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# Poteng Local Food Potential with isolate Lactobacillus Plantarum In Preventing Depression

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***Abstract***
*Depression is a global problem whose symptoms are easier to observe than cure. With a fairly high prevalence in Indonesia, which is up to 6.1% in 2018, this problem practically does not only affect the sufferer but also has an impact on the people around him which in turn will further reduce the quality of life of the sufferer. Lombok Island has a local food called poteng which is the result of fermented sticky rice. Poteng is able to act as a probiotic because it contains Lactobacillus plantarum. Probiotics can play a role in helping people with depression with the Gut Brain Axis mechanism by reducing Interleukin-6, increasing gamma-Aminobutyric Acid, and influencing Vitamin D and its receptors. In a depressed state, Interleukin-6 was observed to increase whereas GABA was observed to decrease. The Gut Brain Axis mechanism affects depression through neuroanatomical pathways, regulation of microbial metabolites (Short-Chain Fatty Acid), Tryptophan metabolism, and Immune Regulation.*

***Keywords: Depression; Probiotics; Lactobacillus plantarum; Gut Brain Axis***

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## Introduction

### Depression. Global Issues to the Importance of Effective Preventive Strategies to Respond to the Challenges of Sustainable Development

Depression is a health problem that is often difficult to diagnose and cure, but nowadays its symptoms are easier to observe than in previous decades (McCarter, 2008). Depression is defined as a group of symptoms that are specific to the underlying disorder (Thapar et al., 2012). Based on data from the World Health Organization (WHO) in 2018, more than 300 million people were diagnosed or affected by depression and it is estimated that by 2020 depression is the second largest cause of death and disability after heart disease (Ranjbar et al., 2015). In line with global conditions, the incidence of depression in Indonesia is quite high and increased from 6% based on Riskesdas data in 2013 to 6.1% in Riskesdas data in 2018 or approximately 14 million people with depression in Indonesia (Ministry of Health of the Republic of Indonesia, 2018; Ministry of Health of the Republic of Indonesia, 2013).

The health problem of depression does not only affect the sufferer but also his family and those around him. Various disorders that arise due to bad mood swings can bring negative things to sufferers and their environment. Depression causes patients to slightly lose their normal social life in general due to limitations in carrying out daily activities such as extreme fatigue, decreased concentration ability to suicidal ideation which in turn will reduce the patient's quality of life (Fried & Nesse, 2014)

One of the things that underlie this high incidence is the unavailability of appropriate and effective preventive and curative measures for cases of depression. An innovation in preventive efforts needs to be done to help solve one of the mental health problems, especially in Indonesia. This innovation is expected at the same time to answer Sustainable Development Goals in the third place, namely ensuring a healthy life and supporting prosperity for all ages.

### Lombok Island with Functional Local Wisdom of Food as a Source of Probiotics

Lombok Island is one of the islands in West Nusa Tenggara Province which has special foods that have the potential to be a source of local probiotics. Poteng is a typical food of the island of Lombok which is derived from fermented sticky rice which contains approximately the same probiotic content as cassava tape, namely Lactobacillus plantarum (Barus & Wijaya, 2011)

Currently, the use of these two foods is only limited to traditional food and there has been no further research on the use of poteng. Soybeans which are popular for the Indonesian people have a high enough oligosaccharide content so that they can be used as a source of prebiotics that can improve the quality and quantity of probiotics (Ma et al., 2017). Based on this description, the author aims to create and provide an innovation of soy milk synbiotic drink with bacterial isolates from poteng as a form of preventive and adjuvant therapy in cases of depression with themechanism Gut Brain Axis. This innovation is expected to help reduce the incidence and prevalence of depression in Indonesia.

## Method

This review was written based on articles collected through several scientific search engines, namely Google Scholar, Pubmed and ScienceDirect. Types of data obtained in the form of secondary data that is qualitative and quantitative sourced from various references or literature relevant to the topic of the problems discussed. The inclusion criteria used were articles, journals, and learning books and were the result of research or expert exposure, while the exclusion criteria were articles in the form of opinions without including the author's name. Data were obtained through the internet, scientific journals and various trusted sources such as JAMA, Pubmed, and others with keywords: depression, prebiotics, gut-brain axis, L. plantarum, reviews, and meta analysis.

The writing of this scientific paper uses the literature study method which is based on the results of a study of various literature whose validity has been tested, relates to each other, is relevant to the study of writing, and supports the description or analysis of the discussion. After the necessary data is collected, data processing is carried out by arranging it systematically and logically. The basic method used in compiling this paper is the exposition method which is the exposure of a mechanism, with descriptive writing, describing the potency of Poteng with isolate L. Plantarum in its role as an antidepressant agent.

## Result and Discussion

### Understanding the Mechanism of Depression

To find out effective and efficient depression prevention strategies, it is necessary to know the mechanism of depression. There are several theories and hypotheses regarding the causes of depression, including inflammatory processes, disorders of the hypothalamic-anterior pituitary axis, and vitamin D deficiency (Verduijn et al., 2015)

A study showed that depressed patients had increased levels of the pro-inflammatory cytokine IL-6 (Howren et al., 2009). Increased inflammatory activity can reduce the production of monoamines such as serotonin and increase the toxic metabolites of tryptophan in the brain, resulting in depression. Hyperactivity of the anterior hypothalamic-pituitary axis causes glucocorticoid receptor malfunctions which will lead to depression through decreased neurogenesis and hippocampal volume (Pariante & Lightman, 2008). Another hypothesis suggests that a decrease in vitamin D causes depression or is the cause of the progression of depression because vitamin D is a neuroprotective substance that can reduce neurotoxic calcium in the brain (Kalueff et al., 2004)

**Relationship of probiotic Lactobacillus Plantarum with depression**

**a. Interleukin-6**

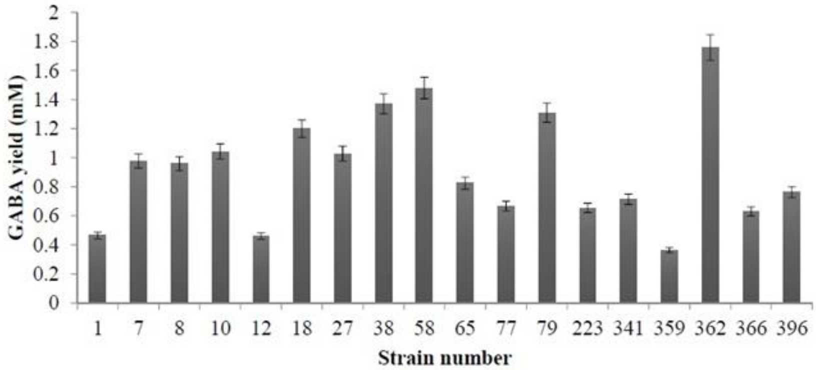
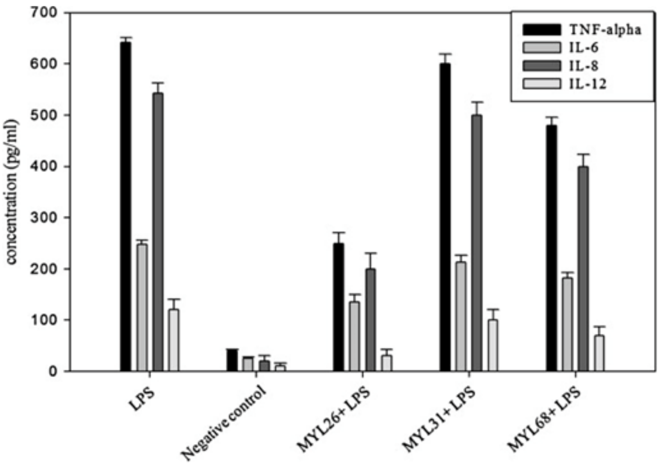



Figure 1. The amount of GABA produced by Lactobacillus plantarum.

Lactobacillus plantarum which is a probiotic that is able to reduce the production of proinflammatory cytokines such as TNF-a, IL-6, IL-8, and IL-12 as shown in the table (Chiu, 2013). Proinflammatory cytokines have been reported to contribute to stress sensitivity because they found an increase in IL-6 in respondents who exhibited depression-like behavior (Hodes, 2016). Increased IL-6 will stimulate an inflammatory response that is highly correlated with the occurrence of depression. By decreasing IL-6 levels due to the probiotic Lactobacillus plantarum, it is expected that it will have a significant impact on a person's level of depression.

Figure 2. Comparison of Pro-Inflammatory Cytokine Levels before and after probiotic administration




**b. GABA**

*The* Taj-Apis362 strain of bacteria is *Lactobacillus Plantarum* reported to have the ability to produce gamma-AminoButyric *Acid (GABA)* a fairly high (Tajabadi et al., 2015). GABA has a very close relationship with a person's depression.

The link in question is in the form of a decrease in a person's GABA levels when the person is depressed (Gabbay et al., 2017). This relationship is corroborated by the fact that with successful depression treatment, GABA levels have also been reported to increase (Pehrson, 2015). So, with its ability to produce GABA which is quite high, it is hoped that it can be an alternative therapy for depression.

**c. Vitamin D**

Lactobacillus Plantarum is a probiotic that can increase the expression of protein Vitamin D Receptor (VDR) which is useful for binding to Vitamin D. Oral administration of probiotics, either alone or in combination with probiotics, can maintain the homeostasis of the small intestine and prevent preneoplastic or neoplastic lesions (Shang & Sun, 2017). VDR and Vitamin D have been shown to have the ability to regulate the innate immune system response to the microbiome by regulating the balance of biota in the gastrointestinal tract. Vitamin D has been reported to reduce the production of proinflammatory cytokines in the gastrointestinal tract (Shang & Sun, 2017). In addition, Vitamin D also stimulates the expression of cathelicidin and Beta-2-Defensin which has an effect on reducing opportunistic pathogens and increasing bacterial richness.

**Microbiota-Gut-Brain Axis Mechanism**

Currently, the mechanism of communication between the gut microbiota and the brain is not fully understood and clarified. However, recently a number of studies suggest that the relationship between the gut and the brain is bidirectional (Pochu & David, 2017). In general, the gut microbiota affects the functioning of the brain through the nervous system, endocrine system, immune system and metabolic system (Wang & Wang, 2016)

**Neuroanatomical pathway**

Modulation of the autonomic nervous system is one of the pathways by which gut microbiota can influence brain function (Bravo et al., 2011). The interaction between the gut and the brain occurs through two pathways neuroanatomical, namely the exchange of information directly through the ANS (Autonomic Nervous System) and VN (Vagus Nervous); and two-way communication between the gut and the brain through the ENS (Enteric Nervous System) in the gut and the ANS and VN in the spinal cord (Wang & Wang, 2016). pathways Neuroanatomical form four integrated hierarchical levels; the first level is the ENS which includes the myenteric ganglia, submucosal ganglion, and intestinal glial cells (Schemann & Neunlist, 2004); the second level is the prevertebral ganglia which regulates peripheral visceral reflex responses; the third level is the ANS in the spinal cord (from T5-L2 sympathetic nerves and S2-S4 parasympathetic nerves) and the brainstem nuclei of the tract solitaries and the dorsal motoric nucleus of the VN (Chang, et al., 2003); the fourth level is the higher brain center (Schemann & Neunlist, 2004)

The gut microbiota can activate the vagus nerve where this nerve has an important role in the sensory pathway that connects the gut to the brain. For example, Lipopolysaccharide (LPS) is a major component of the outer membrane of gram-negative bacteria. LPS can activate cytokines such as IL-1β which play a role in inducing inflammation. After vagotomy, it is seen that there is a blockade of cytokine induction which will ultimately inhibit the induction of inflammation (Bluthé et al., 1994)

**Metabolic Microbial (Short-Chain Fgamma-Amino)**

Intestinal bacteria can synthesize gamma amino acids, butyric acid, 5-HT, dopamine, and SCFA. These substances can exchange between cells of microorganisms, especially intestinal cells can produce 5-HT in large quantities which can affect brain function SCFAs play a role in inhibiting histone deacetylation and binding to the receptor-coupled G protein to induce intracellular signaling. SCFA derivatives, namely butyric acid and propionic acid, can increase the gene expression of tyrosine hydroxylase (an enzyme that limits the rate of synthesis of dopamine and noradrenaline) and dopamine-β-hydroxylase (an enzyme that converts dopamine to noradrenaline). Research has shown that long-term treatment with propionic acid can reduce levels of GABA, serotonin, and dopamine (Nankova et al., 2014)

SCFAs formed by gut microbiota can affect the CNS by acting on glial cells including microglial cells and astrocytes, but the specific effect depends on the type of SCFA and target cells. Studies have shown that the anti-inflammatory action of LPS-induced microglial cells in mice is induced by butyric acid (Huuskonen et al., 2004)

**Tryptophan Metabolism**

Tryptophan is an amino acid that acts as an important precursor in the production of serotonin and kynurenine. Reduced tryptophan levels have a close relationship with the emergence of depression (Ogawa et al., 2014). The gut microbiota has an important role in tryptophan metabolism. A study showed that germ-free mice were reported to have elevated blood levels of tryptophan and serum serotonin compared to normally colonized mice, suggesting that the intestinal expression of tryptophan hydroxylase may be reduced in germ-free mice (Yano et al., 2015). In a further animal study, administration of the probiotic Bifidobacterium infantis increased inflammatory markers and tryptophan levels and decreased the kynurenine-to-tryptophan ratio (Desbonnet et al., 2008)

**Immune Regulation**

When the gut microbiota causes infection, the cells can spread to the CNS and trigger an inflammatory reaction. Chronic low-grade inflammation causes cytokines to be released into the blood, which can affect the immune system. The gut microbiota contains molecules that can cause inflammation. For example, LPS and peptidoglycan are substances that stimulate inflammation. LPS is recognized by the TLR-4 receptor, which is widely distributed in monocytes, macrophages, and brain microglia. Studies have shown that TLR4-mediated inflammatory response activation by gut microbiota occurs in IBS (Irritable Bowel Syndrome) patients with depression (Kelly et al., 2015)

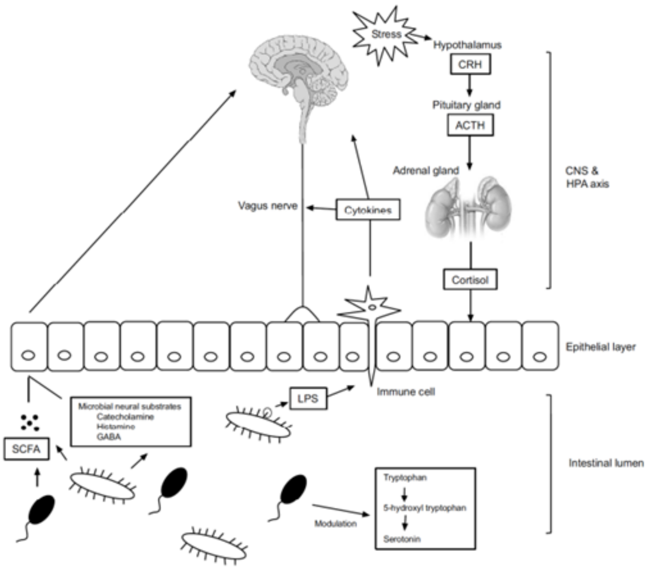



Figure 3. Microbiota-Gut-Brain Axis Interaction Pathways

The gut and brain microbiota interact in a variety of pathways. Activation of the HPA axis by stress causes cortisol secretion. This can affect gut integrity, motility, and mucus secretion, leading to changes in the composition of the gut microbiota. LPS on the surface of gram-negative bacteria can affect the brain by meditating immune cells and the vagus nerve. Microbial metabolites such as SCFA and microbial neuronal substrates including catecholamines, histamine, and GABA can affect the brain directly or indirectly. Intestinal microorganisms control serotonin levels by modulating tryptophan metabolism. CRH, corticotropin-releasing hormone; ACTH, Adrenocorticotropic hormone; CNS, central nervous system; HPA, Hypothalamus-pituitary-adrenal; SCFA, short-chain fatty acids; GABA, Gamma-aminobutyric acid; LPS, Lipopolysaccharide. (Kim & Shin, 2018)

**Connclusion**

Depression is a health problem that is often difficult to diagnose and treat, but its symptoms are easier to observe today than they were a few decades ago. Depression is defined as a group of symptoms that are specific to the underlying disorder. Based on data from the World Health Organization (WHO) in 2018, more than 300 million people were diagnosed or affected by depression and it is estimated that by 2020 depression is the second largest cause of death and disability after heart disease. In line with global conditions, the incidence of depression in Indonesia is quite high and increased from 6% based on Riskesdas data in 2013 to 6.1% in Riskesdas data in 2018 or approximately 14 million people with depression in Indonesia. Because of this problem, it is necessary to take preventive measures to overcome this problem, with the presence of a natural probiotic source owned by poteng from this food, namely Lactobacillus Plantarum, it is hoped that this problem can be prevented so that the prevalence of depression in Indonesia can be reduced.

## REFERENCE

Barus, T., & Wijaya, L. N. (2011). Mikrobiota dominan dan perannya dalam cita rasa tape singkong. *Biota: Jurnal Ilmiah Ilmu-Ilmu Hayati*, *16*(2), 354–561.

Bluthé, R.-M., Walter, V., Parnet, P., Laye, S., Lestage, J., Verrier, D., Poole, S., Stenning, B. E., Kelley, K. W., & Dantzer, R. (1994). Lipopolysaccharide induces sickness behaviour in rats by a vagal mediated mechanism. *Comptes Rendus de l'Academie Des Sciences. Serie III, Sciences de La Vie*, *317*(6), 499–503.

Bravo, J. A., Forsythe, P., Chew, M. V, Escaravage, E., Savignac, H. M., Dinan, T. G., Bienenstock, J., & Cryan, J. F. (2011). Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. *Proceedings of the National Academy of Sciences*, *108*(38), 16050–16055.

Desbonnet, L., Garrett, L., Clarke, G., Bienenstock, J., & Dinan, T. G. (2008). The probiotic Bifidobacteria infantis: an assessment of potential antidepressant properties in the rat. *Journal of Psychiatric Research*, *43*(2), 164–174.

Fried, E. I., & Nesse, R. M. (2014). The impact of individual depressive symptoms on impairment of psychosocial functioning. *PloS One*, *9*(2), e90311.

Gabbay, V., Bradley, K. A., Mao, X., Ostrover, R., Kang, G., & Shungu, D. C. (2017). Anterior cingulate cortex γ-aminobutyric acid deficits in youth with depression. *Translational Psychiatry*, *7*(8), e1216–e1216.

Howren, M. B., Lamkin, D. M., & Suls, J. (2009). Associations of depression with C-reactive protein, IL-1, and IL-6: a meta-analysis. *Psychosomatic Medicine*, *71*(2), 171–186.

Huuskonen, J., Suuronen, T., Nuutinen, T., Kyrylenko, S., & Salminen, A. (2004). Regulation of microglial inflammatory response by sodium butyrate and short-chain fatty acids. *British Journal of Pharmacology*, *141*(5), 874–880.

Kalueff, A. V, Eremin, K. O., & Tuohimaa, P. (2004). Mechanisms of neuroprotective action of vitamin D 3. *Biochemistry (Moscow)*, *69*(7), 738–741.

Kelly, J. R., Kennedy, P. J., Cryan, J. F., Dinan, T. G., Clarke, G., & Hyland, N. P. (2015). Breaking down the barriers: the gut microbiome, intestinal permeability and stress-related psychiatric disorders. *Frontiers in Cellular Neuroscience*, *9*, 392.

Kim, Y.-K., & Shin, C. (2018). The microbiota-gut-brain axis in neuropsychiatric disorders: pathophysiological mechanisms and novel treatments. *Current Neuropharmacology*, *16*(5), 559–573.

Ma, Y., Wu, X., Giovanni, V., & Meng, X. (2017). Effects of soybean oligosaccharides on intestinal microbial communities and immune modulation in mice. *Saudi Journal of Biological Sciences*, *24*(1), 114–121.

McCarter, T. (2008). Depression overview. *American Health & Drug Benefits*, *1*(3), 44.

Nankova, B. B., Agarwal, R., MacFabe, D. F., & La Gamma, E. F. (2014). Enteric bacterial metabolites propionic and butyric acid modulate gene expression, including CREB-dependent catecholaminergic neurotransmission, in PC12 cells-possible relevance to autism spectrum disorders. *PLoS One*, *9*(8), e103740.

Ogawa, S., Fujii, T., Koga, N., Hori, H., Teraishi, T., Hattori, K., Noda, T., Higuchi, T., Motohashi, N., & Kunugi, H. (2014). Plasma L-tryptophan concentration in major depressive disorder: new data and meta-analysis. *The Journal of Clinical Psychiatry*, *75*(9), 0.

Pariante, C. M., & Lightman, S. L. (2008). The HPA axis in major depression: classical theories and new developments. *Trends in Neurosciences*, *31*(9), 464–468.

Ranjbar, E., Memari, A. H., Hafizi, S., Shayestehfar, M., Mirfazeli, F. S., & Eshghi, M. A. (2015). Depression and exercise: a clinical review and management guideline. *Asian Journal of Sports Medicine*, *6*(2).

Schemann, M., & Neunlist, M. (2004). The human enteric nervous system. *Neurogastroenterology & Motility*, *16*, 55–59.

Shang, M., & Sun, J. (2017). Vitamin D/VDR, probiotics, and gastrointestinal diseases. *Current Medicinal Chemistry*, *24*(9), 876–887.

Tajabadi, N., Ebrahimpour, A., Baradaran, A., Rahim, R. A., Mahyudin, N. A., Manap, M. Y. A., Bakar, F. A., & Saari, N. (2015). Optimization of γ-aminobutyric acid production by Lactobacillus plantarum Taj-Apis362 from honeybees. *Molecules*, *20*(4), 6654–6669.

Thapar, A., Collishaw, S., Pine, D. S., & Thapar, A. K. (2012). Depression in adolescence. *The Lancet*, *379*(9820), 1056–1067.

Verduijn, J., Milaneschi, Y., Schoevers, R. A., Van Hemert, A. M., Beekman, A. T. F., & Penninx, B. (2015). Pathophysiology of major depressive disorder: mechanisms involved in etiology are not associated with clinical progression. *Translational Psychiatry*, *5*(9), e649–e649.

Wang, H.-X., & Wang, Y.-P. (2016). Gut microbiota-brain axis. *Chinese Medical Journal*, *129*(19), 2373.

Yano, J. M., Yu, K., Donaldson, G. P., Shastri, G. G., Ann, P., Ma, L., Nagler, C. R., Ismagilov, R. F., Mazmanian, S. K., & Hsiao, E. Y. (2015). Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis. *Cell*, *161*(2), 264–276.