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MINI REVIEW

# Psychobiotics and Dietary Supplementation in the Clinical Practice: A Mini Review

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## ABSTRACT

Mental health defined as a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make meaningful contribution to his or her community reflects the individual ability to adapt to changing environment through thoughts, emotions and behaviors. Recently, the prevalence of psychiatric diseases is an emerging health issue that significantly impact on the quality of life and productivity of societies worldwide. Despite recent research advancements, the effectiveness of the curative approaches for the mental illness are still limited to pharmacologic treatments and/or psychotherapy, thereby indicating the need of development of alternative strategies. Growing number of research efforts into the better understanding of mental health determinants, prompted scientific interests into the use of dietary interventions, as potential approach to modify the mental state and improve wellbeing. A growing body of evidence to demonstrate the importance of diet, in particular intake of plant foods, in achieving optimal nutritional and health status, which has been attributed to plant-derived bioactives that consumed as whole food or dietary supplement may provide benefits for mental health, therefore providing an alternative for common pharmacotherapies in the psychiatry practice applied to treat mental conditions, including anxiety, depression, ADHD or schizophrenia. In addition, the discovery of a bidirectional communication between brain and gut microbiome, followed by the studies linking the gut microbiota composition with behavior and mood, support use of microbial-derived metabolites in the form of live probiotic bacteria (probiotics), as well as their metabolites (post-biotics) may help in stress management and prevent anxiety-/depression-like symptoms in high-risk populations.

## Abbreviations

5-HT: 5-Hydroxytryptamine; ADHD: Attention Deficit Hyperactivity Disorder; ASD: Autism Spectrum Disorder; BDI: Beck Depression Inventory; BMI: Body Mass Index; BDNF: Brain-Derived Neurotrophic Factor; CFU: Colony Forming Unit; CRP: C-Reactive Protein; DASS: Depression Anxiety And Stress Scale; g: grams; GABA: Gamma-Aminobutyric Acid; GHQ: General Health Questionnaire; HPA: Hypothalamic-Pituitary-Adrenal; HAMD-17: Hamilton Depression Rating Scale; MDD: Major Depressive Disorder; ml: milliliters; NO: Nitric Oxide; SCFA: Short Chain Fatty Acids

## Introduction

Mental illnesses, including depression, anxiety, schizophrenia, chronic stress and insomnia, are common mental health problems with high economic and social burden, which significantly affect the mental health, which can be defined, a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make meaningful contribution to his or her community [1]. Clinical depression

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in particular, is one of the five most common diseases in the world that affects the majority of the world's population and has a huge impact on quality of life and the ability to function in society) [2]. Despite the wide availability of many treatments, such as psychotherapy or pharmacotherapy with antidepressants, safety concerns, side effects, including low libido, dry mouth and constipation, mood herbals, weight gain and limited efficacy followed by poor tolerance are important issues in clinical psychiatric practice. A growing number of epidemiological studies demonstrating the correlation between certain dietary patterns and the individual nutritional status, and psychiatric conditions, such as anxiety and depression, is of the particular interest, owing to the potential of gut microbiota manipulation in the treatment of mental illness, as well as improving behavior and mood [3]. Therefore, a bidirectional communication between the brain and gut microbiota, known as gut-brain axis, increases interest in the potential of plant and microbial-based preparations in mental health applications.

Therefore, diet is of great importance for maintaining mental health. It has been shown that diet not only influences body composition and physical health status, but it also may affect mood and general well-being. Interestingly, a well-balanced diet, like traditional diets of people living in Japan, the Scandinavian countries or the Mediterranean area, rich in low-processed plant foods, (e.g., Fresh vegetables and fruits, whole grains or legumes), with moderate consumption of fish and dairy, may support our physical health, but it is also effective in relieving some of the symptoms of depression. For example, introducing appropriate changes in eating habits aimed at increasing the amount of fresh vegetables and fruits, as well as dietary fiber in the form of low-processed whole grain products (e.g., groats, cereals, whole grain bread), including food sources of polyunsaturated fatty acids (e.g. in the form of olive oil or fatty species of marine fish), it is most effective in decreasing depression symptoms when compared to group therapy or physical activity [4]. Although there are many possible mechanisms for how diet can modify our mental state, the influence of nutritional factors of microbial communities is the most appealing. The complexity and diversity of microbial communities found in the gut, including more than  $1 \times 10^{14}$  microbial cells, have an important role in maintaining human health, through modulating activities linked to the gastrointestinal tract and nervous system function [5]. Although gut microbiota in adults is relatively stable over the life course of the person, it may substantially differ between individuals due to various factors, like BMI, exercise (type and frequency), culture, lifestyle and indeed, dietary habits [6]. It must be mentioned that continuous disruption of the gut microbiome, especially in the early life, can increase risk of health issues in adulthood, including higher chances for developing depression [7]. For example, patients diagnosed with irritable bowel syndrome, in most cases also suffer from depression and/or anxiety disorders [8]. Furthermore, composition of gut microbiota of individuals diagnosed

with mental health conditions, such as Alzheimer's and Parkinson's disease, as well as schizophrenia significantly differ from gut microbiota of apparently healthy people [9-11] characterized by increased bacteroidetes followed by decreased Firmicutes and Bifidobacterium found in Alzheimer's patients [10].

### Dietary interventions for gut microbiota

In the past decade, there is an increasing interest in examining the link between dietary patterns and mental health outcomes. Among these, the Mediterranean diet seems to be the most studied under the 'whole diet', however a growing number of studies also focuses on the health effects after adopting plant based-, and western-style eating, as well as intake of diets rich in saturated fat and sugar.

The Mediterranean diet is a diet based on what is consumed in the Mediterranean countries and involves daily intake of fruit and vegetables, whole grains, legumes, nuts, fish, white meats, olive oil, fermented dairy products, a low intake of red meat, and some intake of red or white wine [12]. Nutritionally, it is low in saturated fat and animal proteins while being rich in foods of plant origin, being an excellent source of antioxidants, dietary fibers and monounsaturated fats. Additionally, the Mediterranean diet has an adequate ratio of omega-6/omega-3 fatty acids [13], which is important for cardiovascular health. In addition to gut microbiota, the Mediterranean diet promotes microbial diversity while promoting bacteria which enhance a healthy gut environment [14]. The results of an international study called Nutrition in Elderly People (NU-AGE) 12 months after the start of the intervention aimed at implementing the recommendations and practices typical of the Mediterranean diet contributed to an increase in the percentage of microorganisms that were previously associated with improved cognitive function and a reduced risk of bone fragility and the prevalence of inflammation in the elderly [15].

Furthermore, the Mediterranean diet brings positive mental health outcomes when implemented in patients suffering from depression [16], additionally promoting a cognitive ability [17] and reducing the need to use antidepressants [18]. Furthermore, the Nordic diet, also known as the Scandinavian diet, similarly to Mediterranean diet, relies on the frequent consumption of fresh, low-processed foods, such as local vegetables and fruits, e.g. cruciferous vegetables, root/tuber vegetables; and apples, pears or blueberries, blueberries and raspberries. In addition, the Nordic diet is rich in whole grains (e.g., barley and rye), which are excellent sources of dietary fibers and micronutrients valuable from the point of view of mental health. The Scandinavian diet also includes eggs and dairy products, cheese or Icelandic yogurts (high in protein, low in fat), eggs, fish and seafood, seeds and nuts; whereas red meat is eaten rarely and is often replaced with fish and seafood.

Interestingly, the fermented foods, including Swedish fermented milk "filmjöl", kefir and kimchi (the spicy equivalent of sauerkraut) positively affects the functioning of the intestinal microflora [19]. Studies conducted among young women aged 18 to 25 years have shown that following the Nordic diet, and especially the regular consumption of large amounts of vegetables (including cruciferous vegetables), which are a source of dietary fiber, B vitamins and folic acid, is the opposite. Proportional to the measure of stress and drug symptoms and is also associated with improved health-related quality of life [20].

### Psychobiotic potential of fermented foods

Recently, microbial-based products gained a significant public interest, which has been reflected by the increasing number of foods and dietary supplements that claim to contain probiotic microorganisms, such as bifidobacteria (e.g., *Bifidobacterium animalis* subsp. *lactis*, *B. bifidum*, and *B. longum*) and lactobacilli (e.g., *Lactobacillus acidophilus* and *Lactobacillus helveticus*, as well as *L. casei* group, *Lactocaseibacillus casei*, *Lactocaseibacillus paracasei*, and *Lactocaseibacillus rhamnosus*). There is

evidence to suggest that regular intake of fermented foods or beverages, by impacting on gut microbiota, can positively influence mood and behavior [21]. Although these effects are predominantly attributed to the strain used for the fermentation, it must be mentioned that other ingredients found in this particular food product may also exert some effect on the gut-brain by themselves [22] (Table 1). Among all fermented foods, milk and dairy products are the most common; what is related to the fact that lactic bacteria are widely used in fermented dairy foods, either as starter cultures, or is naturally found in the raw material. These probiotic strains are widely associated with improved health outcomes [23]. A wide range of studies attributed the potential psychobiotic effects resulting from the regular intake of fermented milk products to the presence of certain lactobacilli and bifidobacteria strain, such as *Lactobacillus casei* Shirota and *Lactobacillus helveticus*; as well as their combinations: *Lactobacillus acidophilus* + *Lactobacillus casei* + *Bifidobacterium bifidum* + *Lactobacillus fermentum*; *Lactobacillus fermentum* LAB9 + *Lactobacillus casei* LABPC and *Bifidobacterium animalis* subsp *lactis* + *Streptococcus thermophilus* + *Lactobacillus bulgaricus* + *Lactococcus lactis* subsp *lactis*. Similarly, consumption of kefir and

**Table 1:** Potential psychobiotic properties of various fermented foods based on the clinical evidence reviewed by [22].

Food Product	Strain(s)	Doses	Psychobiotic Effects
Black soybean milk	<i>Lactobacillus helveticus</i> IDCC3801	500, 1000, or 2000 mg of tablets of skim milk powder fermented for 12 weeks	Improvements in cognitive function in healthy old adults
	<i>Lactobacillus helveticus</i>	190 g of fermented milk once a day for 8 weeks	Improved cognitive function in healthy middle-aged adults
Fermented milk	<i>Lactobacillus gasseri</i> CP2305	190 g of fermented milk once a day for 5 weeks	Improved sleep quality and alleviated stress-associated symptoms in healthy students
	<i>Lactobacillus casei</i> Shirota	100 mL of fermented milk once a day for 8 weeks	Increased fecal serotonin levels and reduced physical symptoms in healthy subjects when exposed to stressful situations
		65 mL of probiotic-containing milk drink for 3 weeks	Improved the mood of adults whose mood was initially poor/depressive
	<i>Bifidobacterium animalis</i> subsp <i>lactis</i> I-2494, <i>Streptococcus thermophilus</i> I-1630, <i>Lactobacillus bulgaricus</i> I-1632 and I-1519, and <i>Lactococcus lactis</i> subsp. <i>lactis</i> I-1631	125 g of fermented milk twice daily for 4 weeks	Affected the activity of brain regions that control central processing of emotion and sensation in healthy women
	<i>Lactobacillus acidophilus</i> , <i>Lactobacillus casei</i> , <i>Bifidobacterium bifidum</i> , and <i>Lactobacillus fermentum</i>	200 mL/day for 12 weeks	Positively affected cognitive function and some metabolic statuses in Alzheimer's disease patients (60-95 years old)
Fermented Laminaria japonica	<i>Lactobacillus brevis</i> BJ20	1.5 g/day of fermented Laminaria japonica for 6 weeks	Provided a protective mechanism against cognitive impairment associated with dementia in elderly
Fermented soybean	<i>Lactobacillus plantarum</i> C29	800 mg/day for 12 weeks	Improved cognitive function in individuals with Mild Cognitive Impairment
Kefir	<i>Acetobacter aceti</i> , <i>Acetobacter</i> sp., <i>Lactobacillus delbrueckii</i> , <i>Lactobacillus fermentum</i> , <i>Lactobacillus fructivorans</i> , <i>Enterococcus faecium</i> , <i>Leuconostoc</i> spp., <i>Lactobacillus kefirifaciens</i> , <i>Candida famata</i> , and <i>Candida krusei</i>	2 mL/Kg/daily for 90 days	Improvement in memory, abstraction abilities, and executive/language functions
Unpasteurized milk and dairy products	Lactobacilli	Free consumption before and after 12 weeks	Decreased stress and anxiety in adults
Yogurt	<i>Lactobacillus acidophilus</i> LA5 and <i>Bifidobacterium lactis</i> BB12	100 g once a day for 6 weeks	Improvement of depression, anxiety and stress symptoms in adults
	<i>Lactobacillus gasseri</i> SBT2055 and <i>Bifidobacterium longum</i> SBT2928	100 g once a day for 12 weeks	Reduced levels of the stress-induced hormone in adults

yogurt, which are another examples of dairy beverages produced upon fermentation with LAB, such as *Lactobacillus gasseri* SBT2055, *Bifidobacterium longum* SBT2928, *Lactobacillus acidophilus* LA5, *Bifidobacterium lactis* BB12, also been studied for their psychobiotic effects. Interestingly, an emerging fermented food products recently gaining attention are soya-based products, which are produced during fermentation soy-based milk following addition of *Lactobacillus brevis* FPA 3709 and *Lactobacillus plantarum* C29 strains.

### Dietary fiber and prebiotic fibers

Dietary fiber is a key element of a healthy and balanced diet, mainly because of its beneficial effects on the gut microbiota. Epidemiological evidence consistently has shown a link between dietary fiber consumption and the risk of depression. For example, observational studies conducted on 69,000 postmenopausal women indicated that intake of 21g a day of the dietary fiber in the Beijing of the study resulted in a 14% lower risk of developing depression symptoms three years later. Interestingly, people with a lower dietary fiber intake in this study of about 14 grams a day had depression risk reduced by 4% [24]. Interestingly, the increased consumption of soluble but not insoluble fiber was associated with a lower frequency of depressive symptoms in both men and women; and similarly an increased proportion of vegetable fiber from soy-based products has been associated with a lower risk of depression for both groups [25]. Dietary fiber is a key component of a healthy diet, which, compared to other nutrients such as carbohydrates, fats and proteins, is not broken down by the human digestive system. Consequently, intact, it passes into the further structures of the gastrointestinal tract, eventually reaching the large intestine, where it is fermented by the gut bacteria, what results in the production of microbial-derived bioactives, such as SCFAs (e.g., acetate, propionate and butyrate). In the gut microbiota, SCFA are mostly produced by abundant Bacteroidetes (acetate and propionate producers), and Firmicutes (butyrate producers) [26]. Bacterial SCFA production is considered by many scientists to be one of the main mechanisms in which dietary fiber may influence inflammation and risk of diseases related to its presence, including depression.

### Microbial-based preparations and their effects on mental health - psychobiotics

Probiotic supplements are predominantly known for their role in achieving an optimal digestive and immune health, however less is known about their effects on hypothalamic, adrenal and pituitary functions [27]. Psychobiotics, similarly to probiotics, are living microorganisms which administered in sufficient amounts can produce a health benefit for patients with psychiatric or neurological conditions [28]. Recently, the psychobiotics definition was extended to include microbial metabolites and their components (postbiotics) as well as their substrates (prebiotics), that

causing a positive change in the gut microbiota function, may have a favorable influence on mental health, characterized by changes in emotional, cognitive, systemic, and neural indices [29,30]. The most common bacterial strains with attributed potential psychobiotic effects as *Lactobacilli*, *Streptococci*, *Bifidobacteria*, *Escherichia* and *Enterococci*, and their substrates (prebiotic dietary fibers), such as fructooligosaccharides and galactooligosaccharides [31]. To date, evidence obtained from clinical studies, demonstrated that microbial preparations involving single or multi strains possess psychobiotic properties [31] (Table 2), which may help to manage symptoms of mental disorders, including mood swings, anxiety and stress, as well as may delay progression of clinical disorders like Alzheimer's and Parkinson's disease.

### Potential mechanism how microbial-based interventions can modulate the gut-brain axis

There is growing evidence to demonstrate that microorganisms with attributed psychobiotic properties might be involved in the cross-talk between the brain and the gastrointestinal system, thereby implicating for a bidirectional communication within the gut-brain-axis [3,31] via the vagus nerve, which being a parasympathetic nerve combines the neurological and digestive functions [31]. Although many support the gut microbiota as a modifier of the brain functions [32], the exact mechanism still remains unclear. To date, several mechanisms have been proposed in order to explain how microbial metabolites (e.g. SCFAs), enteroendocrine hormones, cytokines and neurotransmitters can influence brain and nervous system function [33,34].

Gut microbiota has been shown to be involved in the production of a range of neurochemicals, including brain neurotransmitters (e.g., GABA, noradrenaline, serotonin, dopamine, and acetylcholine), as well as other bacterial metabolites like short-chain fatty acids (e.g., acetate, butyrate, lactate, and propionate) have been attributed to neuroactive properties [35] that all together can stimulate production of a variety of neurotransmitters in the strain-dependent manner. For example, serotonin (5-HT), a neurotransmitter involved in the regulation of human behavior and mood can be induced by *Enterococci* and *Streptococci* families in the enterochromaffin cells, which are neuroendocrine cells located in gastric glands [34]. Similarly, accessible levels of dopamine and epinephrine, catecholamine neurotransmitters, with play vital roles in motor control, learning, memory formation, and stress response, as well as with regulatory effects on the carbohydrates and fats metabolisms [36,37] can be influenced by gut microbiota plays, in particularly *Bacillus* family. Interestingly, also increased abundance of *Clostridium* in the gut has been associated with a drastic elevation of free dopamine and norepinephrine [38]. Furthermore, GABA and glutamate, primary neurotransmitters of the nervous systems, having a modulatory role on neurotransmission,



**Table 2:** Microbial-based formulations with potential psychobiotic effects based on the clinical evidence reviewed [22].

Bacteria	Dose	Findings
Bacillus coagulans MTCC 5856	2 billion spores	Efficient in treatment of patients experiencing IBS symptoms with major depressive disorder
Bifidobacterium longum 1714	1 × 10 <sup>9</sup> CFU/day	Reduced stress and improved memory.
Bifidobacterium longum NCC3001	1 × 10 <sup>10</sup> CFU/g	Reduction in depression scores and reduced responses to negative emotional stimuli.
Clostridium butyricum MIYAIRI 588	60 mg/day	In combination with anti-depressants, effective in the treatment of treatment-resistant major depressive disorder.
Lactobacillus casei Shirota	1 × 10 <sup>9</sup> over 8 weeks	Decrease in the cognitive state anxiety perceived stress.
Lactobacillus casei Shirota	100 mL of a fermented beverage containing more than 1 × 10 <sup>9</sup> CFU/mL/day	Lower rate of subjects experiencing common abdominal and cold symptoms, and total number of days experiencing these physical symptoms.
Lactobacillus gasseri CP2305	1 × 10 <sup>10</sup> CFU	Improved stress behaviours and sleep quality.
Bifidobacterium bifidum W23, Bifidobacterium lactis W52, Lactobacillus acidophilus W37, Lactobacillus brevis W63, Lactobacillus casei W56, Lactobacillus salivarius W24, and Lactococcus lactis (W19 and W58)	2.5 × 10 <sup>9</sup> CFU/g	Reduced overall cognitive reactivity to low mood.
Lactobacillus acidophilus, Lactobacillus casei and Bifidobacterium bifidum	2 × 10 <sup>9</sup> CFU/g of each strain	Significant improvement in depression scores. Reduced insulin. Increased total glutathione levels.
Lactobacillus acidophilus, Lactobacillus casei, Bifidobacterium bifidum and Lactobacillus fermentum	1 capsule containing 2 × 10 <sup>9</sup> CFU/g daily for 12 weeks	Improved general health, depression anxiety and stress symptoms. Changes in levels of pro-inflammatory markers (e.g. CRP, NO metabolites, and malondialdehyde).

neuronal excitability, synaptic plasticity, and cognitive functions (e.g., learning and memory functions) can be produced by certain Bifidobacteria and Lactobacilli. For example, lactic acid bacteria isolated from Italian cheeses, especially *Lactobacillus paracasei* PF6, *Lactobacillus delbrueckii* subsp. *bulgaricus* PR1, *Lactococcus lactis* PU1, and *Lactobacillus brevis* PM17; as well as LAB strains isolated from traditional dairy products made from raw milk, mostly *Lactococcus lactis* subsp. *lactis* and *Streptococcus thermophiles*, have been shown to produce high GABA concentrations during the fermentation of reconstituted skimmed milk [39,40]. Bacterial metabolites, such as SCFAs, short aliphatic organic acids (e.g., acetate, propionate, and butyrate) produced by gut bacteria during fermentation of resistant to digestion carbohydrates (prebiotic fibres) have been implicated in regulating cellular metabolism, appear to play an important role in regulating the integrity of the epithelial barrier, regulating the immune system and inflammatory response [41]. Moreover, SCFAs was proposed to directly influence neural function by reinforcing blood-brain barrier integrity, modulating neurotransmission, and influencing levels of neurotrophic factors [42].

Furthermore, gut microbiota can modulate response to stress through the HPA Axis, which is a part of the system of the body response to physiological and physical stress, composed of the hypothalamus, pituitary gland, and adrenal cortex, as well as regulatory factors and hormones, such as cortisol (a stress hormone). Imbalances in the gut microbiota can lead to the prolonged activation of the HPA axis, while achieving the microbial balance might help to restore homeostasis within the HPA axis. For example, use of probiotic formulation containing *Lactobacillus*

*helveticus* R0052 and *Bifidobacterium longum* R0175, as well as *Lactobacillus plantarum* 299v has been shown to significantly reduce the HPA axis response to stress [43,44] characterized by reduced salivary cortisol levels [44].

Finally, the immunomodulatory activity of the gut microbiota may help to maintain balance between the innate and adaptive responses within the brain [45] leading to the immune homeostasis. Disruption of gut microbiota composition are linked with aberrant immune responses followed by overproduction of pro-inflammatory mediators and consequently higher risk of the brain inflammation, as those cytokines, including IL-6, IL-1 $\beta$ , and TNF- $\alpha$ , have been also found to increase in the individuals with psychiatric disorders [22].

### Supplementation with microbial preparations in mental health diseases

**Depression:** Combining a psychobiotic strain of *Clostridium Butyricum* (CBM588) with the pre-prescribed antidepressants significantly decreased (e.g.,  $\geq 50\%$  reduction in HAMD-17 total score) in Hamilton rating scale for depression and BDI scores in the group of patients diagnosed with treatment-resistant MDD when compared to the control receiving placebo [46]. This beneficial effect psychobiotic use on MDD treatment, characterized by decreased BDI scores has been also observed after patients were given probiotic capsules containing *Lactobacillus acidophilus*, *Lactobacillus casei* and *Bifidobacterium bifidum* [47], as well as *L. helveticus* R0052 and *B. longum* R0175, while 5 g galactooligosaccharide showed no significant effects on

the parameter after 2 months [48]. The beneficial effects on low-to-moderate depression treatment attributed to *L. helveticus* R0052 and *B. longum* R0175 are probably associated with higher BDNF levels within the brain, observed in those who received probiotics, but not prebiotic or placebo. Interestingly higher levels of BDNF were also linked with depression severity [49]. On the other hand, providing moderately depressed patients a synbiotic consisting of *L. casei*, *L. acidophilus*, *L. bulgaricus*, *L. rhamnosus*, *Bacillus breve*, *B. longum*, *Streptococcus thermophilus* and prebiotic fructooligosaccharides (prebiotic) resulted in significant reductions of HAM-D scores compared to the group receiving placebo [50].

**Exposure to stress:** There is some indication, that consumption of probiotic yogurt with added *L. acidophilus* LA5 and *B. lactis* BB12 strains, or dietary probiotic supplementation containing *L. casei*, *L. acidophilus*, *L. rhamnosus*, *L. bulgaricus*, *B. breve*, *B. longum* and *S. thermophilus* strains, after 6 weeks may bring some benefits for mental status, characterized by improved GHQ and DASS scores in the group of 70 petrochemical workers. Nevertheless, these effects were no significant in those who received conventional yogurt group [49], what highlight the need for further research into this direction.

**Autism:** A study conducted in the group of Taiwanese boys with ASD, have shown that supplementation with *Lactobacillus plantarum* PS128 might bring some benefits for behavioral outcomes, suggesting its potential in ameliorating opposition/defiance behaviors, and significantly improve the total score of SNAP-IV for younger children compared to the placebo group. Although the authors of that trial concluded that *L. plantarum* PS128 might help to improve some of the autism symptoms, such as disruptive and rule breaking behaviors and hyperactivity [51]; nevertheless, more research needs to be done in order to confirm that effect.

## Conclusion

Mental disorders are serious problems for people's mental health that reduce their quality of life and their ability to function properly in society. To develop alternative options for current medications for emotional disorders, natural products, especially those of plant origin, which contain numerous bioactive compounds with a pharmacological effect on the function of the central nervous system, are attracting more and more interest. The evidence to demonstrate effects of the whole diet interventions (such as Mediterranean diet) on gut microbiome function in mental health is limited to promoting consumption of particular food groups. For example, increasing intake of fruits, vegetables and other edible plants have been shown to increase the gut, promoting beneficial bacteria, while western-style diets, abundant with highly processed foods with added saturated fats and sugars may negatively impact on symbiotic strains

and promote inflammatory bacteria [52]. In this case, the microbiome diversity is of particular interest, owing to its ability to promote overall health through production of microbial-derived metabolites, including vitamins, minerals, amino-acids, and polyphenols, necessary for optimal functioning organisms as a whole [53]. These studies suggest that intentional modification of the diet leading to desired impact on microbiome activity, have potential could promote mental health and provide alternative aid for treatment of psychiatric conditions. Nevertheless, there is an emerging need for a large cohort, high-quality studies, that would expand understanding of mechanisms how whole diet interventions may impact mental health. While more research is needed to assess their safety profile before they can be implemented into approved clinical practice, it can already be concluded that naturally derived compounds present in medicinal fruits, vegetables and medicinal herbs may be applicable to the potential treatment of psychiatric disorders, including anxiety and depression, and help reduce symptoms of chronic stress.

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