

Review Article

Multifaceted applications of lactic acid bacteria: From food preservation to mental health enhancement

Wei Wei Chuah¹, Kar Shin Goh¹, Hui Suan Ng^{2,3}, John Chi-Wei Lan^{4,5}, Jest Phia Wong⁶ and Joo Shun Tan^{1,*}

¹School of Industrial Technology, Universiti Sains Malaysia, 11800 Gelugor, Pulau Pinang, Malaysia.
 ²Department of Chemical and Materials Engineering, National Yunlin University of Science and Technology, 123 University Road, Section 3, Douliu, Yunlin 64002, Taiwan.

³College of Future, National Yunlin University of Science and Technology, 123 University Road, Section 3, Douliu, Yunlin 64002, Taiwan.

⁴Biorefinery and Bioprocess Engineering Laboratory, Department of Chemical Engineering and Materials Science, Yuan Ze University, Chung-Li 32003, Taiwan.

⁵Graduate School of Biotechnology and Bioengineering, Yuan Ze University, Chung-Li 32003, Taiwan. ⁶Westwood Clinic, UG-23, PJ Midtown, Jalan Kemajuan, Seksyen 13, 46200 Petaling Jaya. Selangor.

*jooshun@usm.my

Received: 3 January 2024

Accepted: 11 March 2024

Published: 28 March 2024

Doi: https://10.51200/ijf.v1i1.4955

ABSTRACT

various functional inhibitory compounds which includes bacteriocins, organic acids, fatty acids, enzymes and other chemical substances that exhibit inhibitory effects on certain harmful microorganisms. Therefore, LAB is often found in fermented food which adds value to the nutritional composition of the food, and thereby offers a range of health benefits to human beings upon consumption. This review explores the diverse applications of LAB, focusing on their role in enhancing food safety, contributing to nutritional well-being, and their emerging significance in mental health as psychobiotics, specifically to tackle depression. The paper synthesises current research and advancements in LAB applications, providing insights into their potential in addressing contemporary health and nutritional challenges.

Lactic acid bacteria (LAB) are beneficial microorganisms with capability to produce

Keywords: bacteriocin; fermentation; food preservation; lactic acid bacteria; mental health

1. Introduction

The link between food security, nutrition, and food safety is crucial, as emphasised by the World Health Organization (WHO). Globally, contaminated food affects 1 in 10 people each year, causing illness, and leads to approximately 420,000 deaths. This translates to a loss of 33 million healthy life years. Particularly impacted are low and middle-income countries, where the economic burden due to lost productivity and medical expenses is around 110 billion US dollars per year. Children under five are disproportionately affected, accounting for 40% of the foodborne disease burden and resulting in 125,000 deaths each year.

Foodborne infectious diseases not only strain healthcare systems but also hinder socioeconomic progress by impacting economies and sectors like tourism and commerce (Faour-Klingbeil & Todd, 2020). Another global challenge is the prevalence of mental health disorders and psychiatric illnesses, affecting

one in eight people worldwide. Symptoms include significant difficulties in thought, emotion control, or behaviour. Despite the availability of effective prevention and treatment strategies, access to high-quality healthcare remains limited for the majority (Wainberg *et al.*, 2017).

In this context, the role of lactic acid bacteria (LAB) in addressing these issues is noteworthy. LAB, during lactic acid fermentation, produce metabolites like bacteriocin and gamma-aminobutyric acid (GABA) (Cui *et al.*, 2020, Mokoena, 2017). Bacteriocins or bacteriocin-like inhibitory substances (BLIS), are a type of proteinaceous or peptide toxin that acts as an antimicrobial peptide. They have antimicrobial abilities, especially against strains of bacteria that come from closely related species (Kurnianto *et al.*, 2022). Unlike bacteriocins, which have well-defined structures and mechanisms of action, BLIS may not be as thoroughly characterized in terms of their molecular structure or genetic basis. In current, one bacteriocin has been widely used as a product, which is nisin. Nisin has been widely utilized in the food industry as a biopreservative because of their ability to prevent a wide variety of foodborne pathogens (Ng *et al.*, 2020).

GABA is a four-carbon non-protein amino acid with antioxidant properties. Recognized as Generally Recognized as Safe (GRAS) by the Food and Drug Administration (FDA). GABA inhibits lipid, protein, and carbohydrate oxidation. It enhances the activity of antioxidant enzymes in fruits and plants, thereby extending their storage life and minimizing damage from environmental stresses (Yang *et al.*, 2011). The infusion of exogenous GABA considerably extended the storage life of the fruit by increasing the buildup of citrate and amino acids (Sheng *et al.*, 2017), minimizing the damage caused by freezing (Shang *et al.*, 2011) and altering the carbon and nitrogen metabolism (Zhu *et al.*, 2019). Besides its function as a food bio-preservative, GABA is used clinically as an antidepressant and stress reliever in the form of a dietary supplement (Tette, Kwofie, & Wilson, 2022). It does this by inhibiting and blocking the transmission of certain brain signals, which leads to a reduction in the amount of activity in our neurological system. Human bodies experience a sense of relaxation and calmness when GABA attaches to the receptors that are specifically designed to respond to its presence (Nuss, 2015). Psychobiotics, a new class of probiotics producing neuroactive compounds like GABA, show promise in mental wellness by exhibiting effects on brain function, including the treatment of anxiety, the promotion of sleep and the regulation of the metabolic process of energy (Zielińska *et al.*, 2022).

The potential of LAB to produce both GABA and BLIS opens avenues for their use as psychobiotics and food bio-preservatives. Their dual production can enhance food safety, shelf life, health benefits, and marketability. Consuming fermented foods with both bacteriocins and GABA could offer comprehensive health benefits. Moreover, research indicates that co-culture environments or the presence of stress signals like additional bacteria can enhance bacteriocin production (Gutiérrez-Cortés *et al.*, 2018). Studies have shown that *Lactobacillus brevis*, in particular, can produce high amounts of GABA, but the induction systems using *Lactobacillus* extracts need further exploration. Additionally, using natural mediums like fruit and vegetable-based substrates for LAB cultivation could be a more efficient and cost-effective method for producing GABA-enriched nutrition.

In light of these challenges, this review delves into the versatile roles of LAB and their metabolites, particularly focusing on their contributions to food safety and mental health. We explore the dual roles of LAB in producing bacteriocin and GABA, highlighting their applications as psychobiotics and food biopreservatives. The paper underscores how LAB's antimicrobial properties, particularly against closely related bacterial strains, enhance food preservation, and their role in producing GABA, which offers therapeutic potential in treating mental disorders. We also discuss the innovative use of natural mediums for LAB cultivation, enhancing the nutritional value of food products. This review aims to provide a comprehensive overview of the current advancements in LAB applications, their potential health benefits, and their alignment with global health and safety goals. By examining these aspects, the review contributes to a deeper understanding of LAB's multifaceted roles in contemporary health and nutrition challenges, offering insights into their practical applications and future research directions.

2. LAB in Food Preservation and Safety

Lactic acid bacteria are Gram-positive bacteria primarily belonging to the Firmicutes phylum, encompassing genera such as *Lactobacillus, Streptococcus, Leuconostoc, Pediococcus, Lactococcus,* and *Enterococcus* (Mokoena, 2017). They are characterized by their ability to produce lactic acid as the major metabolic product of carbohydrate fermentation (Goa *et al.,* 2022). LAB can be classified based on their morphology into rods and cocci and based on their glucose fermentation into homofermentative (producing lactic acid as the sole product) and heterofermentative (producing lactic acid along with other compounds such as ethanol, acetic acid, and carbon dioxide).

During fermentation, LAB produce various metabolites including bacteriocins, lactic acid, organic acids, amino acids, antibiotic chemicals, antifungal compounds, sulphur compounds, aldehydes, esters, alcohols, and carbon dioxide (Emkani *et al.*, 2022). LAB have played a crucial role in food preservation for centuries, primarily due to their ability to produce lactic acid, which acts as a natural preservative. Lactic acid lowers the pH of the environment, creating conditions inhospitable for the growth of spoilage and pathogenic microorganisms. This acidic environment inhibits the growth of harmful bacteria, yeasts, and molds by denaturing microbial proteins and disrupting membrane integrity. This finding make bacteriocin becomes an interesting topic to be discussed. The next section will explore the specific mechanisms through which bacteriocin exerts its preservative effects.

3. Bacteriocins

Bacteriocins are proteinaceous molecules synthesised by ribosomal processes, primarily aiming at inhibiting the growth of other bacterial strains, especially those closely related to the producing bacterium. They can be classified into three primary classes based on their structural and physicochemical characteristics.

Class I bacteriocins, also known as lantibiotics, are small peptides typically below 5 kDa in size. They are heat-stable peptides with unique post-translational modifications such as lanthionine and methyl-lanthionine (Simons *et al.*, 2020). Lantibiotics can be further divided into type A (linear molecules) and type B (globular molecules), each with distinct mechanisms of action. Type A lantibiotics, like nisin, disrupt the target organism's cell membrane, leading to depolarization and cell death. Type B lantibiotics interfere with intracellular enzymatic activities (Chakraborty *et al.*, 2023; Bakhtiary *et al.*, 2017). Class II bacteriocins are small peptides usually less than 10 kDa in size (Negash & Tsehai, 2020). They lack lanthionine and other post-translational modifications, with their antimicrobial activity attributed to their ability to insert into the target cell membrane, leading to cell depolarization and death. Class II bacteriocins can be further classified into subclasses IIa (antilisterial pediocin bacteriocins type), IIb (composed of two peptides), and IIc (circular bacteriocins) (Kaur & Kaur, 2015; Darbandi *et al.*, 2022; Gabrielsen *et al.*, 2014). Class III bacteriocins are large peptides, typically greater than 30 kDa in size, and are heat-sensitive. They exert their antibacterial activity by targeting the cell wall of Gram-positive pathogens, causing cell lysis (Kaur & Kaur, 2015).

3.1 Mechanisms of bacteriocin action

Bacteriocins employ various mechanisms to inhibit bacterial growth, broadly categorized into two groups: those acting on the cell envelope and those affecting gene expression and protein production within the cell (Darbandi *et al.,* 2022). Certain bacteriocins, particularly those targeting Gram-positive bacteria, target the cell membrane (Negash & Tsehai, 2020). Class I bacteriocins, like nisin, inhibit lipid-II, impeding peptidoglycan formation and inducing apoptosis (Pérez-Ramos *et al.,* 2021). They also utilize lipid-II to initiate membrane insertion and pore formation, leading to cell death. Lantibiotics like lacticin 3147 possess dual activities dispersed over peptides, while others like mersacidin solely bind lipid-II (Islam *et al.,* 2012).

Conversely, bacteriocins targeting Gram-negative bacteria disrupt DNA, RNA, and protein synthesis. For instance, MccJ25 inhibits RNA polymerase, microcin B17 targets DNA gyrase, and MccC7-C51 inhibits aspartyl-tRNA synthetase (Cotter *et al.*, 2013; Negash & Tsehai, 2020). Enzymatic activities, like DNase and RNase, also contribute to bacteriocins' antibacterial action activity (Rodali *et al.*, 2013). Class II peptides have amphiphilic helical structures enabling them to insert into the target cell membrane, depolarizing and causing cell death. Class III bacteriocins, like lysostaphin, act directly on the cell wall of Gram-positive pathogens, lysing the target cell. These diverse mechanisms illustrate bacteriocins' effectiveness against a range of bacteria, highlighting their potential as antimicrobial agents in various applications (Negash & Tsehai, 2020).

3.2 Applications of bacteriocins in food preservation

Bacteriocins are useful compounds that find applications in a variety of fields, including agriculture, the pharmaceutical sector and the food industry. Bio-preservatives are those that are generated by the metabolites of LAB. During the process of carbohydrate fermentation by LAB, these bacteria will release certain metabolites that have the ability to inhibit the growth of foodborne pathogenic bacteria. Nisin is an example of a bio-preservative that is available for use. *Lactococcus lactis* is the bacterium responsible for producing the bacteriocin known as nisin (Anumudu *et al.*, 2021). It can kill bacteria that are genetically related to itself. The use of bio-preservatives is Generally Recognized as Safe (GRAS). They do not pose any danger to human health, can be degraded quickly by the human body, can be used effectively to preserve food even in very low concentrations and are non-toxic.

There has been a significant amount of research conducted on the application of bacteriocins in the food industry, specifically with regard to dairy products, eggs, vegetables and meat products (Verma *et al.,* 2022). Nisin has been approved by the FDA and is utilized in over 48 countries. It demonstrates remarkable effectiveness in various food systems by inhibiting the growth of a broad range of Gram-positive bacteria, including important foodborne pathogens like *Listeria monocytogenes*. Nisin is commonly employed in canned foods and dairy products, particularly in the production of processed cheese and spreads, where it provides protection against heat-resistant spore-forming microorganisms such as those from the Bacillus and *Clostridium* genera (Negash & Tsehai, 2020).

There are many bacteriocins that have not yet been brought to market, including lacticin 3147 and lacticin 481, both of which have shown promise for use as natural preservatives and flavour enhancers but have not yet been marketed. Pediocin PA-1 is a broad-spectrum lactic acid bacteriocin that is used as a food preservative. It is particularly effective against *L. monocytogenes* and possesses a high level of activity against this pathogen (Khorshidian *et al.*, 2021). A few years ago, there was a commercial PA-1 product in the market; however, to the best of our knowledge, it is no longer being sold under that name. While certain cultures or bio-preservative "fermentates" are currently available, they are not marketed as new ingredients, which allows them to avoid regulatory scrutiny. It is important to note that the exact bacteriocin content of these products may not be disclosed.

There are approximately three methods that bacteriocins can be incorporated into a portion of food in order to increase its safety. These include the use of a purified or semi-purified bacteriocin preparation as a component in a food, the incorporation of an ingredient that has previously been fermented with a bacteriocin-producing strain, and the use of a bacteriocin-producing culture to substitute all or part of the starter culture in fermented foods (Surati, 2021). Additionally, bacteriocins are utilized to enhance the overall quality and sensory attributes of the food. For instance, they can be utilized to increase the rate of proteolysis or to prevent gas blowing fault in cheese. This means that cheese can age for a longer period, allowing for increased proteolysis to occur over time, leading to improved flavour development and texture. Bacteriocins also have applications in bioactive packaging, a process designed to protect food from external contaminants, thereby improving food safety and extending its shelf life (Negash & Tsehai, 2020).

During the fermentation of carbohydrates, LAB produce certain metabolites, and certain of these metabolites such as bacteriocins and hydrogen peroxide can prevent the growth of foodborne pathogenic organisms. Furthermore, LAB are employed as starter cultures in foods and beverages that have been fermented. It is possible to describe starter culture as a microbial preparation consisting of cultures of one

or more microorganisms. This preparation is then added to a raw material to produce a fermented food by speeding and controlling the fermentation process. The food industry also makes use of LAB in the production of gelling agents, bio-thickeners and food sweeteners (Florou-Paneri, Christaki, & Bonos, 2013). Table 1 shows the use of LAB's bacteriocin in food preservation.

Bacteriocin	Probiotic strains	Effects	References
Nisin	Lactococcus lactis	Inhibit the growth of a broad range of Gram- positive bacteria	(Anumudu <i>et</i> <i>al.</i> , 2021)
Pediocin PA-1	Pediococcus spp.	Preserve meat and meat products against <i>L.</i> monocytogenes	(Khorshidian <i>et al.,</i> 2021)
Lacticin	<i>Lactococcus lactis</i> CNRZ481	Control non-starter lactic acid bacteria proliferation in cheese.	(O'sullivan <i>et</i> <i>al.,</i> 2003)
Bacteriocin	<i>Lactobacillus brevis</i> C23	Inhibit and kill the cells of <i>L.monocytogenes</i>	(Chuah <i>et al.,</i> 2023)

Table I use of bacteriocin in rood preservatio
--

4. LAB and Mental Health

Psychobiotics, a subset of probiotics, are increasingly recognized for their role in mental health, particularly through the production of neurotransmitters like GABA (Sasso *et al.*, 2023). Lactic acid bacteria, a type of psychobiotic, shows promise in positively influencing mental health by interacting with the nervous system. The mechanisms of action for LAB as psychobiotics are multifaceted. They may alleviate symptoms of common mental health issues like depression and anxiety by modulating the enteric nervous system or the immune system (Picó-Monllor *et al.*, 2023). LAB can impact mental health in three ways: by modulating the hypothalamic-pituitary-adrenal (HPA) axis to reduce stress and systemic inflammation, directly influencing the immune system, and secreting beneficial molecules like neurotransmitters, proteins, and short-chain fatty acids (Toro-Barbosa *et al.*, 2020). These actions highlight the potential of LAB as a novel approach to mental health treatment.

The gut-brain axis refers to the bidirectional communication network that links the emotional and cognitive centres of the brain with peripheral intestinal functions. Recent studies have increasingly acknowledged the impact of gut microbiota on this axis, noting that imbalances in gut flora can affect mental health (Carabotti *et al.*, 2015). LAB, as a major component of the gut microbiota, has been shown to play a pivotal role in this interplay. Research demonstrates that LAB can modulate gut microbiota, thereby influencing the gut-brain axis and potentially alleviating psychiatric symptoms (Oroojzadeh, Bostanabad & Lotfi, 2022).

LAB's influence on mental health is primarily exercised through three mechanisms: the production of neurotransmitter-like substances, modulation of the immune system, and direct effects on brain function. Certain strains of LAB have been found to produce GABA, the primary inhibitory neurotransmitter in the central nervous system. This production of GABA by LAB can influence mood and anxiety. Additionally, LAB can modulate the immune response, reducing inflammation which is often linked to several psychiatric disorders (Singh *et al.*, 2022).

Several human trials have explored the effects of LAB on mood and anxiety disorders. For instance, a study reported that participants consuming LAB-rich probiotics showed significant improvements in mood, illustrating the potential of LAB as a non-pharmacological treatment for depression (Jach *et al.*, 2023). The

first study involving *L. plantarum* PS128TM (PS128TM) focused on high-stress IT specialists, revealing significant improvements in stress levels, mood symptoms, and other psychological health indicators over an 8-week intervention. These findings indicate that PS128TM may offer unique benefits in stress reduction and mental health improvement, particularly for individuals in high-stress occupations. This aligns with the psychobiotic paradigm, which posits a substantial influence of gut microbiota on mental health through the gut-brain axis (Wu *et al.*, 2021).

Comparatively, another study in the field tested the impact of psychobiotics on anxiety symptoms, highlighting the role of genetic factors. The study revealed that consuming psychobiotics significantly reduced anxiety symptoms over 12 weeks, particularly in individuals with a genetic predisposition to anxiety, suggesting the potential for tailored psychobiotic treatments in anxiety disorders. This study complements the broader narrative of psychobiotics' effectiveness but also emphasizes the importance of considering genetic variations in treatment efficacy (Gualtieri *et al.*, 2020). In a similar vein, another investigation examined the effects of psychobiotic supplementation in clinically stressed nurses for eight weeks. This study employed a different heat killed probiotic strain, HK-PS23, and found significant reductions in stress hormones, particularly in subgroups with higher anxiety levels. These findings are crucial as they demonstrate the potential of psychobiotics in professions with inherent high-stress levels, like nursing, and suggest possible anxiolytic effects of these supplements (Wu *et al.*, 2022).

Moreover, the study involving *L. plantarum* JYLP-326 among college students with test anxiety provided a unique insight into the psychobiotic's impact on a younger demographic. This study not only reported improvements in anxiety, depression, and insomnia symptoms but also illustrated changes in gut microbiota and fecal metabolomics. The identification of specific faecal metabolites affected by JYLP-326 underscores the complex interplay within the microbiota-gut-brain axis and its potential role in stress-induced disorders (Zhu *et al.,* 2023). Each study contributes uniquely to the understanding of psychobiotics in mental health. While they collectively support the potential of psychobiotics in reducing stress and improving mood disorders, they also highlight the importance of personalized approaches, considering individual genetic makeup and specific strains of bacteria. The variation in results across different demographics and stress environments underscores the complexity of psychobiotic interventions and the need for further, more nuanced research.

Despite promising results, research on LAB as psychobiotics is still in its nascent stages. Most studies to date have been limited by small sample sizes, short durations, and variability in LAB strains used, making it challenging to generalize findings. Future research should focus on long-term effects, standardized LAB strains, and larger, more diverse population samples to fully elucidate the potential of LAB as psychobiotics. In conclusion, the burgeoning research on LAB as psychobiotics opens new doors in understanding and treating mental health disorders. By modulating the gut-brain axis, LAB shows potential in improving mood, reducing anxiety and stress, and enhancing cognitive functions. As research in this field advances, LAB could become a cornerstone in the holistic approach to mental health, complementing traditional psychiatric treatments and offering a natural, side-effect-free alternative to improve mental well-being. Table 2 summarises the use of probiotics for mood and anxiety in previous studies.

4.1 Applications of LAB derived GABA

GABA, a neurotransmitter crucial for regulating neuronal excitability and promoting calmness, is not only produced by the human body but also found in certain LAB. These GABA-producing LAB hold promise for influencing brain function via the gut-brain axis, particularly in psychobiotics research. By synthesizing and releasing GABA, these bacteria offer a natural means to address disorders linked to GABA deficiencies (Rashmi *et al.*, 2018). Exploring the role of GABA-producing LAB in psychobiotics could yield innovative treatments for mental health and neurological disorders, serving as potential alternatives to traditional pharmaceutical approaches. Understanding how these bacteria modulate GABA pathways highlights the interconnectedness between gut microbiota and brain function, providing insights into novel therapeutic strategies. As research in this area progresses, GABA-producing LAB may emerge as valuable tools for promoting mental well-being and managing neurological conditions, offering new avenues for holistic health

interventions. GABA has so many applications which can be found in the medical, food and cosmetics industries, as shown in Table 3.

Method	Probiotic strains	Effects	References
Oral Administration	<i>L. plantarum</i> PS128TM	Improvement in stress, mood symptoms, cortisol levels, psychological health, anxiety, depression, sleep disturbances, and quality of life	(Wu <i>et al.,</i> 2021)
Oral Administration	Not specified	Reduction in HAM-A total score; effective in mitigating anxiety symptoms, especially in IL-1 β carriers	(Gualtieri <i>et</i> <i>al.</i> , 2020)
Oral Administration	Heat-Killed PS23	Significant reduction in blood cortisol levels; effective in improving perceived anxiety and stress hormone levels in highly stressed clinical nurses.	(Wu <i>et al.,</i> 2022)
Oral Administration	<i>L. plantarum</i> JYLP- 326	Alleviation of anxiety, depression, and insomnia symptoms; modification of gut microbiota and faecal metabolomics; potential biomarkers for diagnosing and treating stress and anxiety disorders	(Zhu <i>et al.,</i> 2023)
Oral Administration	<i>L. plantarum</i> DR7	Reduced symptoms of stress (P=0.024), anxiety (P=0.001), and total psychological scores (P=0.022) as early as 8 weeks among stressed adults compared to the placebo group as assessed by the DASS-42 questionnaire.	(Chong <i>et</i> <i>al.</i> , 2019)
Oral Administration	B. longum	One week of B. longum did not significantly reduce stress, depression, or anxiety in young adults.	(Chong <i>et</i> <i>al.</i> , 2019)

Table 2 Use of probiotics for mood and anxiety.

In the realm of medicine, these LABs are emerging as powerful psychobiotics. They show promise in treating a range of psychiatric conditions like anxiety, depression, and stress. By producing GABA, these bacteria can modulate brain activity. It does this by inhibiting or blocking particular brain signals, reducing the amount of activity in the neurological system and bringing about a calming effect on the brain. When GABA attaches to its receptors in the brain, the responsiveness of the nerve cell is decreased.

GABA is an inhibitory neurotransmitter, which indicates that it reduces a nerve cell's capability to receive, manufacture or deliver chemical messages to other nerve cells. This unique approach offers a natural and potentially side-effect-free alternative to conventional psychiatric medications. In food science, GABA-producing LABs have a crucial role in food preservation. Their antioxidant properties help prevent food spoilage by inhibiting lipid oxidation, thereby extending the shelf life of various food products. Because of its antioxidant characteristics, GABA can help keep food from going bad due to oxidation, which can happen over time.

Industry	Applications	Description	References
Medication	Psychobiotic medication for psychiatric conditions	 Treats conditions like anxiety, melancholy, stress, schizophrenia. Inhibits brain signals, reduces neurological activity, creates calming effect. As an inhibitory neurotransmitter, decreases nerve cell communication capabilities. 	(Liwinski <i>et.</i> <i>al,</i> 2023)
Food Additives	Food preservation	 Utilizes antioxidant properties to prevent food spoilage through oxidation. Prevents formation of lipoxidation end products in foods. Enhances antioxidant activities in fruits and barley seedlings, improves storage performance, reduces chilling injury, alters carbon and nitrogen metabolism. 	(Khaliq, Ali, & Abdi, 2023; Liang <i>et al.,</i> 2022; Chuah <i>et al.,</i> 2023)
Dietary Supplements	Nutritional supplement	 Promotes muscle hypertrophy, increases skeletal muscle mass, and prevents mass decline. Induces increase in growth hormone levels and muscle protein synthesis. 	(Sakashita <i>et</i> <i>al.</i> , 2019; Uehara & Hokazono, 2022)
Cosmetics	Skin care and enhancement	 Incorporated into cosmetic products for skin benefits. Absorbs into skin to relax muscles, reduce fine lines and wrinkles. Improves cuticle barrier function, reduces skin roughness due to environmental factors. Stimulates fibroblast proliferation and production of hyaluronic acid and collagen, increasing skin moisture and elasticity. 	(Nguyen <i>et</i> <i>al.</i> , 2021)

 Table 3 Applications of GABA in various industries.

Researchers discovered that GABA has the ability to prevent the formation of lipid oxidation end products because of its scavenging effects on reactive carbonyl compounds (Deng *et al.*, 2010). They also discovered that GABA can alleviate oxidative damage to fruits (Khaliq, Ali, & Abdi, 2023, Liang *et al.*, 2022) and barley seedlings (Song *et al.*, 2010). By enhancing the activities of antioxidant enzymes and that it can enhance the storage performance of fruits by increasing the accumulation of citrate and amino acids (Sheng *et al.*, 2017), lowering chilling injury (Khaliq, Ali, & Abdi, 2023) and altering the metabolism of carbon and nitrogen (Chen *et al.*, 2020). This natural preservation method can be especially valuable in maintaining the quality and nutritional value of perishable goods, offering a healthier alternative to synthetic preservatives. The study on LAB, specifically *L. brevis*, producing γ -aminobutyric acid (GABA), presents a significant advancement in food science and biotechnology with implications for natural food preservation

and health. In a study, dual functionality of GABA and BLIS by *L. brevis* C23 were studied (Chuah *et al.,* 2023). The innovative use of plant-based media and optimization using Response Surface Methodology (RSM) highlights a potential shift towards more sustainable and acceptable food preservation methods, yet the scalability, economic viability, and regulatory compliance pose challenges. The study's findings on the high antioxidant activity and effectiveness against microbial growth suggest a natural alternative to synthetic preservatives, but comprehensive testing is needed to assess long-term food quality, safety, and health impacts. Overall, this research offers exciting prospects but underscores the necessity for further exploration in practical applications, safety, and broader health implications.

Apart from that, GABA is employed in the form of a nutritional supplement. GABA supplements can promote exercise-induced muscle hypertrophy, which both increases skeletal muscle mass and prevents the decline of that mass (Sakashita *et al.*, 2019). GABA is also capable of inducing a rise in the concentration of growth hormone as well as a rise in the amount of muscle protein that is synthesised inside the human body (Uehara & Hokazono, 2022).

GABA are valuable for their skin-enhancing properties. The amino acid GABA is frequently included as a component in a wide variety of cosmetic products. GABA has the ability to quickly absorb into the skin, where it can work to relax tense muscles and diminish the appearance of fine lines and wrinkles (Nguyen *et al.*, 2021). In the dermis, GABA can stimulate the proliferation of fibroblasts as well as the production of hyaluronic acid and collagen, leading to an increase in both the skin's moisture content and its elasticity. This results in the skin appearing smooth and firm. The association of increased GABA ligand and GABA receptor expression in psoriatic skin indicates a potential link between the GABA system and psoriasis pathogenesis, especially regarding pruritus. However, considering GABA as an alternative therapy for psoriasis requires a critical evaluation of its efficacy and mechanism of action in this specific context. While the existing evidence suggests a promising direction, further research is needed to fully understand GABA's role and to establish it as a reliable treatment option for psoriasis.

4.2 Stimulation of Oxytocin by LAB

The burgeoning field of psychobiotics has unearthed intriguing connections between gut microbiota and mental health, particularly spotlighting the role of LAB in influencing brain chemistry. Recent studies have ventured into this fascinating interplay, exploring how LAB might stimulate the production of oxytocin, a hormone pivotal for social bonding and emotional well-being (Danhof *et al.*, 2023). Oxytocin, often dubbed the 'love hormone,' plays a crucial role in regulating emotional responses and social interactions. Maternal supplementation with *L. reuteri* during developmental exposure to polybrominated diphenyl ethers (PBDEs) in mice was found to mitigate PBDE-induced autistic-like behaviors and neurodevelopmental disruptions in a sex-dependent manner. This normalization effect of *L. reuteri* is potentially linked to its influence on oxytocin levels and thyroid hormones, demonstrating its therapeutic potential in neuroendocrine disruption caused by environmental toxins. The hypothesis that LAB can enhance oxytocin levels suggests a groundbreaking approach to mental health treatment, potentially offering a natural and non-invasive alternative to traditional pharmaceuticals. This research, part of a broader exploration of the gut-brain axis, could revolutionize our understanding of mental health disorders and their management, underscoring the profound impact of gut microbiota on our overall psychological state.

The implications for treating conditions like anxiety, depression, and stress-related disorders are particularly compelling, offering a ray of hope for millions affected by these issues.

5. Conclusion

Research on LAB as psychobiotics is promising but is in its early stages, limited by small samples, short in duration, and strain variability. Future research should focus on long-term effects, standardizing LAB strains, understanding mechanisms, and conducting extensive clinical trials. LAB shows potential in improving mood, reducing anxiety, and enhancing cognitive functions through the gut-brain axis. As research progresses, LAB could revolutionize mental health care, offering a natural, side-effect-free

alternative to traditional treatments, complementing existing approaches, and enhancing mental well-being holistically.

Conflict of interest

There are no conflicts to declare.

References

- Anumudu, C., Hart, A., Miri, T., & Onyeaka, H. (2021). Recent advances in the application of the antimicrobial peptide nisin in the inactivation of spore-forming bacteria in foods, Molecules, 26(18), 5552.
- Bakhtiary, A., Cochrane, S. A., Mercier, P., McKay, R. T., Miskolzie, M., Sit, C. S., & Vederas, J. C. (2017). Insights into the mechanism of action of the two-peptide lantibiotic lacticin 3147. Journal of the American Chemical Society, 139(49), 17803-17810.
- Carabotti, M., Scirocco, A., Maselli, M. A., & Severi, C. (2015). The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. Annals of Gastroenterology, 28(2), 203.
- Chakraborty, N., Joshi, A., Ahuja, K., Vashisht, A., Basu, A., Purty, R. S., & Chatterjee, S. (2023). Immunogenicity studies on lantibiotics. In Lantibiotics as Alternative Therapeutics (pp. 255-275). Academic Press.
- Chen, W., Meng, C., Ji, J., Li, M. H., Zhang, X., Wu, Y., Xie, T., Du, C., Sun, J., Jiang, Z., & Shi, S. (2020). Exogenous GABA promotes adaptation and growth by altering the carbon and nitrogen metabolic flux in poplar seedlings under low nitrogen conditions. Tree physiology, 40(12), 1744-1761.
- Chong, H. X., Yusoff, N. A. A., Hor, Y. Y., Lew, L. C., Jaafar, M. H., Choi, S. B., Yusoff, M. S. B., Wahid, N., Abdullah, M. F. I. L., Zakaria, N., Ong, K. L., Park, Y. H., & Liong, M. T. (2019). *Lactobacillus plantarum* DR7 alleviates stress and anxiety in adults: a randomised, double-blind, placebo-controlled study. Beneficial microbes, 10(4), 355-373.
- Chuah, W. W., Tan, J. S., Hazwani Oslan, S. N., & Bothi Raja, P. (2023). Enhancing food preservation with postbiotic metabolites γ-aminobutyric acid (GABA) and bacteriocin-like inhibitory substances (BLIS) produced by *Lactobacillus brevis* C23 co-cultures in plant-based medium. Preparative Biochemistry & Biotechnology, 1-12.
- Cotter, P. D., Ross, R. P., & Hill, C. (2013). Bacteriocins-a viable alternative to antibiotics?. Nature Reviews Microbiology, 11(2), 95-105.
- Cui, Y., Miao, K., Niyaphorn, S., & Qu, X. (2020). Production of gamma-aminobutyric acid from lactic acid bacteria: A systematic review. International Journal of Molecular Sciences, 21(3), 995.
- Danhof, H. A., Lee, J., Thapa, A., Britton, R. A., & Di Rienzi, S. C. (2023). Microbial stimulation of oxytocin release from the intestinal epithelium via secretin signaling. Gut Microbes, 15(2), 2256043.
- Darbandi, A., Asadi, A., Mahdizade Ari, M., Ohadi, E., Talebi, M., Halaj Zadeh, M., ... & Kakanj, M. (2022). Bacteriocins: Properties and potential use as antimicrobials. Journal of Clinical Laboratory Analysis, 36(1), e24093.
- Deng, Y., Xu, L., Zeng, X., Li, Z., Qin, B., & He, N. (2010). New perspective of GABA as an inhibitor of formation of advanced lipoxidation end-products: it's interaction with malondiadehyde. Journal of Biomedical Nanotechnology, 6(4), 318-324.
- Emkani, M., Oliete, B., & Saurel, R. (2022). Effect of lactic acid fermentation on legume protein properties, a review. Fermentation, 8(6), 244.
- Faour-Klingbeil, D., & Todd, E. (2020). Prevention and control of foodborne diseases in Middle-East North African countries: Review of national control systems. International Journal of Environmental Research and Public Health, 17(1), 70.
- Florou-Paneri, P., Christaki, E., & Bonos, E. (2013). Lactic acid bacteria as source of functional ingredients. In Lactic acid bacteria-R & D for food, health and livestock purposes. IntechOpen.

- Gabrielsen, C., Brede, D. A., Nes, I. F., & Diep, D. B. (2014). Circular bacteriocins: biosynthesis and mode of action. Applied and Environmental Microbiology, 80(22), 6854-6862.
- Goa, T., Beyene, G., Mekonnen, M., & Gorems, K. (2022). Isolation and characterization of lactic acid bacteria from fermented milk produced in Jimma Town, Southwest Ethiopia, and evaluation of their antimicrobial activity against selected pathogenic bacteria. International Journal of Food Science, 2022.
- Gualtieri, P., Marchetti, M., Cioccoloni, G., De Lorenzo, A., Romano, L., Cammarano, A., ... & Di Renzo, L. (2020). Psychobiotics regulate the anxiety symptoms in carriers of allele A of IL-1β gene: a randomized, placebo-controlled clinical trial. Mediators of inflammation, 2020.
- Gutiérrez-Cortés, C., Suarez, H., Nero, L. A., & Todorov, S. D. (2018). Enhanced bacteriocin production by *Pediococcus pentosaceus* 147 in co-culture with Lactobacillus plantarum LE27 on cheese whey broth. Frontiers in Microbiology, 9, 395385.
- Islam, M. R., Nishie, M., Nagao, J. I., Zendo, T., Keller, S., Nakayama, J., ... & Sonomoto, K. (2012). Ring A of nukacin ISK-1: a lipid II-binding motif for type-A (II) lantibiotic. Journal of the American Chemical Society, 134(8), 3687-3690.
- Jach, M. E., Serefko, A., Szopa, A., Sajnaga, E., Golczyk, H., Santos, L. S., ... & Sieniawska, E. (2023). The role of probiotics and their metabolites in the treatment of depression. Molecules, 28(7), 3213.
- Kaur, S., & Kaur, S. (2015). Bacteriocins as potential anticancer agents. Frontiers in pharmacology, 6, 165109.
- Khaliq, G., Ali, S., & Abdi, G. (2023). γ-Aminobutyric acid is involved in overlapping pathways against chilling injury by modulating glutamate decarboxylase and defense responses in papaya fruit. Frontiers in Plant Science, 14, 1233477.
- Khorshidian, N., Khanniri, E., & Yousefi, M. (2021). Antibacterial activity of pediocin and pediocin-producing bacteria against Listeria monocytogenes in meat products. Frontiers in microbiology, 12, 709959.
- Kurnianto, M. A., Lioe, H. N., Chasanah, E., & Kusumaningrum, H. D. (2022). Purification, HR-LC-ESI-MS-MS identification, and peptide prediction of bacteriocin-like inhibitory substances produced by Streptomyces sp. isolated from Chanos chanos. International Journal of Food Science, 2022.
- Liang, J., Guo, F., Cao, S., Zhao, K., Zhao, K., Wang, H., ... & Xu, F. (2022). γ-aminobutyric acid (GABA) alleviated oxidative damage and programmed cell death in fresh-cut pumpkins. Plant Physiology and Biochemistry, 180, 9-16.
- Liwinski, T., Lang, U. E., Brühl, A. B., & Schneider, E. (2023). Exploring the therapeutic potential of gamma-aminobutyric acid in stress and depressive disorders through the gut–brain axis. Biomedicines, 11(12), 3128.
- Mokoena, M. P. (2017). Lactic acid bacteria and their bacteriocins: classification, biosynthesis and applications against uropathogens: a mini-review. Molecules, 22(8), 1255.
- Negash, A. W., & Tsehai, B. A. (2020). Current applications of bacteriocin. International Journal of Microbiology, 2020.
- Ng, Z. J., Zarin, M. A., Lee, C. K., & Tan, J. S. (2020). Application of bacteriocins in food preservation and infectious disease treatment for humans and livestock: a review. RSC advances, 10(64), 38937-38964.
- N Nguyen, T. Q., Zahr, A. S., Kononov, T., & Ablon, G. (2021). A randomized, double-blind, placebo-controlled clinical study investigating the efficacy and tolerability of a peptide serum targeting expression lines. The Journal of Clinical and Aesthetic Dermatology, 14(5), 14.
- Nuss, P. (2015). Anxiety disorders and GABA neurotransmission: a disturbance of modulation. Neuropsychiatric disease and treatment, 165-175.
- Oroojzadeh, P., Bostanabad, S. Y., & Lotfi, H. (2022). Psychobiotics: the influence of gut microbiota on the gut-brain axis in neurological disorders. Journal of Molecular Neuroscience, 72(9), 1952-1964.
- O'sullivan, L., Ross, R. P., & Hill, C. (2003). A lacticin 481-producing adjunct culture increases starter lysis while inhibiting nonstarter lactic acid bacteria proliferation during Cheddar cheese ripening. Journal of Applied Microbiology, 95(6), 1235-1241.
- Pérez-Ramos, A., Madi-Moussa, D., Coucheney, F., & Drider, D. (2021). Current knowledge of the mode of action and immunity mechanisms of LAB-bacteriocins. Microorganisms, 9(10), 2107.

Picó-Monllor, J. A., Sala-Segura, E., Tobares, R. A., Moreno-Ochando, A., Hernández-Teruel, A., & Navarro-Lopez, V. (2023).

Influence and Selection of Probiotics on Depressive Disorders in Occupational Health: Scoping Review. Nutrients, 15(16), 3551.

- Rashmi, D., Zanan, R., John, S., Khandagale, K., & Nadaf, A. (2018). γ-aminobutyric acid (GABA): Biosynthesis, role, commercial production, and applications. Studies in Natural Products Chemistry, 57: 413-452.
- Rodali, V. P., Lingala, V. K., Karlapudi, A. P., Indira, M., Venkateswarulu, T. C., & John Babu, D. (2013). Biosynthesis and potential application of bacteriocins. Journal of Pure and Applied Microbiology, 7, 2933-2945.
- Sakashita, M., Nakamura, U., Horie, N., Yokoyama, Y., Kim, M., & Fujita, S. (2019). Oral supplementation using gammaaminobutyric acid and whey protein improves whole body fat-free mass in men after resistance training. Journal of Clinical Medicine Research, 11(6), 428.
- Sasso, J. M., Ammar, R. M., Tenchov, R., Lemmel, S., Kelber, O., Grieswelle, M., & Zhou, Q. A. (2023). Gut microbiome-brain alliance: a landscape view into mental and gastrointestinal health and disorders. ACS Chemical Neuroscience, 14(10), 1717-1763.
- Shang, H., Cao, S., Yang, Z., Cai, Y., & Zheng, Y. (2011). Effect of exogenous γ-aminobutyric acid treatment on proline accumulation and chilling injury in peach fruit after long-term cold storage. Journal of Agricultural and Food Chemistry, 59(4), 1264-1268.
- Sheng, L., Shen, D., Luo, Y., Sun, X., Wang, J., Luo, T., ... & Cheng, Y. (2017). Exogenous γ-aminobutyric acid treatment affects citrate and amino acid accumulation to improve fruit quality and storage performance of postharvest citrus fruit. Food Chemistry, 216, 138-145.
- Simons, A., Alhanout, K., & Duval, R. E. (2020). Bacteriocins, antimicrobial peptides from bacterial origin: Overview of their biology and their impact against multidrug-resistant bacteria. Microorganisms, 8(5), 639.
- Singh, S., Sharma, P., Pal, N., Kumawat, M., Shubham, S., Sarma, D. K., ... & Nagpal, R. (2022). Impact of environmental pollutants on gut microbiome and mental health via the gut–brain axis. Microorganisms, 10(7), 1457.
- Song, H., Xu, X., Wang, H., Wang, H., & Tao, Y. (2010). Exogenous γ-aminobutyric acid alleviates oxidative damage caused by aluminium and proton stresses on barley seedlings. Journal of the Science of Food and Agriculture, 90(9), 1410-1416.
- Surati, S. (2020). Bacteriocin, antimicrobial as a new natural food preservative: its potential and challenges. Eruditio: Indonesia Journal of Food and Drug Safety, 1(1), 63-82.
- Tette, F. M., Kwofie, S. K., & Wilson, M. D. (2022). Therapeutic anti-depressant potential of microbial GABA produced by Lactobacillus rhamnosus strains for GABAergic signaling restoration and inhibition of addiction-induced HPA axis hyperactivity. Current Issues in Molecular Biology, 44(4), 1434-1451.
- Toro-Barbosa, M., Hurtado-Romero, A., Garcia-Amezquita, L. E., & García-Cayuela, T. (2020). Psychobiotics: mechanisms of action, evaluation methods and effectiveness in applications with food products. Nutrients, 12(12), 3896.
- Uehara, E., & Hokazono, H. GABA (γ-aminobutyric acid) promotes cell proliferation, increases MyoD and PGC-1α expression, and decreases myostatin expression in C2C12 myoblasts. International Journal of Food Science and Nutrition, 7(4), 8-12.
- Verma, D. K., Thakur, M., Singh, S., Tripathy, S., Gupta, A. K., Baranwal, D., ... & Srivastav, P. P. (2022). Bacteriocins as antimicrobial and preservative agents in food: Biosynthesis, separation and application. Food Bioscience, 46, 101594.
- Wainberg, M. L., Scorza, P., Shultz, J. M., Helpman, L., Mootz, J. J., Johnson, K. A., ... & Arbuckle, M. R. (2017). Challenges and opportunities in global mental health: a research-to-practice perspective. Current Psychiatry Reports, 19, 1-10.
- Wu, S. I., Wu, C. C., Cheng, L. H., Noble, S. W., Liu, C. J., Lee, Y. H., ... & Tsai, Y. C. (2022). Psychobiotic supplementation of HK-PS23 improves anxiety in highly stressed clinical nurses: a double-blind randomized placebo-controlled study. Food & Function, 13(17), 8907-8919.
- Wu, S. I., Wu, C. C., Tsai, P. J., Cheng, L. H., Hsu, C. C., Shan, I. K., ... & Tsai, Y. C. (2021). Psychobiotic supplementation of PS128TM improves stress, anxiety, and insomnia in highly stressed information technology specialists: a pilot study. Frontiers in Nutrition, 8, 614105.
- Yang, A., Cao, S., Yang, Z., Cai, Y., & Zheng, Y. (2011). γ-Aminobutyric acid treatment reduces chilling injury and activates the defence response of peach fruit. Food Chemistry, 129(4), 1619-1622.

- Zhu, R., Fang, Y., Li, H., Liu, Y., Wei, J., Zhang, S., ... & Chen, T. (2023). Psychobiotic Lactobacillus plantarum JYLP-326 relieves anxiety, depression, and insomnia symptoms in test anxious college via modulating the gut microbiota and its metabolism. Frontiers in Immunology, 14, 1158137.
- Zhu, X., Liao, J., Xia, X., Xiong, F., Li, Y., Shen, J., ... & Fang, W. (2019). Physiological and iTRAQ-based proteomic analyses reveal the function of exogenous γ-aminobutyric acid (GABA) in improving tea plant (Camellia sinensis L.) tolerance at cold temperature. BMC plant biology, 19, 1-20.
- Zielińska, D., Karbowiak, M., & Brzezicka, A. (2022). The role of psychobiotics to ensure mental health during the covid-19 pandemic—a current state of knowledge. International Journal of Environmental Research and Public Health, 19(17), 11022.