



# International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher  
RS Global Sp. z O.O.  
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## ARTICLE TITLE

NUTRITIONAL FACTORS AND THEIR ROLE IN MENTAL HEALTH -  
A CLINICAL REVIEW

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## DOI

[https://doi.org/10.31435/ijitss.4\(48\).2025.4390](https://doi.org/10.31435/ijitss.4(48).2025.4390)

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## RECEIVED

16 September 2025

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## ACCEPTED

08 December 2025

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## PUBLISHED

23 December 2025

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# NUTRITIONAL FACTORS AND THEIR ROLE IN MENTAL HEALTH - A CLINICAL REVIEW

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**ABSTRACT**

The aim of this study was to review the current scientific evidence on the effects of selected nutrients on mental health in the general population. Randomized controlled trials, metaanalyses, and systematic reviews published between 2018 and 2025 were analyzed, retrieved from the PubMed, Embase, and Google Scholar databases. The review considered associations between the intake of omega-3 fatty acids, B-group vitamins, vitamin D, zinc, magnesium, probiotics, prebiotics, and antioxidants (vitamins C, E, carotenoids, and polyphenols) and the occurrence of depressive, anxiety, and cognitive symptoms. Literature data indicate that deficiencies of these nutrients may affect neurotransmitter function, neuronal plasticity, inflammatory processes, and oxidative stress, linking diet to the pathophysiological mechanisms of mood disorders. Supplementation with omega-3 fatty acids, folic acid, magnesium, zinc, vitamin D, and selected probiotics demonstrated moderate improvement in mood and reduction of anxiety symptoms in most analyzed studies, while the results for vitamins C, E, and B<sub>12</sub> remain inconclusive. Beneficial effects of curcumin and  $\beta$ carotene were also observed in reducing oxidative stress and improving psychological wellbeing. The collected data suggest that an adequate supply of micronutrients and antiinflammatory components may support mental health, but the current evidence is limited by small sample sizes, short observation periods, and heterogeneity of interventions. In clinical practice, a balanced diet remains essential, while supplementation should be individualized and applied in cases of confirmed deficiency. This article summarizes the current state of knowledge and indicates directions for future research.

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**KEYWORDS**

Mental Health, Omega-3 Fatty Acids, Vitamin B<sub>6</sub>, Vitamin B<sub>12</sub>, Folic Acid, Zinc, Magnesium, Probiotics, Prebiotics, Antioxidants

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**CITATION**

Oliwia Wróblewska, Jakub Majewski, Barbara Pająk, Maria Kaniecka, Anna Karcz, Artur Koza, Hubert Boldys-Żegocki, Małgorzata Dworniczak, Sofiya Salash, Aleksandra Romaniuk. (2025) Nutritional Factors and Their Role in Mental Health - A Clinical Review. *International Journal of Innovative Technologies in Social Science*. 4(48). doi: 10.31435/ijitss.4(48).2025.4390

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**1. Introduction**

Mental health is a key component of human well-being and an important area of public health that requires integrated strategies for protection and promotion. Depressive and anxiety disorders are among the most common and burdensome mental illnesses, leading to reduced quality of life and disability. It is estimated that depression affects about 5.7% of the adult population, whereas anxiety disorders affect about 4.05% of the global population (1,2). Pharmacotherapy and psychotherapy remain the fundamental treatments for mental disorders, but the effectiveness of these interventions is limited, and some patients do not achieve full remission of symptoms (3). Additionally, adverse effects of psychotropic medications and heterogeneous clinical responses have prompted the search for complementary and supportive therapies. In recent years, there has been growing interest in the impact of diet and micronutrient intake on brain function, neurotransmitter metabolism, inflammatory processes, and oxidative stress.

A new field known as *nutritional psychiatry* analyzes the relationship between diet and mental state and explores the potential role of nutrients in the prevention and treatment of depressive, anxiety, and cognitive disorders (3). Data from the scientific literature indicate that deficiencies of omega-3 fatty acids, B vitamins, vitamin D, zinc, magnesium, and probiotics may influence neurotransmission, synaptic plasticity, and regulation of the hypothalamic-pituitary-adrenal (HPA) axis, thereby linking diet with the pathophysiological mechanisms of mood disorders (4,13,20,23,27).

The aim of the present work is a comprehensive review of recent clinical data on the role of these nutrients in maintaining mental health, including biological mechanisms, results of interventional studies, and potential clinical implications in the general population. The results of randomized controlled trials, metaanalyses, and large observational studies were taken into account, and potential controversies and research gaps were discussed.

## 2. Methodology of the Review

This review covered literature published between 2018 and 2025. Searches were conducted in the PubMed, Embase, and Google Scholar databases using keywords: “omega-3”, “EPA”, “DHA”, “vitamin B6”, “vitamin B12”, “vitamin D”, “folic acid”, “zinc”, “magnesium”, “probiotic”, “prebiotic”, “antioxidant”, “vitamin C”, “vitamin E”, “polyphenol” and “depression”, “anxiety”, “mental health”, “randomized controlled trial”, “meta-analysis”. Inclusion criteria included randomized controlled trials or meta-analyses examining the effect of a given substance on mental health, publications in English with full text available online, and a publication date between 2018 and 2025.

## 3. Omega-3 Fatty Acids (EPA and DHA)

### 3.1 Mechanisms of action:

Omega-3 fatty acids, especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are crucial for proper brain function. They are components of neuronal membrane phospholipids, strengthening membrane structure and maintaining fluidity. Proper membrane fluidity influences the efficiency of neural signal transmission by modulating

neurotransmitter binding and maintaining cellular signaling integrity (5). N-3 polyunsaturated fatty acids (PUFAs) have anti-inflammatory effects by limiting immune cell activation and reducing the production of classical inflammatory mediators such as prostaglandins (PG) and leukotrienes (LT) derived from arachidonic acid (6). They also reduce the production of proinflammatory cytokines and chemokines, including interleukin-1 $\beta$  (IL-1 $\beta$ ), interleukin-6 (IL6), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), which contributes to weakening the inflammatory response in the body (7). Increased inflammation can contribute to depression and anxiety. The antidepressant mechanism of omega-3 PUFAs may be related to their enzymatic metabolites. COX, LOX, and CYP450 enzymes convert omega-3 fatty acids into specialized lipid mediators such as resolvins, protectins, and maresins, which regulate the inflammatory response and immune function (8). Depression is a heterogeneous central nervous system disorder whose symptoms include anxiety, reduced energy, feelings of guilt, and loss of interest in daily activities. There is growing evidence linking low omega-3 intake to a higher risk of developing depression. Maintaining an appropriate omega-3 to omega-6 ratio supports proper neurotransmitter synthesis, and DHA - as a key component of neuronal membranes - supports hippocampal neurogenesis, which may play an important role in preventing and alleviating depressive symptoms (9).

### 3.2 Clinical Trials

A randomized controlled trial conducted in Japan in 2023 involved 60 patients with major depressive disorder (MDD) who were given 3.2 g/day of an EPA+DHA mixture or placebo

(soybean oil) for 12 weeks. The results showed a significantly greater reduction in Hamilton Depression Rating Scale (HAM-D) scores in the omega-3 group compared to placebo at weeks 4, 6, 8, and 12. It was found that patients with MDD treated with omega-3 had somewhat higher rates of remission and clinical response after 12 weeks compared to the placebo group, although these differences did not reach statistical significance. The authors suggested that omega-3 monotherapy may alleviate depressive symptoms and could be a potential alternative therapy for patients with MDD (10).

A 2024 meta-analysis including 23 randomized trials with 2,189 participants evaluated the effect of omega-3 supplementation on anxiety symptoms. It found that an additional 1 gram per day of EPA/DHA resulted in a moderate reduction in anxiety symptoms (SMD: -0.70), with the greatest improvement observed at doses around 2 grams per day. Doses below 2 g/day had no effect on anxiety, and doses above 2 g/day provided no additional benefit; supplementation was considered safe. The meta-analysis noted the limited quality of available evidence and substantial heterogeneity of results, underscoring the need for further well-designed clinical trials to obtain more reliable conclusions (11).

**Controversies:** Some studies have not confirmed the benefits of omega-3 supplementation for depression or anxiety, possibly due to differences in dosage, supplement composition

(EPA vs. DHA), duration of intervention, and characteristics of the populations studied. In the VITAL-DEP randomized clinical trial with over 18,000 adult participants, the impact of longterm omega-3 supplementation (1 g/day EPA+DHA) on the risk of developing depression and mood was assessed versus placebo. After a mean follow-up of 5.3 years, no significant difference was found between the groups in the incidence of new depressive episodes or in average mood scores. The authors emphasized that omega-3 supplementation did not confer tangible benefits in preventing depression in the general population, which may be due to participant heterogeneity, dose differences, and interactions with other dietary factors. These results suggest that the impact of omega-3 on mental health may be limited to selected patient groups and requires further, more precise clinical studies (12).

## **4. B Vitamins**

### **4.1 Vitamin B<sub>12</sub> (Cobalamin)**

Vitamin B<sub>12</sub> is an essential coenzyme in two key biochemical reactions: the conversion of Lmethylmalonyl-CoA to succinyl-CoA and the remethylation of homocysteine to methionine. The human body does not synthesize B<sub>12</sub> - its main sources are animal products (meat, fish, eggs, dairy) - thus, vegans and individuals with absorption disorders are at risk of deficiency. B<sub>12</sub> absorption is complex and requires release from food proteins, the presence of intrinsic factor, and absorption in the ileum; B<sub>12</sub> is also stored relatively well in the body (primarily in the liver). Vitamin B<sub>12</sub> plays a key role in metabolic processes involving carbohydrates, fats, and proteins, as well as in the maturation of red blood cells and the normal functioning of the central nervous system. Symptoms of B<sub>12</sub> deficiency are often observed in people with chronic neurological conditions and can include sensory disturbances, balance problems, memory and mood disorders, and cognitive impairment (13).

A Mendelian randomization study conducted in 2025 evaluated the relationship between genetically determined B<sub>12</sub> levels and the risk of mental disorders. The results showed that higher B<sub>12</sub> concentrations were associated with a reduced risk of pernicious anemia, but were not correlated with a reduced risk of depression, anxiety disorders, or cognitive decline (14). Nevertheless, in people with vitamin B<sub>12</sub> deficiency neurological disorders can occur, such as myelin damage, cognitive impairment, and psychiatric symptoms (15).

### **4.2 Vitamin B<sub>6</sub> (Pyridoxine)**

Vitamin B<sub>6</sub> plays a key role in numerous metabolic pathways important for nervous system function. As a coenzyme, it participates in the biosynthesis of major neurotransmitters such as serotonin, dopamine, and noradrenaline, thus influencing mood and emotion regulation. It also functions as a cofactor in the kynurenine pathway, where it reduces the formation of quinolinic acid - an NMDA receptor agonist that, in excess, can cause excessive neuronal excitation. Vitamin B<sub>6</sub> is also involved in the conversion of homocysteine to cysteine, leading to a decrease in homocysteine levels, which are known for their neurotoxic properties and NMDA receptor agonist activity. By participating in this pathway, vitamin B<sub>6</sub> indirectly supports the synthesis of glutathione, which regulates glutamate levels in the brain, protecting nerve cells from damage caused by excessive stimulation (16).

A randomized controlled trial from 2022 involving 478 young adults compared the effect of monthly high-dose vitamin B<sub>6</sub> supplementation (100 mg/day) and vitamin B<sub>12</sub> supplementation against placebo on mood and neuronal functions. Vitamin B<sub>6</sub> supplementation was shown to significantly reduce self-reported anxiety symptoms and showed a trend toward reducing depressive symptoms, while vitamin B<sub>12</sub> produced only a slight improvement. The authors suggested that the anxiolytic effect of vitamin B<sub>6</sub> may be due to its influence on increasing the synthesis of gamma-aminobutyric acid (GABA), which promotes inhibition of excessive neuronal excitation and restores the balance between excitatory and inhibitory processes in the central nervous system (16).

### **4.3 Folic Acid (Vitamin B<sub>9</sub>)**

Folic acid is an essential nutrient that must be obtained from the diet, and it is partly synthesized by gut microbiota. As a water-soluble vitamin, it plays a key role in cellular metabolism, including the synthesis of monoamine neurotransmitters such as dopamine, epinephrine, and serotonin. Enzymes such as methylenetetrahydrofolate reductase (MTHFR) and methionine synthase reductase (MTRR) are crucial for folate transformations, enabling the proper functioning of the one-carbon cycle and methylation processes in the central nervous system (17).

An umbrella meta-analysis from 2024 covering 11 meta-analyses on folate in depression treatment showed that folic acid supplementation significantly reduces depressive symptoms (standardized mean difference -0.42) and lowers depression scale scores by about 3 points. Observational studies indicate that low folate levels are associated with an increased risk of developing depressive symptoms - individuals with folic acid deficiency have about a 35% higher probability of developing depression. The results of meta-analyses also suggest that folate supplementation may be an effective adjunct to pharmacotherapy, alleviating depressive symptoms (18).

#### 4.4 Controversies about B Vitamins

Recent genetic studies using Mendelian randomization do not confirm a causal link between higher levels of vitamin B<sub>12</sub> and a reduced risk of mental disorders. In an analysis including various conditions, such as depression, anxiety disorders, and schizophrenia, higher genetically determined levels of B<sub>12</sub> were associated only with a significantly reduced risk of pernicious anemia, whereas no significant effect on mental health was found. These results suggest that vitamin B<sub>12</sub> supplementation may be beneficial primarily in individuals with its deficiency, but does not constitute a protective factor in the general population (19).

### 5. Zinc

#### 5.1 Role of Zinc

Zinc is an essential micronutrient that must be obtained through the diet to maintain normal levels in the body. It plays a critical role in protein synthesis, nucleic acid metabolism, gene expression regulation, as well as in processes of cell growth and division. An important role of zinc is its influence on the proper development and functioning of the central nervous system. Adequate zinc levels are necessary for correct neural tube formation and the proliferation of stem cells during development. Zinc modulates NMDA and GABA receptors and participates in glutamatergic neurotransmission. It also affects receptor activity at synapses. Fluctuations in zinc concentration can impact the central nervous system and may contribute to disorders such as depression or Alzheimer's disease (20).

#### 5.2 Clinical Trials

A randomized trial conducted in Iran in 2020 with 150 older adults (>60 years) examined the effect of supplementation with 30 mg of zinc daily for 70 days on levels of depression and anxiety. Participants were randomly assigned to either a zinc supplement group or a control group (no supplement). After the intervention, there was a statistically significant decrease in anxiety and depression levels in the zinc-supplemented group compared to the control group.

Additionally, the supplementation group showed an increase in serum zinc levels ( $p < 0.05$ ). The results indicate that regular zinc supplementation may alleviate symptoms of depression and anxiety in older adults. (21)

In the double-blind randomized clinical trial ZINCAiD (2025), the effect of zinc supplementation on cognitive function was evaluated in individuals with mild cognitive impairment (MCI) of Alzheimer's etiology. Forty-eight participants received 135 mg of zinc daily for 12 weeks (followed by 65 mg daily) or placebo in a 2:1 ratio. A pharmacodynamic response was defined as a decrease in ceruloplasmin levels by at least 20%. In the primary analysis, no significant differences were observed between the groups in cognitive function. However, post-hoc analysis showed that participants who responded biochemically to supplementation (the "responders") maintained stable cognitive function over 24 weeks, whereas those in the placebo group and non-responders showed cognitive decline ( $\Delta = -2.72$ ;  $p < 0.0001$ ). Additionally, the responder group had favorable changes in the Clinical Dementia Rating-Sum of Boxes (CDR-Sob) score ( $p = 0.017$ ) and a trend toward improvement in the Mini-Mental State Examination (MMSE) score ( $p = 0.09$ ). The authors suggest that zinc supplementation may help stabilize cognitive function in selected patients with MCI who exhibit a biochemical response, although further, larger studies are needed to confirm these observations (22).

### 6. Magnesium

#### 6.1 Role of Magnesium

Magnesium is an essential micronutrient required to maintain important physiological functions of the body. It is involved in nerve conduction, regulation of blood pressure, heart rhythm, and muscle contraction. Magnesium (Mg<sup>2+</sup>) acts as a cofactor for over 300 enzymes. It plays a key role in regulating ion channels, including the NMDA receptor for glutamate, which is critical for proper neuronal function. Magnesium is involved in modulating electrical conductance by controlling the activity of channel proteins at electrical synapses and regulating ion influx during chemical neurotransmission. As a result Mg<sup>2+</sup> supports both electrical and chemical neuronal communication, underlining its importance for synaptic plasticity and the formation of neural networks (23).

## 6.2 Clinical Trials

A meta-analysis and systematic review conducted in 2023 (325 adults, aged 20-60) compiled seven randomized trials evaluating the effectiveness of magnesium supplementation in treating depression. The studies showed a significant reduction in depression among individuals taking magnesium compared to those receiving placebo (standardized mean difference -0.919). The authors concluded that magnesium could be a valuable adjunct in depression therapy, but noted that further research is needed to fill gaps in knowledge (24).

A cross-sectional study of 3,172 Iranian adults aged 18-55 found a significant inverse association between magnesium intake and the risk of mental disorders. After adjusting for confounders, individuals with the highest magnesium intake had significantly lower risk of anxiety and depression symptoms. Women with the highest magnesium intake had a 39% lower risk of anxiety disorders (odds ratio [OR] = 0.61; 95% confidence interval [CI] 0.40-0.93), while normal-weight men and overweight women showed significantly lower risk of depression (OR = 0.45; 95% CI 0.20-0.99 and OR = 0.45; 95% CI 0.24-0.85, respectively). In summary, higher dietary magnesium intake was associated with reduced symptoms of depression and anxiety, whereas no significant association was observed with levels of psychological stress (25).

## 7. Probiotics and Prebiotics

### 7.1 Definition and Mechanisms

Probiotics are live microorganisms that, when consumed in adequate amounts, have a beneficial effect on human health. Prebiotics are selectively utilized by gut microbes and also positively influence human health. Synbiotics are combinations of probiotics and prebiotics, which together support the balance of the gut microbiota (26). It has been shown that probiotics and prebiotics can modulate activity along the gut-brain axis, which may support central nervous system function and contribute to the prevention and alleviation of certain mental disorders. In addition, prebiotics, probiotics, and synbiotics may have beneficial effects on cognitive processes such as attention, perception, and memory (27).

### 7.2 Clinical Trials

A 2023 meta-analysis of 13 randomized trials involving 786 participants showed that probiotics, prebiotics, and synbiotics significantly improved symptoms of depression compared to a placebo group (standardized mean difference -0.34). This effect was observed in both clinical populations and healthy individuals, with a stronger impact in patients diagnosed with depression. The greatest efficacy was noted in interventions lasting at least eight weeks and using strains of *Lactobacillus* and *Bifidobacterium*. The authors suggest that the beneficial effect may arise from modulation of the gut-brain axis and reduction of inflammatory processes, but they emphasize the need for further research (26).

In a randomized controlled trial from 2022 involving 119 adults with moderate psychological stress and low prebiotic intake, the effects of a high-prebiotic diet, probiotic supplementation, and a combination of both (synbiotic) on mental health were compared. It was shown that a high-prebiotic diet significantly improved overall well-being and reduced symptoms of low mood compared to placebo (effect size  $d = -0.60$ ,  $p = 0.039$ ). No significant improvement was observed in the groups receiving only probiotics ( $d = -0.19$ ,  $p = 0.51$ ) or the synbiotic combination ( $d = -0.03$ ,  $p = 0.92$ ). Additionally, the high-prebiotic diet had favorable effects on anxiety, stress, and sleep quality. The authors stress that despite promising results, further studies with larger populations, including clinical trials, are needed to confirm the efficacy and elucidate the mechanisms of action of the gut-brain axis (28).

**Controversies:** Despite these promising findings, research on probiotics is characterized by great heterogeneity in the preparations used. Some strains demonstrate beneficial effects (e.g., reducing symptom severity on depression scales), while others do not produce significant outcomes. Many studies have a limited duration of observation, and the lack of long-term trials makes it difficult to assess the durability of effects and the safety of prolonged use (29).

## 8. Antioxidants: Vitamins C, E, and Polyphenols

### 8.1 Oxidative Stress in Mental Health

Increased oxidative stress and decreased activity of antioxidant enzymes are observed in individuals with depression and anxiety. The body has an antioxidant defense system that helps counteract the negative biochemical changes resulting from oxidative stress. Among the elements of this defense are non-enzymatic antioxidants such as vitamins C and E, which play key roles in neutralizing free radicals (30).

### 8.2 Vitamin C

A randomized, double-blind, placebo-controlled trial was conducted in 50 healthy young adults with insufficient serum vitamin C levels ( $<50 \mu\text{mol/L}$ ). Participants received 500 mg of vitamin C twice daily or placebo for 4 weeks. The supplementation significantly increased serum vitamin C levels and positively affected certain measures of psychological functioning and general vitality. However, it did not significantly impact levels of stress, depression, or anxiety, although it did improve attention and response time in a Stroop test. These results suggest that vitamin C may support cognitive functions, but does not necessarily improve mood (31).

A meta-analysis of 10 randomized clinical trials involving a total of 836 participants showed that vitamin C supplementation did not lead to a statistically significant improvement in mood in the general population (Hedge's  $g = 0.09$ ; 95% CI: -0.15 to 0.33;  $p = 0.465$ ). However, in the subgroup of individuals with subclinical depression who were not receiving pharmacological treatment, a moderate, statistically significant improvement in mood was observed (Hedge's  $g = -0.18$ ; 95% CI: -0.35 to -0.01;  $p = 0.041$ ). The authors emphasize that while the overall effect of vitamin C on mood is limited, the results suggest its potential supporting action in individuals with mild mood disturbances. Further well-designed studies with larger samples are necessary to confirm the efficacy of this intervention (32).

### 8.3 Vitamin E

A 2022 meta-analysis including 306 participants evaluated the effect of alpha-tocopherol (vitamin E) supplementation on symptoms of anxiety and depression. In the analysis of anxiety outcomes, no significant therapeutic effect was found (SMD = -0.86; 95% CI: -2.11 to 0.40), while in the analysis of depression outcomes a moderate, statistically significant antidepressant effect was observed (SMD = -0.88; 95% CI: -1.54 to -0.21). The authors emphasize that vitamin E, due to its antioxidant and anti-inflammatory properties, may support neuronal function and reduce symptoms of mood disorders, but further studies with larger samples and standardized supplementation protocols are needed (33).

In a randomized, double-blind trial involving 40 women with polycystic ovary syndrome

(PCOS), supplementation with omega-3 fatty acids (1000 mg/day) combined with vitamin E (400 IU/day) for 12 weeks significantly improved measures of mental health compared to placebo. The treatment group showed a greater decrease in Beck Depression Inventory (BDI) scores ( $-2.2 \pm 2.0$  vs.  $-0.2 \pm 1.3$ ;  $p = 0.001$ ) as well as improvements in General Health Questionnaire (GHQ) and Depression Anxiety Stress Scales (DASS) scores ( $p < 0.001$  for both) than the placebo group. These improvements were accompanied by beneficial changes in the expression of genes related to inflammatory processes - a decrease in IL-8 and TNF- $\alpha$  and an increase in PPAR- $\gamma$  expression - suggesting that the psychological effects may be mediated by anti-inflammatory and metabolic mechanisms. These results indicate a possible synergistic effect of combining omega-3 fatty acids and vitamin E, as their combined antioxidant and anti-inflammatory properties correlated with a reduction in depressive symptoms. It should be noted, however, that the study population (women with PCOS,  $n = 40$ ) was specific and the sample size was small, therefore these results require confirmation in further, well-designed clinical trials on larger and more diverse groups (34).

### 8.4 Polyphenols (Curcumin)

Curcumin is a bioactive phenolic compound found in the rhizome of *Curcuma longa* (turmeric, a member of the ginger family). It is used as an ingredient in numerous dietary supplements due to its anti-inflammatory and antioxidant properties. Curcumin exhibits a strong antioxidant action - even several times greater than that of vitamins C and E. It increases glutathione production and neutralizes free radicals, protecting cells from oxidative stress. Additionally, it modulates the inflammatory response by regulating cytokines (IL-4, IL-6, IL-8, TNF- $\alpha$ ) and affects neurotransmission, for example by increasing the release of serotonin and dopamine and inhibiting monoamine oxidase (MAO) activity (35).

A randomized, double-blind RCT conducted in 2025 with 96 first-time mothers found that supplementation with curcumin (500 mg daily for 8 weeks) significantly reduced mean depression scores (MD = -2.5; 95% CI: -3.3 to -1.7;  $p < 0.001$ ) and anxiety scores (MD = -1.4; 95% CI: -2.1 to -0.7;  $p < 0.001$ ) compared to placebo. This study indicates the potential of curcumin as a supportive therapy for alleviating postpartum depression and anxiety symptoms in primiparous women. The observed significant reduction in mood scores confirms the beneficial impact of this natural compound on mental well-being during the postpartum period. However, due to the limited sample size and relatively short follow-up, further clinical

trials are needed to evaluate the long-term efficacy and safety of curcumin in different populations of postpartum women (35).

A narrative literature review published in 2022 by Lopresti analyzed the potential role of curcumin in the treatment of major depressive disorder (MDD). The author discussed the results of seven clinical trials in which curcumin was administered at doses of 500-1500 mg per day for 5-12 weeks, either alone or in combination with antidepressant medications. Most studies showed a statistically significant reduction in depressive symptoms compared to placebo. However, the author emphasized the need for further well-designed randomized trials using standardized high-bioavailability forms of curcumin (36).

## **9. Beta-Carotene and Other Carotenoids**

### **9.1 Role of Carotenoids**

Carotenoids are fat-soluble phytochemical pigments present mainly in fruits and vegetables, characterized by a broad spectrum of biological activities. They exhibit antioxidant, antiinflammatory, antibacterial, anti-aging, and anti-diabetic properties, and also have cardioprotective, neuroprotective, hepatoprotective, and osteoprotective effects. Among the carotenoids,  $\beta$ -carotene is the most important compound in the human diet, serving as a natural plant pigment (37).

### **9.2 Clinical Trial**

In a cross-sectional study conducted in Stockholm involving 1,139 adolescents aged 13-14 years (of whom 1,036 completed the two-day dietary record), researchers examined associations between antioxidant intake ( $\beta$ -carotene, vitamins C and E) and mental health. Participants self-reported their food intake using the RiksmatenFlexDiet tool and completed questionnaires assessing anxiety symptoms (short version of the Spence Children's Anxiety Scale, SCAS-S), psychosomatic symptoms (Psychosomatic Problems Scale, PSP), and health-related quality of life (HRQoL; Kidscreen-10). In regression analyses adjusted for sex, standardized body mass index (BMI), and total energy intake, higher  $\beta$ -carotene intake was significantly associated with lower anxiety levels (-1.23 points in the highest versus lowest tertile; 95% CI: -2.34 to -0.12), fewer psychosomatic symptoms ( $\beta = -0.91$ ; 95% CI: -1.69 to -0.13), and better quality of life ( $\beta = 0.89$ ; 95% CI: 0.11 to 1.68). Additionally, higher vitamin C intake was associated with fewer psychosomatic symptoms ( $\beta = -1.00$ ; 95% CI: -1.79 to -0.21), whereas vitamin E intake showed no significant associations with any of the mental health indicators. Interaction analyses observed some sex differences in relation to  $\beta$ -carotene and vitamin C intake levels, but no positive synergistic effects were identified. Overall, the results indicate that higher  $\beta$ -carotene intake is consistently associated with better mental health functioning in adolescents – including lower anxiety, fewer psychosomatic complaints, and higher quality of life - while vitamin C may have a predominantly beneficial effect on somatic well-being. The authors emphasize that, due to the cross-sectional design of the study, causal inferences cannot be made (38).

### **9.3 Controversies**

The evidence on the effectiveness of vitamins C, E, and other antioxidants in improving mental health is limited. Randomized trials involving young, healthy individuals often show little or no effect of these supplements on mood (31). The meta-analysis of vitamin E included small, heterogeneous populations and did not demonstrate a significant reduction in anxiety symptoms (33).

## **10. Vitamin D**

### **10.1 Vitamin D Function**

Vitamin D is a fat-soluble group of compounds that exists in two forms  $D_2$  and  $D_3$ . Its active metabolite,  $1,25(OH)_2D_3$ , is mainly responsible for maintaining normal calcium and phosphorus levels and proper bone development. The presence of vitamin D receptors in many tissues suggests that it also has extraskeletal functions - it influences immunity, cell proliferation and differentiation, and may modulate the risk of cardiovascular diseases and diabetes (39).

### **10.2 Clinical Trial**

A systematic review and meta-analysis of randomized controlled trials evaluated the effect of vitamin  $D_3$  supplementation on depressive symptoms in adults, including 31 studies with a total of 24,189 participants. The results showed that vitamin  $D_3$  significantly reduced symptoms of depression in both individuals with a diagnosis of depression and those without, with a stronger effect observed in participants already experiencing

depressive symptoms. The greatest benefits were observed with higher doses (around 8,000 IU per day), and interventions of short- to medium-term duration (8-24 weeks) produced better effects than long-term interventions. Supplementation did not show a significant effect on anxiety symptoms. The conclusions suggest that vitamin D<sub>3</sub> can be an effective support in alleviating depressive symptoms, although further studies are needed to determine optimal dosing and its effect on anxiety (40).

### **11. Controversial aspects and limitations of evidence**

Although many studies suggest that specific nutrients have a beneficial effect on mental health, it is important to highlight a number of limitations. Heterogeneity of interventions - differences in dosages, treatment durations, studied populations, and supplement formulations - makes it difficult to compare results and formulate clear recommendations. Additionally, most trials involved small groups of participants and short follow-up periods, limiting the assessment of long-term efficacy and safety. In many cases, supplements were used as adjuncts to standard pharmacotherapy, making it challenging to evaluate their independent effects. Dietary and lifestyle factors were often not controlled for, which can influence the outcomes. In some studies, participants had deficiencies of the nutrient being tested, and supplementation led to improvements in biological parameters - making it hard to generalize these results to a well-nourished general population. There are also studies available in the literature that have not confirmed the benefits of supplementation, which indicates the possibility of a publication bias, whereby positive results are more likely to be published. It is also worth considering the potential interactions between supplements and the risk of adverse effects resulting from overdose.

### **12. Conclusions and Practical Implications**

The literature review indicates that nutrients play an important role in maintaining mental health, and mood disorders, such as depression and anxiety - can be modulated to some extent through dietary and supplementation interventions. The nutrients examined include omega-3 fatty acids, B vitamins, vitamin D, magnesium, zinc, probiotics, and antioxidants such as vitamins C and E, carotenoids, and polyphenols. These nutrients share common mechanisms of action that are neuroprotective, anti-inflammatory, and antioxidant, affecting neuronal plasticity, neurotransmission, and regulation of the HPA axis.

Omega-3 fatty acids, especially EPA and DHA, exhibit antidepressant and anti-inflammatory properties, and their supplementation can alleviate symptoms of depression and anxiety, particularly in individuals with low fish consumption or omega-3 deficiency. B vitamins support the synthesis of neurotransmitters and the metabolism of homocysteine; their deficiencies are associated with worse mental health outcomes. Folate supplementation may enhance the effectiveness of antidepressant medications, whereas routine use of vitamin B<sub>12</sub> supplements is justified primarily in cases of deficiency. Zinc and magnesium act as neuromodulators, and their supplementation may support the treatment of mood disorders if a deficiency is confirmed by laboratory tests. Probiotics and prebiotics, through their impact on the gut-brain axis, can have a beneficial effect on psychological well-being. Meta-analyses indicate moderate mood improvement with interventions lasting at least eight weeks, especially using *Lactobacillus* and *Bifidobacterium* strains. A diet rich in prebiotic fiber further supports microbiota balance and stress reduction.

Antioxidants such as vitamins C and E,  $\beta$ -carotene, curcumin, and other polyphenols can reduce oxidative stress and inflammation, supporting cognitive function and overall wellbeing. Their beneficial effects have been mainly observed in populations with deficiencies or increased oxidative stress, whereas their preventative role in the general population requires further investigation.

Vitamin D may have beneficial effects on mental health, particularly by alleviating symptoms of depression in individuals with low vitamin D levels or existing depressive symptoms, although its effect on anxiety remains less clear. Vitamin D supplementation shows promise in supporting mood and nervous system function.

Despite many positive findings, current data are limited by small study sizes, short intervention durations, and heterogeneity of interventions. In clinical practice, priority should be given to a balanced diet rich in natural foods, and supplementation should be individualized and supervised by a specialist. Future research should focus on long-term effects, nutrient interactions, and the identification of biomarkers to determine which patient groups may benefit most from specific dietary interventions.

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**Funding Statement:** This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Ethics Approval:** Not applicable, as the study did not involve human participants or animals.

**Conflicts of Interest:** No conflicts of interest to declare

**Data Availability Statement:** The authors confirm that the data supporting the findings of this study are available within the article's bibliography

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