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Micronutrients and mood: Exploring nutrition-based therapeutic interventions in psychology

Dipankar Paul[1], Mahmudul Hasan[2], Nirupama Barman[3], Somy Mary Mathew[4], Souvik Tewari[5*]
[1]Assistant Professor and Head, School of Allied and Healthcare Sciences, Dhamma Dipa International Buddhist University, Sabroom, South Tripura, Tripura, India
[2] Nutritionist, Institute of Paediatric Neurodisorder and Autism, Bangladesh Medical University, Dhaka, Bangladesh
[3] Department of Dietetics and Community Nutrition Management, Vidyasagar University, West Bengal, India
[4] Assistant Professor, Department of Food Technology and Quality Assurance, Cochin Arts and Science College, Mankkakadavu, Kakkanad, Ernakulam, Kerala, India
[5] Assistant Professor, Department of Food and Nutrition, Swami Vivekananda University, Barrackpore, West Bengal, India

Abstract
Emerging evidence links micronutrient status to emotional regulation, cognitive function, and the risk and course of mood disorders. This review synthesizes biological mechanisms that connect vitamins and minerals to mood (including neurotransmitter synthesis, neuroinflammation, oxidative stress, and the gut–brain axis), evaluates clinical and epidemiological evidence for specific micronutrients (B-complex vitamins, vitamin D, magnesium, zinc, iron, selenium, vitamin C, and others), and examines the efficacy and safety of nutrition-based therapeutic interventions. We summarize limitations in current research design, identify promising areas for clinical translation, and propose recommendations for future research and clinical practice. The paper is intended as a balanced resource for psychologists, psychiatrists, nutritionists, and researchers interested in integrative approaches to mental health.

Keywords: Micronutrients, mood, depression, anxiety, vitamin d, b vitamins, magnesium, zinc, nutrition therapy, gut–brain axis

Introduction

Mood disorders (major depressive disorder, dysthymia, bipolar disorder, and clinically significant anxiety) are leading causes of disability worldwide. Pharmacotherapy and psychotherapy are front-line treatments (Cafarella *et al*., 2012) [12], but many patients remain partially treated or experience adverse effects. Nutrition — and specifically micronutrient status — has received increasing attention as a modifiable factor that could influence mood and treatment response. Micronutrients (vitamins and minerals required in small amounts) play critical roles in neuronal function, neurotransmitter synthesis, mitochondrial energy production, and regulation of inflammatory and oxidative processes that are implicated in the pathophysiology of mood disorders (Mucci *et al*., 2020) [31].

Mood disorders and food are closely interconnected, with dietary patterns playing a significant role in influencing emotional well-being and mental health. Nutrient-rich foods supply essential vitamins, minerals, antioxidants, and fatty acids that support neurotransmitter synthesis, regulate inflammation, and maintain optimal brain function. Diets high in whole grains, fruits, vegetables, nuts, seeds, and omega-3–rich foods have been linked to reduced symptoms of depression and anxiety, while highly processed foods, refined sugars, and unhealthy fats may worsen mood dysregulation by increasing oxidative stress and inflammatory responses. Additionally, the gut–brain axis highlights how gut microbiota, shaped by diet, influences serotonin production, stress response, and emotional regulation. Thus, dietary choices are not only crucial for physical health but also act as a powerful modifiable factor in preventing and managing mood disorders (Wang and Wang, 2016) [49].

This review addresses three related questions: (1) What biological mechanisms plausibly connect micronutrients to mood and emotional regulation? (2) What is the quality and strength of clinical and epidemiological evidence linking specific micronutrients to mood outcomes? (3) What practical, safe, and evidence-based nutrition-focused interventions have been tested or recommended in psychological practice?

Methods — search strategy and selection criteria

Inclusion/exclusion: Include human interventional and observational studies that measured micronutrient status and mood outcomes or tested micronutrient supplementation. Exclude single-case reports (unless mechanistically informative), studies with highly confounded dietary patterns that do not separate micronutrient effects, and non-peer-reviewed sources (Tapsell *et al*., 2016) [45].

Biological mechanisms linking micronutrients to mood

1. Neurotransmitter synthesis and function

Many micronutrients act as cofactors for enzymes that synthesize and metabolize monoamines and other neurotransmitters. For example, B vitamins (B6, B9/folate, and B12) are essential in one-carbon metabolism and in synthesis of serotonin, dopamine, and norepinephrine precursors. Tetrahydrobiopterin (BH4) –dependent pathways, which require folate and related cofactors, influence phenylalanine and tyrosine hydroxylation (Singh *et al*., 2014) [41].

2. Mitochondrial energy metabolism and neuronal resilience

Micronutrients such as iron, coenzyme Q (a quinone/cofactor), and certain B vitamins are critical for

mitochondrial oxidative phosphorylation and ATP production. Energy deficits in neurons can compromise synaptic function and plasticity — processes implicated in depression (Bansal and Kuhad, 2016) [7].

3. Oxidative stress and antioxidant defenses

Several vitamins and trace minerals (vitamin C, vitamin E, selenium, zinc) participate in antioxidant systems that neutralize reactive oxygen species (ROS). Excessive oxidative stress is associated with neuronal damage and inflammation; micronutrient insufficiency may exacerbate this state (Holton, 2021) [22].

4. Inflammation and immune modulation

Micronutrients modulate innate and adaptive immunity. Low levels of vitamin D, omega-3 fatty acids (often discussed alongside micronutrients but technically macronutrient/essential fatty acid), zinc, and selenium have been associated with higher systemic inflammatory markers, which in turn correlate with depressive symptoms (Erickson *et al*., 2020).

5. Gut–brain axis and microbiome interactions

Micronutrients shape gut microbiota composition and function; the microbiome influences mood via immune signaling, neurotransmitter production, and vagal pathways. Deficiencies in specific nutrients can impair gut barrier function and favor dysbiosis, indirectly influencing mood (Merino del Portillo *et al*., 2024) [30].

6. Epigenetic regulation and neurodevelopmental effects

One-carbon metabolism and methyl donors (folate, B12, choline) are central to DNA methylation, histone modification, and gene expression patterns relevant to neurodevelopment and stress-responsive pathways (Bekdash, 2023) [8].

Evidence for specific micronutrients

1. B-vitamins (B6, folate/B9, B12)

Rationale: Central in homocysteine metabolism and synthesis of monoamines. Elevated homocysteine is associated with depression and cognitive dysfunction.

Evidence summary: Observational studies often find associations between low folate or B12 and higher prevalence of depressive symptoms. Supplementation trials yield mixed results: some RCTs show modest benefit in depressive symptom reduction when folate/B12 are used as adjuncts to antidepressants, particularly in folate-deficient populations; other trials show no effect in unselected samples (Cuskelly *et al*., 1996) [14].

Clinical note: Screening for B12 deficiency is recommended in patients with depressive symptoms, especially older adults and those with malabsorption risks. Folate status may predict antidepressant response in some subgroups (Alpert *et al*., 2003) [4].

2. Vitamin D

Rationale: Vitamin D receptors and metabolizing enzymes are expressed in brain regions implicated in mood regulation; vitamin D influences neurotrophic and immune processes (Kiraly *et al*., 2006) [25].

Evidence summary: Cross-sectional studies report inverse associations between serum 25-OH-D levels and depressive symptoms (Song *et al*., 2016) [42]. RCTs are heterogeneous — some find improvement in mood with vitamin D supplementation in deficient individuals, particularly when baseline levels are low; pooled meta-analyses often report small overall effects with high heterogeneity (Shaffer *et al*., 2014) [40].

Clinical note: Consider checking 25-OH-D in patients with seasonal affective patterns or treatment-resistant depression; correct deficiency according to local guidelines (Jahan-Mihan *et al*., 2024) [24].

3. Magnesium

Rationale: Magnesium modulates NMDA receptor function, GABAergic signaling, and HPA axis activity.

Evidence summary: Small trials have reported rapid improvements in depressive symptoms with oral magnesium supplementation, but sample sizes are limited and methodologies vary. Observational data link low magnesium intake with higher depressive/anxiety symptoms.

Clinical note: Magnesium is generally safe at dietary supplement doses but can cause gastrointestinal upset and should be used cautiously in renal impairment (Botturi et al., 2020) [11].

4. Zinc

Rationale: Zinc is involved in synaptic plasticity, NMDA signaling, and immune modulation.

Evidence summary: Several trials indicate that zinc supplementation as an adjunct to antidepressants may improve outcomes, particularly in treatment-resistant cases. Low serum zinc correlates with depressive severity in some cohorts (da Silva *et al*., 2021) [15].

5. Iron

Rationale: Iron is required for tyrosine hydroxylase and other enzymes; iron deficiency anemia presents with fatigue and cognitive/mood disturbances.

Evidence summary: Iron deficiency — with or without anemia — is associated with higher rates of depressive symptoms, fatigue, and cognitive complaints. Treatment of iron deficiency can improve mood and energy, especially in anemic individuals (Arshad *et al*., 2023) [6].

6. Selenium

Rationale: Selenium is vital for selenoproteins involved in antioxidant defense and thyroid hormone metabolism; thyroid function is closely linked to mood.

Evidence summary: Epidemiological associations exist between low selenium and poor mood; interventional data are limited and inconsistent. Both selenium deficiency and excess carry risks (Santos *et al*., 2025) [39].

7. Vitamin C and other antioxidants

Rationale: Vitamin C participates in neurotransmitter synthesis (e.g., dopamine) and antioxidant defense.

Evidence summary: Few clinical trials focus on vitamin C alone for mood disorders; some small studies show short-term improvements in mood, particularly in stress contexts (Long and Benton, 2013) [28].

8. Multi-micronutrient and comprehensive formulations

Rationale: Because biochemical pathways are interdependent, multi micronutrient formulations may yield broader effects than single nutrient supplementation.

Evidence summary: Trials of broad-spectrum micronutrient formulas (sometimes combined with minerals and cofactors) show promising results in certain populations (e.g., pediatric bipolar spectrum symptoms, stress resilience) though heterogeneity and proprietary formulations complicate generalizability. Adherence, dosing, and safety monitoring are critical (Rucklidge and Kaplan, 2013) [37].

Clinical applications and therapeutic interventions

1. Screening and assessment

Routine dietary and clinical screening forms the foundation of micronutrient-based psychological interventions, particularly among populations at elevated risk such as the elderly, pregnant or postpartum women, individuals with restrictive eating patterns, and those with malabsorption disorders. Early identification of inadequate intake or physiological deficiency allows clinicians to prevent or mitigate mood disturbances linked to micronutrient imbalance. Comprehensive assessment should combine dietary history with targeted laboratory testing—including serum vitamin B12, folate, 25-hydroxyvitamin D, ferritin and iron studies, as well as zinc and magnesium when clinically indicated—to accurately identify deficiencies that may contribute to depressive symptoms, anxiety, cognitive decline, or fatigue. This individualized approach supports precise supplementation strategies, enhances treatment responsiveness, and integrates nutritional assessment as an essential component of holistic mental health care (Voros *et al*., 2025) [48].

2. Supplementation as adjunctive therapy

Supplementation serves as a valuable adjunctive strategy in managing mood disorders, but evidence emphasizes the importance of targeted rather than indiscriminate use. Correcting identified deficiencies—such as vitamin D insufficiency or iron deficiency anemia—has consistently shown meaningful improvements in mood, cognitive function, and overall psychological well-being. Rather than applying universal supplementation, clinicians are encouraged to tailor interventions based on laboratory findings and individual risk profiles. Research further suggests that specific micronutrients, including zinc and various B vitamins, can enhance the therapeutic effects of conventional antidepressant medications, contributing to better symptom reduction and treatment response. This adjunctive approach supports a more comprehensive, personalized treatment model that aligns nutritional status with psychological care (Adams *et al*., 2020) [2].

3. Dietary approaches

Whole-diet interventions are increasingly recognized as effective strategies for supporting mental health, with Mediterranean-style dietary patterns—rich in fruits, vegetables, whole grains, legumes, nuts, seeds, and healthy fats—showing the strongest evidence for mood enhancement. These diets provide a naturally diverse array of micronutrients, antioxidants, fibre, and anti-inflammatory compounds that collectively support neurotransmitter synthesis, gut–brain axis regulation, and oxidative balance. Emphasizing nutrient-dense foods over processed, high-sugar, and high-fat options helps stabilize energy levels, reduce systemic inflammation, and improve overall psychological resilience. Incorporating structured dietary counseling, culturally appropriate food choices, and long-term behavioral support enhances adherence and maximizes the therapeutic benefits of nutrition-based interventions for mood disorders (Kris-Etherton *et al*., 2021) [27].

Table: 1 Summary of Evidence on Micronutrients and Mood from Previous Published Studies

Micronutrient	Psychological/Mood Outcome	Mechanism of Action (Reported in Literature)	Key Findings from Previous Studies	Representative References
Vitamin B6 (Pyridoxine)	Depression, anxiety, irritability	Cofactor in serotonin, dopamine, and GABA synthesis	Supplementation improved depressive symptoms in mild-to-moderate cases, especially when combined with magnesium	Abraham & Hueston (2019) [1]; Young (2007) [50]
Vitamin B9 (Folate)	Major depressive disorder (MDD), cognitive decline	Methylation reactions; synthesis of SAMe, serotonin, norepinephrine	Low folate linked with higher depression risk; folate supplementation improved antidepressant response	Coppen & Bailey (2000) [13]; Gilbody *et al*. (2007) [19]
Vitamin B12	Depression, fatigue, cognitive impairment	Maintains myelin, neurotransmitter function	Deficiency strongly associated with depression and cognitive problems	Penninx *et al*. (2000) [35]; Almeida *et al*. (2010) [3]
Vitamin D	Depression, seasonal affective disorder	Regulates serotonin production; anti-inflammatory effects	Numerous RCTs show vitamin D supplementation reduces depressive scores, especially in deficient individuals	Anglin *et al*. (2013) [5]; Spedding (2014) [43]
Magnesium	Depression, stress, anxiety	NMDA antagonism; HPA-axis regulation	Meta-analyses show significant mood improvement among magnesium-deficient participants	Jacka *et al*. (2009) [23]; Tarleton & Littenberg (2017) [47]
Zinc	Depression, stress tolerance	Modulates glutamate transmission; BDNF expression	Low zinc is consistently linked to depression; supplementation enhances antidepressant efficacy	Swardfager *et al*. (2013) [44]; Nowak *et al*. (2009) [33]
Iron	Fatigue, low mood, cognitive impairment	Oxygen transport; dopamine synthesis	Iron deficiency associated with irritability, poor mood, reduced cognitive performance	Murray-Kolb & Beard (2007); Patterson *et al*. (2001) [34]
Omega-3 Fatty Acids (EPA, DHA)	Depression, bipolar disorder	Anti-inflammatory; modulates neuronal membrane fluidity	Large-scale meta-analyses show EPA-rich omega-3 significantly reduces depressive symptoms	Freeman *et al*. (2006); Grosso *et al*. (2014) [20]
Selenium	Anxiety, depression	Antioxidant; regulates thyroid hormones	Low selenium intake associated with depressed mood; supplementation showed mild improvements	Benton & Cook (1990) [9]; Rayman (2012) [36]

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