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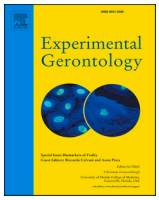

Review

The relationship between nutrition and depression in the life process: A mini-review

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ABSTRACT

Depression is one of the leading health problems, and >300 million people have a major depressive disorder and this number is getting increasing. Depression complicates the management of existing chronic diseases and the management of complications that may arise. A person's mental state can affect their food preferences, and food preferences can also affect their mental state. In this paper, depression and eating behavior, diet quality, folic acid, vitamin B12, vitamin B6, vitamin D, omega-3 fatty acids, magnesium, selenium, zinc and copper, prebiotics and probiotics are discussed. Research on the subject emphasizes that diet quality may also affect the occurrence of depression. However, studies also indicated that dietary nutrients such as folic acid, vitamin B12, vitamin B6, omega-3 fatty acids, zinc, selenium, and magnesium might be associated with the risk of depression.

1. Introduction

The World Health Organization (WHO) stated that >300 million people have major depressive disorder and depression is one of the leading mental problems (The World Health Organization, 2017). Major depressive disorder is responsible for approximately 800,000 suicides per year (Cheung et al., 2019). It is known that depression complicates the management of existing chronic diseases and the management of complications that may occur in individuals. Depression is a risk factor for diabetes and chronic heart disease (Katon, 2022). It has been reported to be associated with education level, body weight, and genetic factors (Wray et al., 2018).

It is known that some foods and dietary habits affect mental health. The situations of individuals can affect their nutritional status, as well as their food preferences, which can affect their mental state. Psychological, physiological, genetic, and social functions affect the eating behaviors of people, food intake, and food preferences (Paans et al., 2018a).

Subtypes of major depressive disorder could affect body weight and appetite. The atypical major depressive disorder causes an increase in appetite, body weight, and body mass index values, leading to an increase in chronic diseases. The melancholic major depressive disorder causes a decrease in appetite and loss of body weight (Mills et al., 2020). Food preferences for increasing food intake due to depression consist of fast food, snacks, low food quality, and high-energy foods. In addition, individuals with severe depression have an unhealthy diet and a decrease in the consumption of vegetables, fruits, fish, chicken, milk, and grains (Paans et al., 2019). Among the reasons for the relationship between depression and obesity; cigarette consumption, a decrease in physical activity level, and bad eating habits are shown (Paans et al., 2018b). While it is thought that excessive consumption of soft drinks may increase the risk of depression, it is thought that consumption of tea and coffee is inversely proportional to the risk of depression, and sugary drinks may increase the risk of depression (Y. Kang et al., 2018; Hu et al., 2019). In one study, it was seen that the risk of depression increased in women who consumed fast food, ketchup, mayonnaise, refined grains, and high amounts of sugar and fat. It was observed that the risk of depression decreased in women with higher consumption of foods such as vegetables, fruits, eggs, nuts, and olive oil (Saeidlou et al., 2021). In a study which is conducted on women with major depressive disorder or anxiety disorder, the incidence of eating disorders was found to be four times higher (Garcia et al., 2020). In another study, it was found that the risk of depression was associated with poor food quality, inadequate protein intake, and irregular meals (Kim and Lee, 2022). In a study examining individuals aged 45–75 with major or subclinical depression, it was determined that the incidence of depressive symptoms decreased as the rate of adherence to the Mediterranean Diet increased (Oliván-Blázquez et al., 2021). In another study, it was reported that the

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incidence of depressive symptoms was higher in individuals with low fruit and vegetable consumption and that adequate fruit and vegetable consumption was associated with a decrease in the prevalence of depression (Ju and Park, 2019; Wolniczak et al., 2017). In addition, it has been reported that the increase in the frequency of eating with family in elderly individuals reduces the risk of suicidal ideation and depression and is inversely proportional (D. Kang et al., 2018).

2. Method

The literature review was realized during the period of February–August 2022 through the chosen websites including the World Health Organization (WHO), Science Direct, PubMed, Google Scholar, Cochrane Central, Web of Science, Embase, The MEDLINE, and www.ClinicalTrials.gov. The articles were searched using the keywords such as "depression nutrition, depression and eating behavior, diet quality, nutrients health benefits/effects, folic acid, vitamin B12, vitamin B6, vitamin D, omega-3 fatty acids, magnesium, selenium, zinc and copper, prebiotics and probiotics, minerals, vitamins". Studies on depression nutrition have investigated clinical human, animal, in vitro and in vivo studies. Articles published only in abstract form were excluded. The year of publication was not restricted. Studies were identified by manually searching the reference lists of relevant original and review articles. Inclusion criteria were as follows: the publication in peer-reviewed journals in English; specific consideration of nutrient intake concerning depression outcomes. Articles published only in abstract form were excluded.

3. The relationship of nutritional status to depression at all stages of the life cycle

It is thought that diet quality is associated with the risk of depression, the mother's diet quality affects the child's mental health, and diet quality is associated with depression at every stage of the life cycle (Marx et al., 2021). It was found that poor diet quality in older women doubled the likelihood of depressive symptoms compared to men with poor diet quality (Gomes et al., 2018). A meta-analysis study concluded that diet quality, micronutrient intake, adherence to the Mediterranean Diet, and food choice may have effects on depression (Ljungberg et al., 2020). In another study, it was found that a strong association between adherence to the Mediterranean Diet and the risk of depression. It has been observed that the severity of depression is lower in individuals with high grain and vegetable consumption (Gibson-Smith et al., 2020). In older adults, alcohol consumption of <40 g/day for men and <24 g/day for women did not appear to have a protective effect on depression, consistent with the moderate Mediterranean Diet (García-Esquinas et al., 2018). As a result of the healthy nutrition program applied to young adults for 3 months, it was observed that there was a decrease in depression scores (Francis et al., 2019). In another study, it was determined that the risk of depression was higher in the group with high consumption of refined sugar and sweets, and low consumption of legumes, vegetables, and fruits (Grases et al., 2019). Another study reported that high-quality carbohydrate consumption was effective in reducing the risk of depression (Sanchez-Villegas et al., 2018). Iron, folic acid, omega-3 fatty acids, selenium, potassium, magnesium, vitamin A, vitamin B12, vitamin B6, and vitamin C, It is thought that the consumption of foods containing thiamine and zinc will increase the Antidepressant Nutrient Score designed for the prevention and treatment of depression (LaChance and Ramsey, 2018).

3.1. Omega-3 fatty acids

Omega-3 fatty acids have an important role in the functioning of the brain with their neuroinflammation, neurogenesis, and neurotransmission effects. The deficiency of omega-3 fatty acids increases the risk of psychological disorders such as attention disorder, attention deficit, schizophrenia, bipolar disorder, depression, and dementia. Docosahexaenoic acid and eicosapentaenoic acids play a role in the pathophysiology of depression (Lange, 2020). The American Psychiatric Association emphasizes that omega-3 fatty acids play a role in brain development and functioning due to their effects on serotonin and dopamine transmission (Clay, 2017). It also recommends giving omega-3 fatty acid supplements for the treatment of depressive disorders, psychotic disorders, and impulse control disorders (Nasir and Bloch, 2019). In the Dutch Depression and Anxiety Study, lower levels of omega-3 fatty acids and DHA were associated with higher rates of depressive symptoms in individuals (Thesing et al., 2018). There was no significant difference in monounsaturated fatty acids, saturated fatty acids, omega-3 fatty acids, and n−3/n−6 ratios between the group with and without major depression (Hamazaki et al., 2021).

The prevalence of depression was found to be lower in individuals consuming moderately fatty fish (about 20-30 g/day) or those with 0.5–0.15 g/day omega-3 fatty acid intake (Sánchez-Villegas et al., 2018). In one study, it was stated that as the omega-3 fatty acid level decreases, the symptoms of depression increase (Milaneschi et al., 2019). It is also thought that consuming 1 g daily of omega-3 fatty acids with an EPA content of 60.0 % or more may have positive effects on depression (Liao et al., 2019).

3.2. Vitamin D

It is known that there is a relationship between the development of depression and vitamin D. Vitamin D plays a role in the production of serotonin (Berridge, 2017). With the conversion of 7-dehydrocholesterol to vitamin D3, the synthesis of vitamin D begins in the skin. In the brain, the vitamin D receptor regulates serotonin synthesis by genetic mechanisms (Ceolin et al., 2021). While vitamin D induces the expression of the tryptophan hydroxylase 2 gene, which is involved in serotonin synthesis, it suppresses the expression of tryptophan hydroxylase 1. Vitamin D is effective in preventing depression by keeping serotonin levels at normal levels. High levels of reactive oxygen species and Ca^{+2} in neuronal cells in those with vitamin D deficiency explain the relationship between vitamin D and depression (Berridge, 2017). It is known that the risk of depression increases by 8.0 %–14 % in people with vitamin D deficiency (Fipps and Rainey, 2020). In a study, it was observed that cholecalciferol vitamin D3 supplementation in a group for three months decreased the depression score and increased serum serotonin levels in individuals with moderate, severe, and extreme depression according to the Beck Depression Scale (Alghamdi et al., 2020). It was reported that older adults with low serum 25-hydroxyvitamin D levels have high depressive symptoms (De Oliveira et al., 2018). Besides, it was found that the risk of developing depression is 3.5 times higher in individuals with vitamin D deficiency (Sherchand et al., 2018). It was observed that vitamin D supplementation was moderately effective in depression symptoms in individuals diagnosed with major depression (Vellekkatt and Menon, 2019). It was found that serum 25-hydroxyvitamin D levels are lower in obese individuals with depression (Kamalzadeh et al., 2021). In this study, it was observed that the daily administration of 70 micrograms of vitamin D to people with depression did not cause any change in depression scores and symptoms of depression (Hansen et al., 2019).

3.3. Vitamin B_{12}

It is known that vitamin B12 deficiency may be associated with depression. It was reported that the incidence of depression is higher in vegetarians due to insufficient intake of vitamin B12. In the case of vitamin B12 deficiency, it is not sufficient to measure serum B12 levels alone. Methylmalonic acid and homocysteine levels should also be checked (Russell-Jones, 2022). Vitamin B12 deficiency plays a role in the formation of depression with its effects on the adrenergic system, glutaminergic system, serotonin system, and dopamine system (Sangle

et al., 2020). People with B12 deficiency experience oxidative stress and changes in mitochondria tropic support, calcium buffering, and energy supply. These changes cause depression by producing atrophy, death of neurons, and decreased neurotransmitter signalling (Sangle et al., 2020). It was found that serum B12 concentrations were lower in omnivorous young people and the incidence of depression was 31.0 % in the vegetarian group and 12.0 % in the omnivorous group (Kapoor et al., 2017). It was observed that high serum B12 concentration in adults increases the risk of depression (Huang et al., 2018). In a study, lasting 6 years in the elderly, it was concluded that there was no relationship between serum vitamin B12 levels and depressive symptoms (Elstgeest et al., 2017). In other study, no relationship was found between vitamin B12 and depression (Markun et al., 2021). However, older adults with depressive symptoms were found to have lower serum vitamin B12 levels, and B12 deficiency and low B12 levels were found to have a significantly greater risk of depression four years later (Laird et al., 2021).

3.4. Vitamin B_6

Vitamin B6 is a cofactor that can affect depression by affecting neurotransmitters such as serotonin and norepinephrine in the brain (Mesripour et al., 2017). Pyridoxal phosphate vitamin, the active form of vitamin B6, plays an active role in plasma homocysteine concentration, decarboxylation reactions, and transamination reactions (Baradia et al., 2018). In a study, it was stated that daily intake of vitamin B6 meets the daily recommended amount, but is not associated with the risk of depression (Jahrami, 2021). In a study conducted by giving dexamethasone and 100 mg/kg vitamin B6 to mice for 7 days, it was found that vitamin B6 prevented depression by showing an antidepressant effect (Mesripour et al., 2019). In another study, it was observed that individuals with anxiety and depression had a lower intake of vitamin B6 than healthy individuals. It was concluded that insufficient intake of vitamin B6 may increase the possibility of developing depression (Kafeshani et al., 2019). It is known that women who use oral contraceptives have low levels of vitamin B6. A 20.0 % decrease was found in the Beck Depression Scale scores of 100 mg B6 daily for 4 weeks in women using oral contraceptives (Curtin and Johnston, 2022). The concentration of pyridoxal-5-phosphate, the active form of vitamin B6, was measured in Latino adults in the 2nd and 5th years of the study, and it was observed that depressive symptoms were higher in individuals with low values (Arévalo et al., 2019). It was found that there is an inverse relationship between only vitamin B6 and the risk of depression in middle-aged and elderly women with moderate and severe depressive symptoms and anxiety (Odai et al., 2020). Another study in adults reported an inverse relationship between vitamin B6 and stress (Mahdavifar et al., 2021).

3.5. Folic acid

Irritability, anaemia, and behavioral disorders are seen in folic acid deficiency. It is known that folic acid contributes to the recovery of depression by increasing the effectiveness of antidepressant drugs (Abdelmaksoud et al., 2019). In the body, folic acid is metabolized as S-adenosylmethionine (Bender et al., 2017). S-adenosylmethionine and folic acid are involved in the synthesis of serotonin, dopamine, epinephrine, and monoamine neurotransmitters (Bender et al., 2017; Zheng et al., 2020). Folic acid deficiency is associated with decreased levels of serotonin, dopamine, and norepinephrine. Decreased levels of norepinephrine, dopamine, and serotonin cause neurochemical deterioration and cause depression (Abdelmaksoud et al., 2019; Halaris et al., 2021). Studies have shown that low folic acid levels are associated with depression. It is also known that the incidence of major depression is lower in Asians with a high intake of folic acid. It has been observed that the efficacy of antidepressant drugs is lower in individuals with low folic acid levels (Mikkelsen et al., 2017). In mice under chronic unpredictable mild stress, folic acid produced antidepressant-like effects through various pathways involving monoamine neurotransmitters (Zhou et al., 2020). It has been observed that oxidative damage and depressive behaviors caused by stress were prevented by folic acid given to mice daily at 50 mg/kg (Réus et al., 2018).

3.6. Magnesium

Magnesium levels are very important for Alzheimer's, stroke, diabetes, hypertension, attention deficit, hyperactivity, migraine, and central nervous system functions (Wang et al., 2018). Magnesium is neurologically important because it plays a role in nerve conduction and neuromuscular transmission. It has a protective effect against overstimulation that leads to neuronal cell death (Kirkland et al., 2018). Considering the relationship of magnesium with the limbic system, it is thought to affect the formation and progression of depression (Wang et al., 2018). It is reported that magnesium has antidepressant properties and increases the effectiveness of antidepressant drugs (Szewczyk et al., 2018). As a result of a seven-year study, it was found that dietary magnesium intake and the risk of depression were inversely related in women, but not in men (Sun et al., 2019). In a study conducted with 60 depressed people with hypomagnesemia, it was found that there was a significant improvement in serum magnesium levels and depression status in the intervention group given 500 mg magnesium oxide for 8 weeks (Rajizadeh et al., 2017). In another study, it was reported that there is a relationship between serum magnesium levels and depression and that magnesium supplementation can improve depressive symptoms in individuals with low serum magnesium levels (Tarleton et al., 2019). According to the meta-analysis results of 17 epidemiological studies conducted to investigate the dose-response relationship between magnesium intake and the risk of depression, it was concluded that 320 mg/day of magnesium intake is effective in reducing the risk of depression (Z. Li et al., 2017; B. Li et al., 2017). In women, higher dietary magnesium intake was associated with lower levels of anxiety. In addition, there was a significant inverse relationship between dietary magnesium intake and depression in overweight women and normal-weight men (Anjom-Shoae et al., 2018).

3.7. Selenium

Selenium plays an important role in antioxidant mechanisms in the brain and nervous system by taking a role in the proper functioning of selenoproteins, and it also has an important role in thyroid metabolism. Thyroid diseases, on the other hand, are known to be associated with mental disorders, and considering this effect on brain functions, it is thought to be associated with depression. Selenium has a protective effect against the risk of depression with its effects on the prevention of inflammation and modulation of serotonin, dopamine, and noradrenaline (Wang et al., 2018). In a study, it was found that high doses of selenium consumption and a 54.0 % reduction in the risk of depression occur (Ferreira de Almeida et al., 2021). Due to the anti-inflammatory and antioxidant properties of 3-((4-chlorophenyl)sulfanyl)-1-methyl-1H-indole (CMI), which contains selenium, its effects on depressive behaviors in mice improve oxidative stress and impaired superoxide dismutase and catalase activity in the hippocampus reduced behaviors (Casaril et al., 2019). In another study, it is thought that there may be an inverse relationship between dietary selenium intake and the risk of depression (Li et al., 2018). In the meta-analysis of fifteen studies, no significant difference was found between the serum selenium levels and depression scores of depressed and healthy individuals. It has been reported that high selenium intake is inversely associated with the risk of depression. It was concluded that depression symptoms decreased in individuals given additional selenium supplementation (Sajjadi et al., 2022).

3.8. Zinc

It is thought that zinc may be effective in neural transmission associated with depression such as dopaminergic, serotonergic, and glutamatergic systems. Zinc shows antidepressant properties by modulating *N*-methyl-D-aspartate receptors and serotonergic functions and increasing brain-derived neurotrophic factor levels (Z. Li et al., 2017; B. Li et al., 2017). The brain is known to have the highest level of zinc compared to other organs. Therefore, zinc deficiency may cause depression by causing changes in glutamatergic transmission in the central nervous system, limbic system, and cerebral cortex (Styczeń et al., 2017). There is a tendency for zinc deficiency to be seen in the elderly population, and in a study, it was found that the majority of elderly individuals did not have sufficient dietary zinc intake, but there was no relationship between depression and zinc intake (Anbari-Nogyni et al., 2020). Another study observed that the serum zinc concentration of individuals with depression was lower than that of healthy individuals (Styczeń et al., 2017). It has been found that daily supplementation of 30 mg of zinc for 70 days in the elderly leads to a significant increase in serum zinc levels. This increase in serum zinc levels was found to be associated with a decrease in depression and anxiety scores (Afzali et al., 2021). An inverse relationship was found between dietary zinc intake and the risk of developing depression in female university students (Hajianfar et al., 2021).

3.9. Copper

Copper is known to have energy metabolism, immune function, and neurobehavioral effects. Copper can affect the regulation of neurotransmitters and noradrenaline concentration and activation (Ni et al., 2018). Cognitive, learning and memory processes, synaptogenesis, neuron growth, glycine receptors, catecholamine metabolism, regulation of the immunological system and regulation of antioxidant processes, etc. copper is involved. It is thought that copper may play an important role in the development of depression due to its effect on the conversion of dopamine to norepinephrine (Słupski et al., 2018). In a study investigating the relationship between dietary copper intake and depression in adults, a negative relationship was found between copper intake and depression (Li et al., 2018).

3.10. Major depressive disorder and prebiotic, probiotic

It is thought that there is a bidirectional interaction between major depressive disorder and gut microbiota. The mechanisms that are thought to provide this communication between the brain and the gut are the autonomic, enteric, and central nervous systems, gastrointestinal systems, immune systems, and neuroendocrine systems. It has been reported that major depressive disorder may be affected by possible changes in the intestinal microbiota (Nikolova et al., 2019). It is known that probiotics produce anti-inflammatory and antioxidant compounds and have anti-inflammatory, anti-infective, immune-supporting and oxidative stress-reducing effects. Probiotics are involved in the production of fatty acids and amino acids, which are necessary for the synthesis of neurochemicals, which are inhibitory factors in the formation of depression (Gayathri and Rashmi, 2017). The mechanism of action of probiotics on depression is given in Fig. 1.

GABA synthesized in the intestinal microbiota by probiotic bacteria plays a role in the synthesis of neurotransmitters such as serotonin, histamine, glutamate, dopamine, norepinephrine, and acetylcholine. For example, probiotic bacteria *Lactobacillus helveticus*, *Lactobacillus plantarum*, *Lactobacillus casei*, and *Lactobacillus bulgaricus* are involved in dopamine synthesis and play a role in the regulation of functions such as concentration, motivation, mood, psychomotor speed, ability to enjoy (Yong et al., 2020). Antidepressant effects of probiotics; *Lactobacillus rhamnosus* and *Lactobacillus casei* are involved in the production of GABA neurotransmitters, which can affect the hypothalamic-pituitary-adrenal axis. *Lactobacillus brevis* probiotic bacteria, on the other hand, play a role in the secretion of GABA neurotransmitters that improve sleep quality. *Lactobacillus reuteri* reduces the synthesis of proinflammatory cytokines by releasing histamine (Yong et al., 2020). Adults aged 18–65 years with major depressive disorder were given probiotic strains containing *Lactobacillus helveticus* and *Bifidobacterium longum* for 16 weeks, and

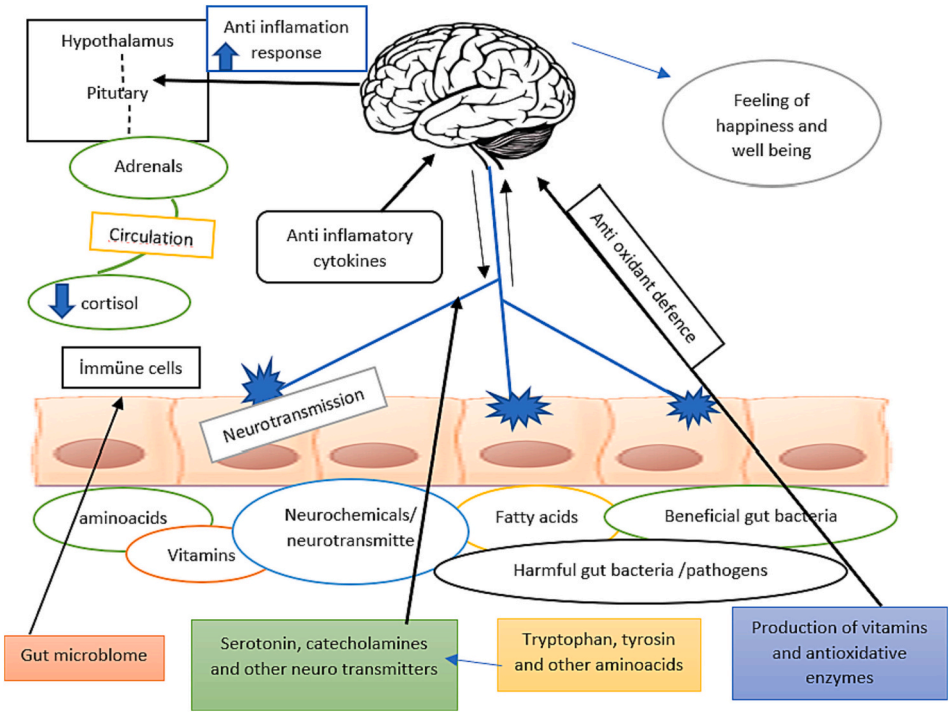

Fig. 1. Mechanism of action of probiotics on depression.
The image is adapted from Gayathri and Rashmi (2017).

symptoms of depression were reduced (Wallace et al., 2020). In the meta-analysis study in which ten clinical studies were examined, it was observed that probiotics were effective in reducing depressive symptoms, but there was no significant change in the anxiety status of the patients (Chao et al., 2020). In another study, it was observed that Beck Depression Scale scores decreased, cortisol levels decreased, and serum inflammatory markers did not change in the probiotic group (Kazemi et al., 2019a). In another study conducted on individuals with major depression, it was observed that the Beck Depression Scale Score decreased in the probiotic group, the kynurenine/tryptophan ratio in the probiotic group decreased significantly compared to the placebo group, and the tryptophan/isoleucine ratio increased significantly (Kazemi et al., 2019b). The probiotic strains *Bifidobacterium breve CCFM6432*, *Bifidobacterium breve CCFM1025*, and *Bifidobacterium longum CCFM687* were found to reduce depression scores and improve gastrointestinal functions in patients with major depressive disorder (Tian et al., 2022).

An increase in the stress level in individuals changes the secretion of cortisol, the function of the hypothalamus-pituitary-adrenal axis, and the functioning of the corticotropin-releasing factor. This increases the risk of infection and suppresses immunity. With immunosuppression, the level of oxidative stress and inflammatory cytokines increases and affects the normal functioning of neurons. It is thought that depression and anxiety affect this change in neural activity. It is associated with increased inflammatory cytokines and decreased tyrosine and tryptophan levels. This reduction in tyrosine and tryptophan levels lowers the levels of neurochemicals such as serotonin and dopamine, which prevent depression (Gayathri and Rashmi, 2017). If the balance of intestinal microbiota is disturbed, blood-brain barrier permeability and intestinal barrier permeability increase. This causes a leaky gut. These changes increase the production of proinflammatory cytokines. It causes a decrease in the levels of 5-hydroxytryptamine, dopamine, brain-derived neurotrophic factor, IDO, TDO, and kynurenine, and this decrease causes depression (Sonali et al., 2022).

4. Conclusions and recommendations

In this study, the relationship between depression and nutrition was examined based on the studies in the literature. As a result of the data obtained from the study; food preferences, nutrient content of the diet were found to be associated with depression. Bioactive components in coffee and tea reduce the risk of depression. It is known that probiotic supplementation can be effective in preventing the occurrence of depression, and omega-3 fatty acids are associated with the severity of depression symptoms. Vitamin D and vitamin B6 are involved in the production of serotonin. Therefore, it is inversely related to the risk of developing depression. Low levels of vitamin B12 are associated with the severity of depression. It is known that folic acid contributes to the recovery of depression by increasing the effectiveness of antidepressant drugs. Selenium, magnesium and zinc play a role in the nervous system and have a protective effect against the formation of depression. Copper is protective against depression by playing a role in the conversion of dopamine to norepinephrine.

Considering the effects of food on depression, people's nutritional status, diet quality, adequate dietary intake of vitamins and minerals are closely related to people's mental health. The roles of nutrients in the treatment of depression are indicated in our study.

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Declaration of competing interest

The authors declare no conflict of interest.

Data availability

No data was used for the research described in the article.

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