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The Role of Probiotics in Depression Therapy: Current State of Knowledge and Therapeutic Perspectives

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ABSTRACT

Depression is one of the most common mental disorders worldwide, leading to a significant reduction in quality of life and an increased risk of suicide. The pathogenesis of major depressive disorder (MDD) remains complex and not fully understood, involving neurotransmitter disturbances, excessive activation of the hypothalamic-pituitary-adrenal (HPA) axis, and reduced levels of brain-derived neurotrophic factor (BDNF). In recent years, an increasing number of studies have highlighted the role of gut microbiota and the gut-brain axis as key elements in the pathogenesis of depression. This review aimed to analyze the current evidence on the impact of probiotic supplementation on depressive symptoms. A PubMed database search was conducted, including randomized clinical trials, meta-analyses, and systematic reviews from the last five years. The results of the analyzed studies suggest that probiotics, particularly Lactobacillus and Bifidobacterium strains, may reduce depressive symptoms, regulate neurotransmitter levels, and decrease inflammation. However, the effectiveness of probiotic supplementation varied depending on the strain used, intervention duration, and the study population. Despite promising results, further research is needed to determine optimal probiotic therapy protocols in depression.

Keywords: depression, gut microbiota, probiotics, gut-brain axis, supplementation, neurotransmitters, inflammation, mental disorders

INTRODUCTION

Depression is one of the most common and debilitating mental disorders in the modern world, leading to a profound reduction in quality of life, social functioning, and overall well-being. It affects individuals across all demographics and is increasingly recognized as a major public health concern. Its effects are far-reaching, with depression not only impairing mental and emotional health but also contributing to the development of comorbid conditions such as cardiovascular disease, diabetes, and various other chronic illnesses. In addition to the personal suffering it causes, depression significantly burdens healthcare systems and society at large, with productivity losses and increased healthcare costs. The World Health Organization (WHO) estimates that approximately 280 million people worldwide are affected by depression, which constitutes about 3.8% of the global population. This statistic underscores the global scale of the problem. Moreover, the prevalence of depression tends to be higher in vulnerable groups, such as the adult population, where it reaches 5%, and even higher in older adults, with a prevalence of 5.7% among individuals over the age of 60 (WHO, 2023). In terms of public health impact, depression is a leading cause of disability and accounts for a significant proportion of the global burden of disease. Each year, depression contributes to around 700,000 suicides, making it the fourth leading cause of death among young people aged 15–29 (WHO, 2023). This alarming statistic further emphasizes the urgency of addressing the issue and finding effective treatments.

The etiology of major depressive disorder (MDD) is extremely complex and multifactorial, encompassing a range of biological, psychological, and environmental factors that interact in a way that is still not fully understood. Researchers have identified a variety of underlying mechanisms that may contribute to the onset and progression of depression. These include disturbances in monoaminergic neurotransmission, which refers to the dysfunction of key neurotransmitters such as serotonin, dopamine, and norepinephrine. Other contributing factors include excessive activation of the hypothalamic-pituitary-adrenal (HPA) axis, which plays a critical role in the body's stress response, as well as decreased levels of brain-derived neurotrophic factor (BDNF), a protein that supports the survival and growth of neurons (Sonali et al., 2022). These mechanisms highlight the complex interplay between brain chemistry, hormonal regulation, and neuroplasticity, all of which are disrupted in depression. Additionally, psychosocial stressors, early life trauma, and genetic predispositions further contribute to the development of depression, making it a highly individualized disorder that requires personalized treatment strategies.

In recent years, there has been increasing interest in the role of gut microbiota and the microbiota-gut-brain axis (MGB) in the pathophysiology of depression. The microbiota-gut-brain axis refers to the bidirectional communication between the gut and the central nervous system, and it is thought to play a pivotal role in regulating mood, cognition, and emotional responses. Disruptions in the balance of gut microbiota, referred to as dysbiosis, have been linked to a range of mental health conditions, including depression, anxiety, and stress-related disorders. Dysbiosis is associated with elevated levels of inflammation, increased oxidative stress, and altered gut permeability, all of which contribute to a dysregulated HPA axis and altered brain function (Simpson et al., 2021; Sonali et al., 2022). Moreover, gut microorganisms play a crucial role in the production and regulation of key neurotransmitters such as serotonin, dopamine, and gamma-aminobutyric acid (GABA), which directly affect brain function and behavior. These findings suggest that the gut microbiota may influence brain chemistry and, consequently, mood and mental health.

Given the emerging evidence linking gut microbiota to depression, there has been growing interest in probiotic supplementation as a potential therapeutic strategy. Probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits to the host. In the context of depression, probiotics, particularly strains from the genera *Lactobacillus* and *Bifidobacterium*, have shown promising effects in regulating inflammation, improving neurotransmitter levels, and modulating the HPA axis. These effects can lead to a reduction in depressive symptoms and cortisol levels, suggesting that probiotics may help to alleviate the physiological imbalances associated with depression (Ferenchick et al., 2019). Probiotics may also help restore a healthy gut microbiota composition, which in turn could support the gut-brain axis and improve overall mental health.

Despite the promising results observed in both clinical and experimental studies, the effectiveness and mechanisms of probiotics in treating depression are still not fully understood. Much of the current research is preliminary, and findings are often inconsistent, with some studies showing significant improvements in depressive symptoms and others demonstrating minimal or no effects. These discrepancies highlight the need for further research to clarify the role of probiotics in depression treatment and identify the specific strains, dosages, and treatment durations that are most effective. Moreover, it is essential to explore the underlying mechanisms through which probiotics exert their effects on the gut-brain axis and how they influence brain function and emotional regulation. Understanding these mechanisms will be critical for developing more targeted and effective therapeutic strategies. This review aims to provide a comprehensive analysis of the current literature on the use of probiotics in depression,

examining the potential benefits, limitations, and future directions for research in this field. While the results to date are encouraging, more robust, well-designed studies are needed to confirm the clinical efficacy of probiotic supplementation as an adjunctive treatment for major depressive disorder and other mood disorders.

METHODS

This systematic review is based on a comprehensive analysis of the most recent scientific literature available, focusing on the relationship between probiotics and depressive symptoms. A thorough search of the PubMed database was conducted, with specific attention to publications from the past five years, to ensure that the most up-to-date evidence was included. Keywords used in the search included "gut microbiota," "depression," "probiotics," "microbiome," "gut-brain axis," "mental health," and "major depressive disorder." The inclusion criteria were limited to peer-reviewed studies published in English, which involved randomized controlled trials (RCTs), systematic reviews, and meta-analyses examining the effects of probiotics on depressive symptoms and their underlying mechanisms in adults diagnosed with depression. Studies that focused on populations other than adults, or those that did not directly address the role of probiotics in the treatment of depression, were excluded from the review. In addition, studies that lacked sufficient clinical data, or those that were not peer-reviewed, were also omitted. The selection process was carried out in several stages. Initially, relevant studies were identified based on the keywords listed above. Chronological filters (2010–2025), language filters (English), and quality filters (peer-reviewed studies) were applied to refine the search results. The reviewed articles included various types of studies: randomized controlled trials, systematic reviews, meta-analyses, observational cohort studies, and clinical trials. Meta-analyses and RCTs, which provide the highest level of evidence, were prioritized for inclusion in this review. This approach enabled the evaluation of the effects of probiotics on depression based on the most robust evidence available. Cohort studies and observational studies were also considered for their long-term observational data, while systematic reviews provided a broader synthesis of the evidence on the topic. The gathered studies were analyzed and synthesized to assess the overall effectiveness of probiotic supplementation in managing depressive symptoms. Special attention was given to factors such as the specific probiotic strains used, the duration of supplementation, the impact on neurotransmitters, and the influence of gut microbiota modulation on mental health. The analysis also critically examined the limitations of the current research, including potential publication bias, variability in study designs, and sample sizes, which may affect the

generalizability of the findings. Additionally, the review identified key trends, gaps in current knowledge, and suggestions for future research in the field.

RESULTS

Current research indicates that probiotic supplementation may have a beneficial impact on depressive symptoms, yet the results are inconsistent and vary depending on several important factors. The effectiveness of probiotics appears to depend on the duration of supplementation, the specific bacterial strains used, and the characteristics of the study populations. A systematic review and meta-analysis by He et al. (2023) found that while probiotic supplementation may contribute to moderate improvements in cognitive functions among patients with depression, the effect on depressive symptoms was minimal and statistically insignificant. This suggests that while probiotics may offer some cognitive benefits, their impact on depressive symptoms requires further investigation and clarification. The variability in findings underscores the necessity for continued research to better understand how probiotics might specifically target the core mechanisms of depression and how they can be optimized for therapeutic purposes (He et al., 2023).

In contrast, a randomized controlled trial conducted by Schaub et al. (2022) found a significant reduction in Hamilton Depression Rating Scale (HAM-D) scores after 31 days of probiotic supplementation, compared to placebo. The study also revealed that the supplementation led to an increase in the abundance of Lactobacillus bacteria and a reduction in the activity of the lenticular nucleus, an area associated with mood regulation. These findings suggest that probiotics might have a direct influence on the neuronal mechanisms underlying depression, potentially through modulation of the gut-brain axis. Such results point to the exciting possibility that probiotics could offer a neurobiological mechanism through which they exert their antidepressant effects, although the precise pathways need further exploration (Schaub et al., 2022).

The impact of probiotics on inflammatory and metabolic markers was also investigated by Kashani-Poor et al. (2016), who demonstrated that eight weeks of probiotic supplementation led to significant reductions in insulin levels, insulin resistance (measured by HOMA-IR), and C-reactive protein (hs-CRP), a key marker of inflammation. Furthermore, they observed an increase in plasma glutathione levels, which points to the potential anti-inflammatory and antioxidant effects of probiotics. These results suggest that probiotics may not only influence the gut microbiota but also contribute to the regulation of metabolic and inflammatory pathways.

Animal studies have further strengthened the hypothesis that probiotics can modulate mental health. Bercik et al. (2011) demonstrated that Bifidobacterium longum NCC3001 exerts anxiolytic effects via vagal pathways, providing substantial evidence for the role of gut-brain communication in anxiety and depression. These findings suggest that probiotics may act through multiple physiological pathways, impacting both emotional regulation and physical health through their interaction with the gut microbiota (Bercik et al., 2011; Bercik et al., 2010).

A meta-analysis by Hofmeister et al. (2021) reviewed the effects of probiotics, prebiotics, and synbiotics on depressive symptoms, concluding that these interventions may offer moderate benefits in reducing symptoms. However, the effects were inconsistent across different study populations, indicating that certain factors, such as individual variability in gut microbiota composition and the duration of treatment, may play a crucial role in determining the efficacy of these therapies. Interestingly, no significant benefits were observed from fecal microbiota transplants or the use of paraprobiotics, highlighting that not all approaches aimed at modulating the gut microbiome are equally effective for treating depression (Hofmeister et al., 2021).

In a similar vein, Reininghaus et al. (2020) confirmed that probiotic supplementation increased gut microbiota diversity and the abundance of beneficial bacteria, such as Ruminococcus gauvreauii and Coprococcus 3. However, no significant clinical improvements were observed compared to placebo, suggesting that longer intervention periods or different probiotic strains may be needed to observe more pronounced effects. This study highlights the importance of optimizing the duration and specific strains of probiotics in order to achieve the desired therapeutic outcomes (Reininghaus et al., 2020).

Another study by Schneider et al. (2023) explored the cognitive effects of probiotics, showing that supplementation improved episodic memory and hippocampal function. These findings suggest that probiotics may influence cognitive processes in individuals with depression, which is particularly important for patients experiencing cognitive deficits alongside their depressive symptoms. The potential therapeutic benefits of probiotics in improving cognitive function could be significant, as cognitive impairment is a common feature in major depressive disorder, and enhancing cognitive functioning may improve overall quality of life (Schneider et al., 2023).

Furthermore, Alli et al. (2022) highlighted substantial differences in the gut microbiota profiles of patients with depression compared to healthy controls. Their analysis indicated that probiotic and synbiotic supplementation in clinical trials resulted in a moderate reduction in depressive symptoms, particularly during supplementation periods of 4 to 9 weeks. This suggests that

probiotics may have a more pronounced effect when used consistently over a longer period, further emphasizing the importance of dosage and duration in probiotic therapy (Alli et al., 2022).

Regarding the association between metabolic disorders and depression, Xiong et al. (2023) emphasized the significant role of gut microbiota in regulating inflammation and neurotransmission. Their research suggests that probiotics could potentially be used to improve both mental and metabolic health by modulating gut microbiota composition, highlighting the broad therapeutic potential of probiotics beyond just mental health (Xiong et al., 2023).

Studies on inflammatory depression subtypes revealed that patients with this form of depression had higher levels of pro-inflammatory bacteria (e.g., Bacteroides) and a reduced abundance of anti-inflammatory bacteria (e.g., Clostridium, Faecalibacterium). Fecal microbiota transplantation (FMT) from patients to mice resulted in increased inflammatory markers and depressive symptoms in the animals, while the administration of Clostridium butyricum had antidepressant effects, suggesting a potential avenue for probiotic interventions in treating inflammatory-related depression (Liu et al., 2024).

Additionally, Liu et al. (2016) observed that the microbiota of patients with both depression and irritable bowel syndrome (IBS) exhibited similar disruptions, suggesting a shared pathophysiological mechanism between these conditions. IBS is often associated with psychiatric comorbidities, including depression, and is thought to be influenced by gut-brain interactions. The relationship between IBS and depression has been well documented, with many IBS patients reporting stress and anxiety as exacerbating factors for their symptoms (Ray, 2017). Thus, probiotic supplementation could play a crucial role in alleviating both depressive and gastrointestinal symptoms, providing a dual benefit for patients suffering from these co-occurring conditions.

In conclusion, available data suggest that while probiotic supplementation holds promise as a therapeutic strategy for managing depression, the effects are still inconsistent and require further exploration. Probiotics may help reduce affective symptoms, improve cognitive function, regulate inflammation, and enhance gut microbiota diversity. However, additional research is essential to determine the optimal strains, dosages, and duration of supplementation needed to maximize the therapeutic benefits of probiotics in depression treatment. Further studies should also aim to refine our understanding of the mechanisms through which probiotics influence the gut-brain axis, as this knowledge could lead to more effective, personalized treatments for depression.

DISCUSSION

The systematic review presented highlights a significant, albeit complex, relationship between probiotic supplementation and the reduction of depressive symptoms. Gut microbiota plays a crucial role in regulating the immune system, influencing brain development, and shaping emotional behaviors, all of which are well-documented in scientific literature (Kelly et al., 2017). Dysbiosis, an imbalance in gut microbiota, may arise due to environmental, genetic, childbirth-related, or early-life stress exposure factors. Such microbiological changes can disrupt the bidirectional communication between the gut and the brain, leading to the development of depressive symptoms (Kelly et al., 2017).

The studies analyzed suggest that the beneficial impact of probiotics on depressive symptoms depends on several factors, including the specific strains of bacteria used, dosage, duration of supplementation, and the characteristics of the studied populations. The most positive effects were observed with Lactobacillus and Bifidobacterium strains, which possess anti-inflammatory properties and regulate neurotransmitter levels such as serotonin, dopamine, and GABA (Alli et al., 2022; Ferenchick et al., 2019). Schaub et al. (2022) confirmed a significant reduction in Hamilton Depression Rating Scale (HAM-D) scores and decreased neuronal activity in the lenticular nucleus after probiotic supplementation, suggesting that probiotics may influence neuronal mechanisms underlying depression. However, meta-analyses by He et al. (2023) and Hofmeister et al. (2021) revealed moderate or limited efficacy of probiotics, emphasizing the need for further studies to determine optimal therapeutic conditions.

A critical issue raised by Wallace and Milev (2017) is the methodological gaps and inconsistencies in existing studies. The authors point out that differences in the duration of interventions, the specific probiotic strains used, and even the definition of depression itself complicate the ability to confirm the effectiveness of this therapy conclusively. Furthermore, studies predominantly focus on probiotics' impact on mood, anxiety, and cognitive functions, leaving other aspects of depression, such as sleep disturbances, underexplored.

It is also important to note that some analyses, such as the study by Reininghaus et al. (2020), did not demonstrate clinically significant differences between probiotics and placebo. This could be attributed to the short intervention periods, the use of specific bacterial strains, or the considerable heterogeneity of the study populations. The high methodological variability and the limitations of the available data constrain the precise comparison of study results. Moreover, the exact mechanisms by which probiotics influence the gut-brain axis remain incompletely understood and require further detailed investigation. Particularly interesting findings were presented by Schneider et al. (2023), who highlighted the positive effects of probiotics on

episodic memory and hippocampal functions, which may have significant therapeutic implications for patients with depression co-occurring with cognitive impairments. Potential benefits from probiotic supplementation are further enhanced when gastrointestinal disorders, such as irritable bowel syndrome (IBS), are also present, as evidenced by Liu et al. (2016).

Given the limitations, future research should adopt more uniform methodologies, involve larger research groups, and clearly define bacterial strains and dosing regimens. This would help establish reliable clinical recommendations for the use of probiotics as an adjunctive treatment for depression. Despite these limitations, probiotics represent a promising therapeutic strategy due to their safety and potential for improving mental health through modulation of the gut microbiota.

CONCLUSIONS

The review of current scientific studies suggests that probiotic supplementation may have a beneficial impact on depressive symptoms, although the findings remain inconclusive and show variability based on several important factors. In particular, the effectiveness of probiotic therapy seems to depend on the duration of the intervention, the specific bacterial strains used, and the characteristics of the study population. He et al. (2023) in their meta-analysis demonstrated that probiotic supplementation could lead to moderate improvements in cognitive functions in patients with depression, though the effect on reducing depressive symptoms was relatively small and statistically insignificant. This highlights the complexity of probiotic interventions, suggesting that while they may offer cognitive benefits, their impact on depression remains more nuanced. The variability in these results further underscores the need for more targeted research to determine which specific strains are most effective for treating depressive symptoms.

In contrast, Schaub et al. (2022) in a randomized controlled trial found a significant improvement in Hamilton Depression Rating Scale (HAM-D) scores after just one month of probiotic supplementation, which was associated with favorable changes in the gut microbiota composition and alterations in the activity of the lenticular nucleus, a brain area linked to mood regulation. These results are promising as they suggest that probiotics can influence not only the gut microbiota composition but also neuronal pathways, such as those related to the lenticular nucleus, which play a crucial role in the development of depressive disorders. Such findings indicate that probiotics may offer a direct mechanism for modulating brain activity, potentially leading to reduced depressive symptoms. However, these results also point to the

need for a more thorough understanding of the precise mechanisms at play, as the relationship between gut microbiota and brain function is still being unraveled.

Despite the promising findings, further well-designed clinical studies are essential to provide a clearer understanding of the effectiveness of probiotic therapy as an adjunctive treatment for major depressive disorder. The complexity of the gut-brain axis means that the clinical application of probiotics in depression treatment should not be over-simplified. Future studies should explore how specific probiotic strains interact with the gut microbiome, neurotransmitter regulation, and the immune system. Moreover, it is crucial to better delineate the mechanisms by which gut microbiota impacts the functioning of the nervous system, as this knowledge will be key in refining probiotic therapies for depression. Investigating these mechanisms will provide deeper insights into how probiotics modulate the brain's neurobiological pathways, which could lead to more effective and personalized treatments.

Additionally, further investigation into the long-term effects of probiotic supplementation and its interaction with other mental health treatments will be necessary to optimize its clinical application. While short-term benefits are evident in some studies, long-term outcomes remain unclear. The interaction between probiotics and other established therapies, such as antidepressants or cognitive-behavioral therapies, should also be explored. Probiotic supplementation could play a complementary role, but it is essential to determine how it can be integrated into existing treatment protocols for maximum efficacy. Furthermore, given the variability in individual responses to probiotics, factors such as genetics, diet, and gut microbiota composition should be considered to develop tailored approaches for patients with depression. This personalized approach could increase the likelihood of successful outcomes, ensuring that probiotic therapy is not just an adjunctive treatment but an effective and integrated component of a holistic depression management plan.

Overall, while the evidence for probiotics in the treatment of depression is promising, there are still significant gaps in our understanding. With more focused research and clearer clinical guidelines, probiotics could become a valuable tool in the management of depressive symptoms, helping to offer a more diverse range of treatment options for individuals suffering from depression.

Disclosure

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References

1. Akkasheh, G., Kashani-Poor, Z., Tajabadi-Ebrahimi, M., Jafari, P., Akbari, H., Taghizadeh, M., Memarzadeh, M. R., Asemi, Z., & Esmaillzadeh, A. (2016). Clinical and metabolic response to probiotic administration in patients with major depressive disorder: A randomized, double-blind, placebo-controlled trial. *Nutrition*, *32*(3), 315–320. https://doi.org/10.1016/j.nut.2015.09.003

2. Alli, S. R., Gorbovskaya, I., Liu, J. C. W., Kolla, N. J., Brown, L., & Müller, D. J. (2022). The gut microbiome in depression and potential benefit of prebiotics, probiotics, and synbiotics: A systematic review of clinical trials and observational studies. *International Journal of Molecular Sciences*, *23*(9), 4494. https://doi.org/10.3390/ijms23094494

3. Bercik, P., Denou, E., Collins, J., Jackson, W., Lu, J., Jury, J., Deng, Y., Blennerhassett, P., Macri, J., McCoy, K. D., Verdu, E. F., & Collins, S. M. (2011). The intestinal microbiota affect central levels of brain-derived neurotropic factor and behavior in mice. *Gastroenterology*, *141*(2), 599-609, 609.e1-3. https://doi.org/10.1053/j.gastro.2011.04.052

4. Bercik, P., Verdu, E. F., Foster, J. A., Macri, J., Potter, M., Huang, X., Malinowski, P., Jackson, W., Blennerhassett, P., Neufeld, K. A., Lu, J., Khan, W. I., Corthesy-Theulaz, I., Cherbut, C., Bergonzelli, G. E., & Collins, S. M. (2010). Chronic gastrointestinal inflammation induces anxiety-like behavior and alters central nervous system biochemistry in mice. *Gastroenterology*, *139*(6), 2102-2112.e1. https://doi.org/10.1053/j.gastro.2010.06.063

5. Doroszkiewicz, J., Groblewska, M., & Mroczko, B. (2021). The role of gut microbiota and gut-brain interplay in selected diseases of the central nervous system. *International Journal of Molecular Sciences*, *22*(18), 10028. https://doi.org/10.3390/ijms221810028

6. Ferenchick, E. K., Ramanuj, P., & Pincus, H. A. (2019). Depression in primary care: Part 1—Screening and diagnosis. *BMJ*, *365*, l794. https://doi.org/10.1136/bmj.l794

7. Foster, J. A., & Neufeld, K.-A. M. (2013). Gut–brain axis: How the microbiome influences anxiety and depression. *Trends in Neurosciences*, *36*(5), 305–312. https://doi.org/10.1016/j.tins.2013.01.005

8. Gutiérrez-Rojas, L., Porras-Segovia, A., Dunne, H., Andrade-González, N., & Cervilla, J. A. (2020). Prevalence and correlates of major depressive disorder: A systematic review. *Brazilian Journal of Psychiatry*, *42*(6), 657–672. https://doi.org/10.1590/1516-4446-2020-0650

9. He, J., Chang, L., Zhang, L., Wu, W., & Zhuo, D. (2023). Effect of probiotic supplementation on cognition and depressive symptoms in patients with depression: A systematic review and meta-analysis. *Medicine (Baltimore)*, *102*(47), e36005. https://doi.org/10.1097/MD.0000000000036005

10. Hofmeister, M., Clement, F., Patten, S., Li, J., Dowsett, L. E., Farkas, B., Mastikhina, L., Egunsola, O., Diaz, R., Cooke, N. C. A., & Taylor, V. H. (2021). The effect of interventions targeting gut microbiota on depressive symptoms: A systematic review and meta-analysis. *CMAJ Open*, *9*(4), E1195–E1204. https://doi.org/10.9778/cmajo.20200283

11. Kelly, J. R., Minuto, C., Cryan, J. F., Clarke, G., & Dinan, T. G. (2017). Cross talk: The microbiota and neurodevelopmental disorders. *Frontiers in Neuroscience, 11*, 490. https://doi.org/10.3389/fnins.2017.00490

12. Kumar, A., Pramanik, J., Goyal, N., Chauhan, D., Sivamaruthi, B. S., Prajapati, B. G., & Chaiyasut, C. (2023). Gut microbiota in anxiety and depression: Unveiling the relationships and management options. *Pharmaceuticals, 16*(4), 565. https://doi.org/10.3390/ph16040565

13. Liu, Y., Zhang, L., Wang, X., Wang, Z., Zhang, J., Jiang, R., Wang, X., Wang, K., Liu, Z., Xia, Z., Xu, Z., Nie, Y., Lv, X., Wu, X., Zhu, H., & Duan, L. (2016). Similar fecal microbiota signatures in patients with diarrhea-predominant irritable bowel syndrome and patients with depression. *Clinical Gastroenterology and Hepatology, 14*(11), 1602–1611.e5. https://doi.org/10.1016/j.cgh.2016.05.033

14. Liu, P., Liu, Z., Wang, J., Wang, J., Gao, M., Zhang, Y., Yang, C., Zhang, A., Li, G., Li, X., Liu, S., Liu, L., Sun, N., Zhang, K. (2024). Immunoregulatory role of the gut microbiota in inflammatory depression. *Nature Communications, 15*(1), 3003. https://doi.org/10.1038/s41467-024-47273-w

15. Ray, K. (2017). IBS: Mindful of probiotics for psychiatric comorbidities in IBS. *Nature Reviews Gastroenterology & Hepatology, 14*(7), 386-387. https://doi.org/10.1038/nrgastro.2017.70

16. Reininghaus, E. Z., Platzer, M., Kohlhammer-Dohr, A., Hamm, C., Mörkl, S., Bengesser, S. A., Fellendorf, F. T., Lahousen-Luxenberger, T., Leitner-Afschar, B., Schöggl, H., Amberger-Otti, D., Wurm, W., Queissner, R., Birner, A., Falzberger, V. S., Painold, A., Fitz, W., Wagner-Skacel, J., Brunnmayr, M., Rieger, A., Maget, A., Unterweger, R., Schwalsberger, K., Reininghaus, B., Lenger, M., Bastiaanssen, T. F. S., & Dalkner, N. (2020). PROVIT: Supplementary probiotic treatment and vitamin B7 in depression—a randomized controlled trial. *Nutrients, 12*(11), 3422. https://doi.org/10.3390/nu12113422

17. Schaub, A.-C., Schneider, E., Vazquez-Castellanos, J. F., Schweinfurth, N., Kettelhack, C., Doll, J. P. K., Yamanbaeva, G., Mählmann, L., Brand, S., Beglinger, C., Borgwardt, S., Raes, J., Schmidt, A., Lang, U. E. (2022). Clinical, gut microbial and neural effects of a probiotic add-on therapy in depressed patients: A randomized controlled trial. *Translational Psychiatry, 12*(1), 227. https://doi.org/10.1038/s41398-022-01977-z

18. Schneider, E., Doll, J. P. K., Schweinfurth, N., Kettelhack, C., Schaub, A. C., Yamanbaeva, G., Varghese, N., Mählmann, L., Brand, S., Eckert, A., Borgwardt, S., Lang, U. E., Schmidt, A. (2023). Effect of short-term, high-dose probiotic supplementation on cognition, related brain functions and BDNF in patients with depression: A secondary analysis of a

randomized controlled trial. *Journal of Psychiatry & Neuroscience, 48*(1), E23–E33. https://doi.org/10.1503/jpn.220117

19. Simpson, C. A., Diaz-Arteche, C., Eliby, D., Schwartz, O. S., Simmons, J. G., & Cowan, C. S. M. (2021). The gut microbiota in anxiety and depression: A systematic review. *Clinical Psychology Review, 83*, 101943. https://doi.org/10.1016/j.cpr.2020.101943

20. Sonali, S., Ray, B., Ahmed, T. H., Rathipriya, A. G., Sunanda, T., Mahalakshmi, A. M., Rungratanawanich, W., Essa, M. M., Qoronfleh, M. W., Chidambaram, S. B., Song, B. J. (2022). Mechanistic insights into the link between gut dysbiosis and major depression: An extensive review. *Cells, 11*(8), 1362. https://doi.org/10.3390/cells11081362

21. Wallace, C. J. K., & Milev, R. (2017). The effects of probiotics on depressive symptoms in humans: A systematic review. *Annals of General Psychiatry, 16*, 14. https://doi.org/10.1186/s12991-017-0138-2

22. World Health Organization. (2023). Depression. Retrieved from https://www.who.int/news-room/fact-sheets/detail/depression

23. Vuotto, C., Battistini, L., Caltagirone, C., & Borsellino, G. (2020). Gut microbiota and disorders of the central nervous system. *Neuroscientist, 26*(5-6), 487–502. https://doi.org/10.1177/1073858420918826

24. Xiong, R.-G., Li, J., Cheng, J., Zhou, D. D., Wu, S. X., Huang, S. Y., Saimaiti, A., Yang, Z. J., Gan, R. Y., Li, H. B. (2023). The role of gut microbiota in anxiety, depression, and other mental disorders as well as the protective effects of dietary components. *Nutrients, 15*(14), 3258. https://doi.org/10.3390/nu15143258

25. Zhu, F., Tu, H., & Chen, T. (2022). The microbiota-gut-brain axis in depression: The potential pathophysiological mechanisms and microbiota combined antidepression effect. *Nutrients, 14*(10), 2081. https://doi.org/10.3390/nu14102081