axis stabilization.*