

Food-Derived Bioactive Compounds as Modulators of Neurotransmitter Pathways in Depression

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Abstract: *Food omics has emerged as an advanced scientific field that combines food science with modern technologies such as genomics, proteomics, metabolomics, and bioinformatics to better understand the relationship between food and human health. By analysing the molecular composition of foods, food omics provides valuable insights into how nutrients and bioactive compounds influence biological processes and contribute to disease prevention and overall well-being. Among the various tools used in food omics, bioinformatics plays a central role in managing and interpreting the large volumes of data generated through high-throughput analytical techniques. It enables researchers to identify genes, proteins, and metabolites present in different food sources and evaluate their nutritional and functional properties. This approach helps in discovering bioactive compounds that may promote health and reduce the risk of chronic diseases. Bioinformatics also contributes significantly to food safety by facilitating the rapid detection and monitoring of foodborne pathogens through genomic sequencing technologies. These tools help identify contamination sources and support effective strategies for preventing foodborne illnesses. In addition, bioinformatics aids in assessing food quality by identifying genetic factors associated with desirable traits such as taste, texture, shelf life, nutritional value, and crop productivity. Furthermore, bioinformatics supports food authenticity and traceability by enabling DNA-based identification of food products, helping to detect adulteration and food fraud while ensuring transparency within the food industry. Overall, the integration of bioinformatics with food omics has revolutionized the evaluation of food quality, safety, and nutritional value. As technological advancements continue, bioinformatics is expected to play an increasingly important role in developing healthier, safer, and more sustainable food systems while strengthening consumer confidence and trust.*

Keywords: Food omics, Bioinformatics, Genomics, Metabolomics, bioactive compounds, Foodborne

I. INTRODUCTION

Depression is one of the most prevalent mental health disorders worldwide and represents a major public health concern. It is characterized by persistent sadness, loss of interest in daily activities, fatigue, impaired concentration, disturbances in sleep and appetite, and reduced quality of life. The disorder affects millions of individuals globally and contributes significantly to disability, healthcare costs, and socioeconomic burden. Depression is also associated with several chronic diseases, including cardiovascular disorders, obesity, diabetes, and neurodegenerative conditions. Although pharmacological and psychological interventions are available, many patients fail to achieve complete remission, highlighting the need for novel and complementary therapeutic approaches (Marx et al., 2017; Marx et al., 2021).

Traditionally, depression was primarily explained by the monoamine hypothesis, which attributes the disorder to deficiencies in neurotransmitters such as serotonin, dopamine, and norepinephrine. However, recent research has



revealed that depression is a multifactorial condition involving complex interactions among neurotransmitter dysregulation, chronic inflammation, oxidative stress, hypothalamic-pituitary-adrenal (HPA) axis dysfunction, impaired neuroplasticity, and alterations in gut microbiota composition. These findings have expanded our understanding of the biological mechanisms underlying depressive disorders (Marx et al., 2021; Cryan et al., 2019). Growing evidence suggests that nutrition plays a crucial role in mental health, leading to the emergence of nutritional psychiatry as a rapidly developing field of research. Nutritional psychiatry investigates the relationship between dietary patterns and psychological well-being. Studies have consistently shown that diets rich in fruits, vegetables, whole grains, fish, nuts, and fermented foods are associated with a lower risk of depression, whereas diets high in processed foods, refined sugars, and unhealthy fats may increase susceptibility to depressive symptoms (Marx et al., 2017; Xu et al., 2021).

Food-derived bioactive compounds have gained considerable attention due to their potential neuroprotective and antidepressant properties. These compounds include polyphenols, flavonoids, carotenoids, omega-3 fatty acids, probiotics, prebiotics, amino acids, and other phytochemicals. They can modulate neurotransmitter synthesis and signaling, reduce inflammation and oxidative stress, and support neuronal function. Furthermore, the gut-brain axis has emerged as a key pathway linking diet and mental health. Through interactions with the gut microbiota, bioactive food components can influence the production of neurotransmitters such as serotonin, dopamine, and gamma-aminobutyric acid (GABA), thereby affecting mood and cognitive function (Cryan et al., 2019; Dinan & Cryan, 2017; Horn et al., 2022).

II. NEUROTRANSMITTER PATHWAYS IN DEPRESSION

Depression is a complex mental disorder that arises from the interaction of genetic, environmental, and biological factors. One of the key biological mechanisms involved in depression is the disruption of neurotransmitter systems. Neurotransmitters are chemical messengers that enable communication between neurons and regulate mood, motivation, cognition, sleep, and emotional responses. Among the various neurotransmitters implicated in depression, serotonin, dopamine, and gamma-aminobutyric acid (GABA) play particularly important roles. Disturbances in these pathways can impair brain function and contribute to the development of depressive symptoms (Marx et al., 2021).

2.1 Serotonin Pathway

Serotonin (5-hydroxytryptamine, 5-HT) is a monoamine neurotransmitter that regulates mood, sleep, appetite, cognition, and emotional behavior. It is synthesized from tryptophan, an essential amino acid obtained through the diet. In serotonergic neurons, tryptophan is converted into 5-hydroxytryptophan (5-HTP) by tryptophan hydroxylase and subsequently into serotonin by aromatic L-amino acid decarboxylase. Once released into the synaptic cleft, serotonin binds to specific receptors on postsynaptic neurons, influencing neuronal signaling and emotional responses. Its action is terminated through reuptake by serotonin transporters (Marx et al., 2021; Gómez-Pinilla, 2008).

Altered serotonergic signaling has long been associated with depression. Reduced serotonin activity may lead to symptoms such as persistent sadness, anxiety, irritability, sleep disturbances, and impaired cognitive function. The effectiveness of selective serotonin reuptake inhibitors (SSRIs), which increase serotonin availability in synapses, further highlights the importance of this neurotransmitter in mood regulation. However, serotonin dysfunction alone cannot fully explain the complexity of depression (Marx et al., 2021)

2.2 Dopamine Pathway

Dopamine is a catecholamine neurotransmitter primarily involved in reward processing, motivation, pleasure, learning, and goal-directed behavior. It is synthesized from the amino acid tyrosine through the intermediate compound L-DOPA. After its release, dopamine interacts with dopamine receptors and is subsequently removed through reuptake and enzymatic degradation (Belujon & Grace, 2017). The mesolimbic and mesocortical dopaminergic pathways are particularly relevant to depression. These pathways regulate reward perception, emotional processing, attention, and decision-making. Impaired dopamine signaling is strongly associated with anhedonia, the inability to experience

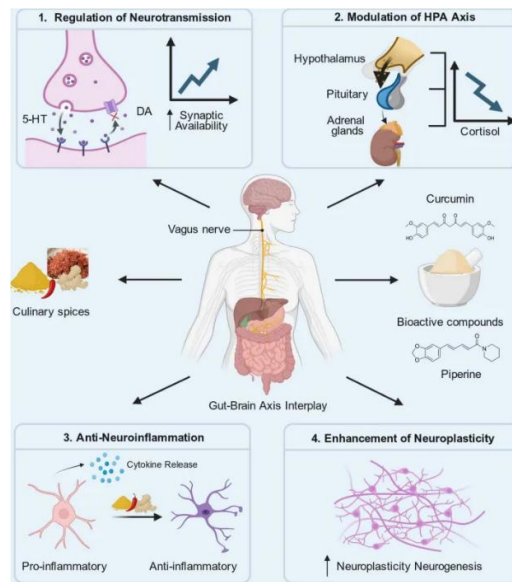


pleasure, which is a hallmark symptom of depression. Reduced dopamine activity may also contribute to decreased motivation, fatigue, social withdrawal, and cognitive difficulties. Chronic stress, inflammation, and oxidative damage can further disrupt dopamine function and worsen depressive symptoms (Belujon & Grace, 2017; Marx et al., 2021).

2.3 GABA Pathway

Gamma-aminobutyric acid (GABA) is the principal inhibitory neurotransmitter in the central nervous system. It is synthesized from glutamate by the enzyme glutamate decarboxylase and acts primarily through GABA-A and GABA-B receptors. By reducing neuronal excitability, GABA helps maintain the balance between excitatory and inhibitory signaling in the brain (Cryan & Kaupmann, 2005).

Evidence suggests that reduced GABA levels and impaired GABA receptor activity are associated with depression. Dysfunction of the GABAergic system may increase stress sensitivity, anxiety, sleep disturbances, and emotional instability. GABA also regulates the hypothalamic-pituitary-adrenal (HPA) axis, which controls the body's stress response. Reduced GABA activity can contribute to excessive cortisol production, a factor frequently linked to depression (Cryan & Kaupmann, 2005).



Interaction Among Neurotransmitter Systems

Serotonin, dopamine, and GABA do not function independently but form an interconnected neurochemical network that regulates mood, motivation, cognition, and stress adaptation. Serotonin can influence dopamine-mediated reward pathways, while GABA regulates the activity of both serotonergic and dopaminergic neurons. Consequently, disturbances in one neurotransmitter system can affect the functioning of others, leading to widespread neurochemical imbalances. Current research recognizes depression as a multifactorial disorder involving interactions among neurotransmitter dysfunction, neuroinflammation, oxidative stress, hormonal imbalance, impaired neuroplasticity, and gut-brain axis disturbances. Therefore, understanding the integrated roles of serotonin, dopamine, and GABA is essential for developing effective therapeutic strategies for depression (Marx et al., 2021; Cryan et al., 2019).

Table 1. Food-Derived Bioactive Compounds and Their Roles in Depression

Bioactive Compound	Major Sources	Target Pathway	Potential Benefit
Polyphenols	Fruits, tea, cocoa	Inflammation/oxidative stress	Neuroprotection
Omega-3 fatty acids	Fish oils	Serotonin & dopamine	Mood improvement



Probiotics	Yogurt, kefir	Gut-brain axis	Stress reduction
Prebiotics	Inulin, FOS	Gut microbiota	SCFA production
Tryptophan	Eggs, milk, nuts	Serotonin synthesis	Emotional stability

III. FOOD OMICS: AN EMERGING TOOL IN NUTRITIONAL PSYCHIATRY

Growing evidence has highlighted the important relationship between nutrition and mental health, leading to the emergence of nutritional psychiatry as a promising field of research. Traditional nutrition studies primarily focused on the role of individual nutrients in maintaining health and preventing disease. However, advances in biotechnology and analytical sciences have revealed that foods contain numerous bioactive compounds capable of influencing biological processes at molecular, cellular, and metabolic levels. Understanding these complex interactions has given rise to the field of food omics (Marx et al., 2017; Horn et al., 2022). Food omics is a multidisciplinary approach that integrates advanced high-throughput technologies to investigate food composition and its effects on human health. It combines several omics disciplines, including genomics, transcriptomics, proteomics, metabolomics, and microbiomics, to provide a comprehensive understanding of how dietary components interact with biological systems. In nutritional psychiatry, food omics has become a valuable tool for exploring the molecular mechanisms through which dietary bioactive compounds influence neurotransmitter pathways, brain function, and mental health (Horn et al., 2022; Marx et al., 2021).

3.1 Genomics and Nutrigenomics

Genomics focuses on the study of an organism's complete genetic material and its functional interactions. In nutrition research, genomics has contributed to the development of nutrigenomics, which examines how nutrients and dietary compounds influence gene expression and how genetic variations affect responses to diet (Horn et al., 2022). Genetic differences can influence neurotransmitter synthesis, receptor function, and metabolic pathways associated with depression. Variations in genes related to serotonin transporters, dopamine receptors, and neurotransmitter metabolism may increase susceptibility to depressive disorders. Research has shown that dietary bioactive compounds such as polyphenols, flavonoids, and omega-3 fatty acids can regulate genes involved in inflammation, oxidative stress, neuroplasticity, and neuronal communication. These findings suggest that personalized dietary interventions based on genetic profiles may help improve mental health and reduce the risk of depression (Marx et al., 2021; Horn et al., 2022).

3.2 Transcriptomics

Transcriptomics involves the study of the transcriptome, the complete set of RNA molecules produced by actively expressed genes. Since RNA acts as an intermediary between genes and proteins, transcriptomic analysis provides insights into how gene activity changes in response to environmental and dietary factors (Horn et al., 2022). In depression research, transcriptomics helps identify gene networks and signaling pathways influenced by dietary compounds. Bioactive substances found in fruits, vegetables, and other plant-based foods can alter the expression of genes involved in neurotransmitter regulation, neuroinflammation, synaptic communication, and neuronal plasticity. (Marx et al., 2021).

3.3 Proteomics

Proteomics is the large-scale study of proteins, their structures, functions, and interactions. Since proteins are directly responsible for most cellular activities, changes in protein expression provide valuable information about physiological and pathological processes (Horn et al., 2022). Proteomic studies have identified alterations in proteins involved in neurotransmission, immune regulation, synaptic plasticity, and neuronal function in individuals with depression. Dietary bioactive compounds such as curcumin, resveratrol, and omega-3 fatty acids have been shown to influence the expression of proteins associated with neuroprotection and cognitive function. Additionally, proteomics aids in the



discovery of biomarkers that may improve the diagnosis, monitoring, and treatment of depressive disorders (Marx et al., 2021; Zhu et al., 2026).

3.4 Metabolomics

Metabolomics examines metabolites, the small molecules produced during metabolic reactions. Because metabolites reflect ongoing biochemical processes, metabolomic analysis provides a direct assessment of an individual's physiological state (Horn et al., 2022). In nutritional psychiatry, metabolomics helps investigate how dietary factors affect pathways involved in neurotransmitter synthesis, inflammation, oxidative stress, and energy metabolism. Studies have identified metabolic disturbances involving tryptophan, serotonin, dopamine, and GABA pathways in individuals with depression. By analyzing these metabolic signatures, researchers can better understand the biochemical basis of depression and evaluate the effectiveness of dietary interventions aimed at improving mental health (Marx et al., 2021).

3.5 Microbiomics and Gut Microbiota

Microbiomics focuses on the study of microbial communities and their genetic material. The human gut contains trillions of microorganisms that contribute to digestion, metabolism, immune regulation, and communication with the nervous system through the gut-brain axis (Cryan et al., 2019; Dinan & Cryan, 2017). Research has demonstrated that gut microbes can influence the production and regulation of neurotransmitters, including serotonin, dopamine, and GABA. Individuals with depression often exhibit alterations in gut microbial composition, known as dysbiosis, which may contribute to inflammation and disrupted gut-brain communication. Dietary bioactive compounds such as polyphenols, dietary fibers, prebiotics, and probiotics can positively modulate gut microbiota composition and promote the production of beneficial metabolites. Consequently, microbiomics provides valuable insights into how dietary interventions may support mental health through modulation of the gut-brain axis (Cryan et al., 2019; Horn et al., 2022). Overall, food omics offers a comprehensive framework for understanding the complex interactions between diet, neurotransmitter regulation, and mental health. By integrating multiple omics technologies, it provides new opportunities for developing personalized nutritional strategies for the prevention and management of depression (Horn et al., 2022; Marx et al., 2021).

IV. FOOD-DERIVED BIOACTIVE COMPOUNDS RELEVANT TO DEPRESSION

Food provides not only essential nutrients but also a variety of bioactive compounds that influence physiological functions beyond basic nutrition. These compounds interact with molecular and cellular pathways involved in brain health and mental well-being. Recent studies have shown that food-derived bioactive compounds can modulate several mechanisms associated with depression, including neurotransmitter regulation, inflammation, oxidative stress, neuroplasticity, and gut microbiota balance. As depression is now recognized as a multifactorial disorder involving biological, psychological, and environmental factors, dietary bioactive compounds have gained considerable attention as complementary approaches for its prevention and management (Marx et al., 2021; Xu et al., 2021).

4.1 Polyphenols

Polyphenols are naturally occurring compounds widely distributed in fruits, vegetables, tea, coffee, cocoa, herbs, spices, and whole grains. They are well known for their antioxidant and anti-inflammatory properties, which contribute to the protection of neuronal cells from oxidative damage and chronic inflammation. Research suggests that polyphenols can influence neurotransmitter activity, support neuronal growth, and enhance neuroplasticity. In addition, many polyphenols interact with the gut microbiota, producing bioactive metabolites that regulate the gut-brain axis and influence neurotransmitter production. Through these mechanisms, polyphenols may help maintain emotional stability and reduce the risk of depressive disorders (Zhu et al., 2026; Marx et al., 2021; Trends in Food Science & Technology, 2025).



4.2 Omega-3 Polyunsaturated Fatty Acids

Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are essential components of neuronal membranes and play a critical role in brain function. Found mainly in fatty fish and fish oils, these fatty acids contribute to membrane fluidity, efficient neurotransmission, and neuronal signaling. Studies have associated low omega-3 intake with an increased risk of depression. Omega-3 fatty acids positively influence serotonin and dopamine pathways, reduce neuroinflammation, and promote neuroplasticity through the enhancement of brain-derived neurotrophic factor (BDNF). Their combined effects make them valuable nutritional agents for supporting mental health and complementing conventional depression treatments (Larrieu & Layé, 2018; Marx et al., 2021).

4.3 Probiotics and Psychobiotics

Probiotics are beneficial microorganisms that support gut health, while psychobiotics refer to specific probiotic strains capable of influencing mental well-being through the gut–brain axis. Species belonging to the genera *Lactobacillus* and *Bifidobacterium* are among the most extensively studied. These microorganisms can stimulate the production of neurotransmitters such as serotonin, dopamine, and gamma-aminobutyric acid (GABA), while also regulating immune responses and reducing inflammation. Evidence suggests that probiotic supplementation may improve mood, reduce anxiety, and alleviate depressive symptoms, highlighting their potential role in mental health management (Cryan et al., 2019; Dinan & Cryan, 2017; Horn et al., 2022).

4.4 Prebiotics

Prebiotics are non-digestible food components that promote the growth of beneficial gut microorganisms. Common examples include inulin, fructooligosaccharides (FOS), and galactooligosaccharides (GOS). Their fermentation by gut bacteria produces short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate, which support intestinal integrity, reduce inflammation, and influence brain signaling pathways. By enhancing gut microbiota balance and strengthening gut–brain communication, prebiotics may contribute to improved emotional regulation and cognitive function (Horn et al., 2022; Cryan et al., 2019).

4.5 Amino Acids and Neurotransmitter Precursors

Certain dietary amino acids serve as precursors for neurotransmitter synthesis. Tryptophan, found in dairy products, fish, eggs, nuts, and seeds, is the primary precursor of serotonin and melatonin. Adequate tryptophan intake supports mood regulation, sleep quality, and emotional stability. Tyrosine, present in protein-rich foods such as dairy products, legumes, fish, and poultry, is the precursor of dopamine, norepinephrine, and epinephrine. Through its role in catecholamine synthesis, tyrosine supports motivation, cognitive performance, stress adaptation, and emotional resilience. Together, these amino acids are essential for maintaining healthy neurotransmitter function and mental well-being (Yılmaz & Gökmen, 2020; Marx et al., 2021).

V. CONCLUSION

Depression is a multifactorial disorder involving disturbances in neurotransmitter pathways, neuroinflammation, oxidative stress, and gut-brain axis dysfunction. Growing evidence suggests that food-derived bioactive compounds, including polyphenols, omega-3 fatty acids, probiotics, prebiotics, and amino acid precursors, can positively influence serotonin, dopamine, and GABA signalling pathways, thereby supporting mental health and emotional well-being.

Advances in food omics technologies have enhanced our understanding of the molecular mechanisms linking diet and depression, enabling the identification of biomarkers and potential therapeutic targets. Furthermore, the integration of genomics, metabolomics, proteomics, and microbiomics has highlighted the importance of personalized nutrition approaches in mental health management.

Although challenges related to bioavailability, individual variability, and clinical translation remain, food-derived bioactive compounds represent promising complementary strategies for the prevention and management of depression.



Future research integrating food omics, artificial intelligence, and precision nutrition is expected to facilitate the development of targeted dietary interventions that support neurotransmitter balance and improve mental health outcomes.

REFERENCES

1. Marx, W., Moseley, G., Berk, M., & Jacka, F. (2017).
Nutritional psychiatry: the present state of the evidence.
Proceedings of the Nutrition Society, 76(4), 427–436.
DOI: <https://doi.org/10.1017/S0029665117002026>
2. Marx, W., Lane, M., Hockey, M., et al. (2021).
Diet and depression: exploring the biological mechanisms of action.
Molecular Psychiatry, 26, 134–150.
DOI: <https://doi.org/10.1038/s41380-020-00925-x>
3. Horn, J., Mayer, D. E., Chen, S., & Mayer, E. A. (2022).
Role of diet and its effects on the gut microbiome in the pathophysiology of mental disorders.
Translational Psychiatry, 12, 164.
DOI: <https://doi.org/10.1038/s41398-022-01922-0>
4. Xu, Y., Zeng, L., Zou, K., et al. (2021).
Role of dietary factors in the prevention and treatment for depression: an umbrella review of meta-analyses of prospective studies.
Translational Psychiatry, 11, 478.
DOI: <https://doi.org/10.1038/s41398-021-01590-6>
5. Larrieu, T., & Layé, S. (2018).
Food for Mood: Relevance of Nutritional Omega-3 Fatty Acids for Depression and Anxiety.
Frontiers in Physiology, 9, 1047.
DOI: <https://doi.org/10.3389/fphys.2018.01047>
6. Yilmaz, C., & Gökmen, V. (2020).
Neuroactive compounds in foods: Occurrence, mechanism and potential health effects.
Food Research International, 128, 108744.
DOI: <https://doi.org/10.1016/j.foodres.2019.108744>

