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LITERATURE REVIEW

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Tempeh's Probiotic Bacteria Content can Boost Its Value as a Functional Food in the COVID-19 Era

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ABSTRACT

The COVID-19 era is far from over, especially with the emergence of new virus variants. Efforts to develop vaccines and treatments have been made, but various prevention strategies must still be developed in order to combat this pandemic. Probiotics are cultures of one type or a mixture of live bacteria that help to maintain the balance of the gut microbiota, which is important for the host's health. Various studies have presented evidence that probiotics have the ability to boost human immunity. Tempe is a fermented Indonesian food, some contain probiotics. Probiotic bacteria found in tempe include *Lactobacillus fermentum*, *Lactobacillus plantarum*, *Lactobacillus paracasei*, *Lactobacillus delbrueckii*, *Lactobacillus agilis*, *Lactobacillus mucosae*, *Lactobacillus paralimentarius*, *Lactobacillus zae*, *Lactococcus sp.*, *Weissella confusa*, *Weissella paramesenteroides*, *Enterococcus faecalis*, *Enterococcus faecium*, *Pediococcus pentosaceus*. In this study, we present the potential of probiotic bacteria origin tempeh that have been shown to improve host health, particularly in terms of increasing immunity, preventing respiratory infections, and lowering risk factors for comorbidities. The data presented is expected to provide an overview of the potential consumption of tempeh as a functional food, particularly in this era of the COVID-19, so that awareness of the benefits of this beneficial food grows.

Keywords: fermentation; health; bacteria

INTRODUCTION

Tempe is a functional food that is highly beneficial to health due to its high concentration of nutrients and bioactive components. According to numerous studies, the nutrients and bioactive components in tempeh are produced by the dynamic composition of the microbiota that plays a role in its production, which includes the main fermenters, *Rhizopus sp.*, molds, kamir, lactic acid bacteria, and other bacteria.^(1,2) The microbiota in tempeh plays an important role, particularly in enzymatic processes that function in converting complex compounds into simpler compounds that are easily absorbed by the body, which contain all essential amino acids, calcium, fatty acids, vitamins, isoflavones, and reduce the content of anti-nutritional substances phytic acid,⁽³⁾ and butyric acid (GABA).⁽⁴⁾

Tempe is a probiotic food source. Besides tempeh, there are many fermented foods in various countries which are also sources of probiotic. These foods include miso yogurt, cheese, kimchi, kombucha, miso, sourdough bread, and tempeh.⁽⁵⁾ Consumption of functional foods with multiple benefits is highly recommended in this COVID-19 era because it can improve consumers' health. Consumption of certain foods is a significant factor, particularly in lowering mortality in Europe.⁽⁶⁾ Countries in Europe, Korea, and Taiwan with large populations that consume foods high in nutrients, anti-oxidants, or anti-angiotensin-converting enzyme (ACE) activity, such as fermented cabbage, have a low COVID-19 mortality rate.⁽⁶⁾ Fermented cabbage, such as kimchi, is a proof-of-concept for dietary manipulations that may enhance nuclear factor erythroid 2-related factor 2 (Nrf2)-associated antioxidant effects, which may be beneficial in reducing COVID-19 severity.⁽⁶⁾ *Lactobacillus*, which are also potent Nrf2 activators, are abundant in fermented foods. *Lactobacillus plantarum* is one of the potential *Lactobacillus* species that can be found in functional foods that can boost Nrf-2 production.⁽⁷⁾ Based on several research reports, one of the probiotic bacteria found in tempeh is *L. Plantarum*.⁽⁸⁻¹¹⁾ As a result, tempeh is one of

the functional foods that could be consumed during a pandemic. As a result, tempeh is one of the functional foods that is especially beneficial for consumption during this pandemic.

Some COVID-19 patients have dysbiosis in certain groups of gut probiotic microbes, including *Lactobacillus* and *Bifidobacterium*.⁽¹²⁾ Furthermore, several studies have found a link between gut microbiota, secondary gastrointestinal infection, and COVID-19 disease.⁽¹²⁻¹⁴⁾ Furthermore, several reports indicate that RNA from SARS-CoV-2 was detected in stool samples from patients who had negative respiratory tract results.⁽¹⁵⁻¹⁷⁾ This shows crosstalk between the gut-lung axis, with a decrease in the diversity of the gut microbiota in COVID-19 patients, which is dominated by opportunistic pathogenic bacteria such as *Streptococcus*, *Rothia*, *Veillonella*, and *Actinomyces*, as well as a decrease in the relative abundance of beneficial symbionts.⁽¹⁴⁾ Therefore, probiotic supplementation is required because it has the potential to reduce the severity of COVID-19 morbidity and mortality.⁽¹⁸⁾ Tempeh, for example, contains a variety of probiotic bacteria, particularly the *Lactobacillus* group, which is the dominant probiotic bacteria in tempeh.⁽¹⁹⁾ The health of the human gut will be maintained as a result of this *Lactobacillus* content, which primarily has a positive effect on the function of the gut-lung axis.

As a result, this article review discusses the potential of probiotics found in tempeh to play a role in COVID-19 prevention. The literature was searched using the keywords probiotics and COVID-19; probiotics in tempeh; probiotics and respiratory infections; and probiotics and coronaviruses, and articles were collected and reviewed for inclusion in this article review.

METHODS

This article review was composed by collecting data from online-published studies. This article describes the various microorganisms found in tempeh. Tempeh can be used as a functional food during the COVID-19 pandemic because its fermented microbes contain health-promoting nutrients. A search for articles using the terms probiotic bacteria in tempeh, the name of the bacterial species, probiotics, and Covid-19 was conducted on the Internet. The processing of data is based on research studies published in an electronic database sourced from Google Scholar, including as many as 100 articles published in Indonesian and English between 2005 and 2022. The article was thoroughly evaluated to determine the tempeh's probiotic bacteria content, which has a beneficial effect on the body's health during the COVID-19 pandemic; all articles have full and accessible versions.

RESULTS

Tempe Provides Probiotic Bacteria

The general characteristics of lactic acid bacteria (LAB) include Gram positive bacteria, negative catalase, negative endospores and non-motile.⁽²⁰⁾ LAB has an important role in fermented foods. The presence of LAB in fermented foods is very important for health.⁽²¹⁻²³⁾ LAB has been reported to play a role in determining the quality of fermented foods.^(24,25) and is extremely important for health as a source of probiotics.⁽²⁶⁾ LAB species isolated from tempeh have probiotic properties such as salt and bile acid tolerance, antimicrobial activity, simulated gastric juice (SGJ) and simulated intestinal juice (SIJ), physiological properties such as the ability to survive at low pH, and enzymatic properties such as the ability to produce phytase and amylase.⁽⁸⁾ These probiotic properties are in accordance with good requirements for probiotics so that they are able to survive through human digestive function and can reach the intestines, as the content of probiotic bacteria in other fermented foods such as kimchi⁽²⁷⁾ and pickles.⁽²⁸⁾

Table 1. Recapitulation of LAB containing probiotic properties in tempe

No	Species
1.	<i>Lactobacillus fermentum</i> ^(8,10,29,30)
2.	<i>Lactobacillus plantarum</i> ^(8-10,31)
3.	<i>Lactobacillus paracasei</i> ⁽⁹⁾
4.	<i>Lactobacillus delbrueckii</i> ^(10,29)
5.	<i>Lactobacillus agilis</i> ^(19,29,30)
6.	<i>Lactobacillus mucosae</i> ⁽¹⁹⁾
7.	<i>Lactobacillus paralimentarius</i> ⁽¹⁹⁾
8.	<i>Lactobacillus zeae</i> ⁽¹⁹⁾
9.	<i>Lactococcus sp</i> ^(19,30)
10.	<i>Weissella confusa</i> ^(10,29)
11.	<i>Weissella paramesenteroides</i> ⁽⁸⁾
12.	<i>Enterococcus faecalis</i> ⁽⁸⁾
13.	<i>Enterococcus faecium</i> ⁽⁸⁾
14.	<i>Pediococcus pentosaceus</i> ^(8,10)

The Potential Clinical Role of Probiotic Bacteria in Tempeh

The relationship between the microbiota in the body and disease demonstrates that bacteria in the human gut can regulate the host immune system. By interacting with TLRs, T regulatory lymphocytes, cytokines, chemokines, and nuclear transcription factors (NF), the metabolites produced can regulate the immune system and affect mucosal immunity.^(32,33) Bacterial metabolites, particularly short-chain fatty acids, have a direct effect on immune and epithelial cells by activating NF- κ B, TNF- α , and decreasing PRR stimulation.⁽³⁴⁾ Probiotics have the potential to boost innate and acquired immunity while also reducing gastrointestinal⁽³⁵⁾ and upper respiratory tract infections.^(36,37) Probiotics are live microorganisms that can improve the immune system and overall health of the host,⁽³⁸⁾ and can be obtained from fermented foods.

There have been numerous reports of the probiotic effect of LAB.⁽³⁹⁾ *Lactobacillus*, *Lactococcus*, *Enterococcus*, *Streptococcus*, *Oenococcus*, *Pediococcus*, *Weissella*, and *Leuconostoc* are the most common lactic acid bacteria (LAB). Tempeh contains several genera of probiotic bacteria, namely *Lactobacillus*, *Lactococcus*, *Weissella*, *Enterococcus* and *Pediococcus*. Because of their health-promoting properties, the *Lactobacillus* genus has received a lot of attention.⁽⁴⁰⁾ The *Lactobacillus* genus is commonly used as a probiotic because it has many important properties, including high tolerance to acid and bile, the ability to adhere to intestinal surfaces, the ability to withstand low pH and gastric juice, the ability to inhibit potentially pathogenic species, the ability to resist antibiotics, the ability to produce exopolysaccharides, and the ability to remove cholesterol.⁽⁴¹⁻⁴³⁾ *Lactococcus* is occasionally recommended as a probiotic. Some *Lactococcus lactis* subsp. *lactis* strains have probiotic properties such as nisin production and are used to treat antibiotic-associated diarrhea.^(13,44) *Weissella* genus are relatively new LAB members. Several *Weissella* strains, including *Weissella confusa*, *W. Cibaria*,⁽⁴⁵⁾ and *W. paramesenteroides*, have also demonstrated probiotic potential in numerous studies.⁽⁴⁷⁾ In the *Pediococcus* genus, *P. pentosaceus* is one type of LAB that has played an increasingly important role in LAB applications in recent years. To date, there is growing experimental evidence that *P. pentosaceus* may be useful as a biopreservative for foods, plants, or animals, or as a potential probiotic candidate.⁽⁴⁸⁾ *P. pentosaceus*, as a probiotic bacteria, improved gastrointestinal peristaltic function⁽³⁰⁾ and has cell adherence function.⁽⁴⁹⁾

The following is a summary of the clinical potential of probiotic bacteria found in tempeh:

1. *Lactobacillus fermentum*

L. fermentum JDFM216 significantly increased macrophage phagocytic activity, sIgA production, and immune cell stimulation in mice. *Lactobacillus* species improve cognitive, psychological, and immune function by modulating the gut microbiota. As a result, its beneficial effect regulates the immune response, making it potentially useful as a functional food.⁽⁵⁰⁾

2. *Lactobacillus plantarum*

Administration of heating-killed *L. plantarum* HKL-137 showed an immune-enhancing effect in mice. Immunity increases due to an increase in non-specific immune responses and adaptive immunity, as well as increased production of IFNs type 1 and Interleukin (IL)-12.⁽⁵¹⁻⁵²⁾ Furthermore, intake of *L. plantarum* HK-137 in healthy humans with high stress levels significantly reduced upper respiratory tract infection (UTRI) symptoms via immune function augmentation.⁽⁵³⁾ *L. plantarum* has been shown to help with gut health, metabolic disorders, and brain health. *L. plantarum* has been shown to help with gut health, metabolic disorders, and brain health. *L. plantarum*'s beneficial role in intestinal disorders such as inflammatory bowel disease, metabolic syndrome, dyslipidemia, hyperblesteromia, obesity, and diabetes, as well as aspects of brain health such as psychological disorders.⁽⁵⁴⁾ Tempeh contains *L. plantarum* that is important in diabetes prevention.⁽⁵⁵⁾

3. *Lactobacillus paracasei* (*L. casei* 431)

Administration of the *L. casei* 431 strain has been reported to reduce upper respiratory tract infections⁽⁵⁶⁾ and regulate the immune system by increasing plasma IgG, IgG1 and IgG3 levels as well as salivary IgA secretion levels.⁽³²⁾

4. *Lactobacillus delbrueckii*

Consumption of fermented yogurt containing *L. delbrueckii* spp *bulgaricus* OLL103R-1 in the elderly can increase NK cell activity and reduce the risk of exposure to the common cold.⁽⁵⁷⁾ Other studies have shown that R-1 and the polysaccharides it produces can boost the immune system by increasing NK cell activity and protect against influenza-related respiratory infections.^(57,58)

5. *Lactobacillus agilis*

Lactobacillus (*L. acidophilus*, *L. agilis*, and *L. casei*) killed by heating had the ability to prevent *Salmonella typhi* and *E. coli* adhesion to Caco-2 cells, a human intestinal cell line. This demonstrates that the killed cells are similar to live cells capable of inhibiting pathogenic bacteria adhesion.⁽⁵⁹⁾

6. *Lactobacillus mucosae*

In humans, *L. mucosae*, along with *Bifidobacterium breve* and *L. gasseri*, is one of the most strongly associated microbiota in intestinal mucosal epithelial cells.⁽⁶⁰⁾ *L. mucosae* can aggregate, adhere to mucus, and inhibit pathogen adhesion to the host gut.⁽⁶¹⁾ *L. mucosae* is not only associated with the intestinal mucosa, but it is

- also found in the cervical and vaginal mucosa.⁽⁶²⁾ *L. mucosae* is acid tolerant and can survive in the human digestive tract,^(61,63) and it can produce antibacterial compounds against a variety of Gram-positive and Gram-negative pathogens.^(61,64) *L. mucosae* also has anti-inflammatory and antioxidant properties.⁽⁶⁵⁾
7. *Lactobacillus paralimentarius*
L. paralimentarius was identified as a lactic acid bacterium isolated from fermented sourdough bread.⁽⁶⁶⁾ *L. paralimentarius* was discovered to be one of the *Lactobacillus* bacteria found in healthy human feces samples.⁽⁶⁷⁾
 8. *Lactobacillus zeae*
L. zeae can be isolated from both raw milk and naturally fermented cow's and goat's milk.⁽⁶⁸⁾ In *Caenorhabditis elegans* in vivo system biology experiments, *L. zeae* LB1 demonstrated the highest level of protection (86 percent) among other *Lactobacillus* against K88⁺ enterotoxigenic *Escherichia coli* (ETEC).⁽⁶⁹⁾
 9. *Lactococcus sp*
Lactococcus sp. is a gram-negative, catalase-negative, non-motile, and non-sporing lactic acid bacterium.⁽⁷⁰⁾ *Lactococcus* bacteria are commonly used as starter bacteria in fermented dairy products such as cheese and yogurt.^(71,72) *Lactococcus* has been isolated from fermented foods such as kimchi⁽⁷³⁾ and tempeh⁽⁷⁴⁾. As a probiotic bacteria, *Lactococcus* has been reported to have multifunctional effects as a probiotic, such as *L. lactis* isolated from kimchi being antimicrobial and able to compete with 6 pathogenic bacteria for attachment to the intestinal wall, namely 3 strains of *Listeria monocytogenes* and 3 strains of *Staphylococcus aureus*.⁽⁷⁴⁾
 10. *Weissella confusa*
Live or dead, *Weissella confusa* strain PL9001 was able to prevent more than 90% of *Helicobacter pylori* attachment to MKN-45 cells, which are human gastric cancer cells. *W. confusa* PL9001 culture supernatant rapidly degraded live *H. pylori* by damaging its cell walls. The findings indicate that PL9001 is a probiotic that can reduce *H. pylori* malignancy and resistance.⁽⁷⁵⁾ *W. confusa* 20 and *W. confusa* 33 demonstrated strong uptake of Caco-2 cells, the most commonly used cell line in assessing probiotic strain absorption capacity in human intestinal epithelial cells.⁽⁴⁵⁾
 11. *Weissella paramesenteroides*
As a producer of bacteriocin and exopolysaccharide, *W. paramesenteroides* can inhibit the growth of *Escherichia coli* and *Staphylococcus aureus*.⁽⁷⁶⁾ In a typhoid-affected murine model, *W. paramesenteroides* WpK4 reduces intestinal cytokine gene expression as well as liver and lymph node injury.⁽⁷⁷⁾
 12. *Enterococcus faecalis*
Some *E. faecalis* and *E. faecium* strains are widely consumed as probiotics, usually in the form of pharmaceutical preparations. This type of probiotic is used to treat diarrhea, antibiotic-associated diarrhea, or irritable bowel syndrome, as well as to lower cholesterol and improve host immunity. However, they must be used with caution because some strains are opportunistic pathogenic bacteria.⁽⁷⁸⁾ Against viruses, the effects of *E. faecalis* FK-23 were reported to reduce alanine aminotransferase (ALT) levels in hepatitis C virus (HCV) positive individuals but did not reduce viral load.⁽⁷⁹⁾
 13. *Enterococcus faecium*
Enterococci are being studied more as potential probiotic candidates. As a probiotic, marketed *E. faecalis* (Symbioflor 1) has been shown to be effective in patients with chronic sinusitis and/or bronchitis.⁽⁷⁸⁾ Few studies have been conducted to evaluate the efficacy of probiotic strains such as *E. faecium* SF68® and *E. faecalis* Symbioflor 1 in humans for the treatment of diarrhea, irritable bowel syndrome, lowering serum cholesterol, and immune regulation.^(78,80,81) Recent study shows *E. faecium* NCIMB 10415 has an effect on the intestinal epithelial cell line Caco-2, which has been induced by Enterotoxigenic *E. coli* (ETEC) strains.⁽²²⁾
 14. *Pediococcus pentosaceus*
P. pentosaceus acts as a flavor enhancer and nutrient in food, as well as a probiotic producing bacteriocin-like substances (BLISs), which are effective as an antimicrobial, anti-inflammatory, anti-cancer, detoxifying antioxidant, and lipid-lowering agent.⁽⁴⁷⁾ The exopolysaccharide fraction of *P. pentosaceus* KFT-18 isolated from kimchi can stimulate the development of thymus and lymphocytes as well as the production of cytokines, which can act as immunomodulators to stimulate protective immune responses and increase nutrient acquisition in rats mediated by cyclophosphamide (CY) to reduce its immune response.^(82,83)

Potential Consumption of Tempeh, a Functional Food, against Several Comorbidity Parameters in COVID-19

As a probiotic bacteria-containing food, research on the role of tempeh in improving health has been conducted, tempeh consumption in Sprague-Dawley rats could increase the population of *Bacterioidetes*, indicating that tempeh could modulate the composition of the gut microbiota to be healthier.⁽⁸⁾ Furthermore, in vitro culture revealed that processed tempeh extract inhibited the growth of *Basilus subtilis* while stimulating the growth of *Bifidobacterium* and *Lactobacillus*, both of which are normal intestinal flora.⁽¹⁸⁾

Diarrheal disease is one of the digestive diseases that can be avoided by eating tempeh.^(23,43,84) Consumption of tempe-based food in male rats can treat EPEC-caused diarrhea.⁽¹⁸⁾ Publications on the role of probiotics in other diseases, in addition to digestive diseases, are widely available. Probiotics have been shown to prevent and improve digestive, allergic, respiratory, and sepsis problems. Probiotics can be used as a coadjuvant therapy for metabolic disorders such as metabolic syndrome, obesity, NAFL (non-alcoholic fatty liver), and type 2 diabetes.⁽⁸⁵⁾

Tempe produced by co-incubating *L. plantarum* and *R. oligosporus* during the fermentation process is an excellent dietary supplement for individuals with abnormal carbohydrate metabolism. The evaluation of tempe consumption can reduce insulin resistance, HbA1C, serum glucose, total cholesterol, triglycerides, free fatty acids, insulin, and low-density lipoprotein (LDL) content, while increasing High-Density Lipoprotein (HDL) content in diabetic hyperglycemic rats. Furthermore, the number of LAB increased, as did the content of bile acids, cholesterol, triglycerides, and short chain fatty acids in the rat feces. The amount of glucose and fat in the serum is modulated by changes in the internal microbiota, which inhibits cholesterol synthesis and increases lipolysis.⁽⁵⁵⁾

Consumption of tempeh is also beneficial to the immune system. Tempe, as an immunomodulator, has been shown to reduce immunoglobulin E levels as well as wound severity.⁽⁸⁶⁾ Furthermore, tempeh consumption can stimulate and increase the secretion of IL-2 and IFN-gamma cytokines.⁽⁶⁹⁾

DISCUSSION

In Indonesia, tempeh is a cheap alternative to meat, and it also has many probiotic bacteria that are very good for the body. Probiotic bacteria found in tempe include *Lactobacillus fermentum*, *Lactobacillus plantarum*, *Lactobacillus paracasei*, *Lactobacillus delbrueckii*, *Lactobacillus agilis*, *Lactobacillus mucosae*, *Lactobacillus paralimentarius*, *Lactobacillus zeae*, *Lactococcus sp.*, *Weissella confusa*, *Weissella paramesenteroides*, *Enterococcus faecalis*, *Enterococcus faecium*, *Pediococcus pentosaceus*. Because it contains probiotic bacteria, tempeh consumption can increase prevention of risk factors for several comorbid diseases in COVID-19, including improving digestive health, reducing insulin resistance, HbA1C, serum glucose, total cholesterol, triglycerides, free fatty acids, insulin, LDL, and increasing HDL. There are 14 different types of LAB found in tempeh, each with a high potential for human health, particularly the species *L. plantarum* as found in kimchi, which has been shown to increase the production of Nrf2, which is useful in reducing the severity of COVID-19 patients. As a result, tempeh is thought to have a high potential for use as a functional food in the COVID-19 era. The diversity of probiotic bacteria in tempeh may vary by region based on the raw materials used in its production, but tempeh always contains probiotic bacteria. Tempeh is a regional staple that is consumed daily in several regions. It is necessary for researchers to educate the public about tempeh's probiotic content and health benefits in order to increase public consumption of tempeh.

CONCLUSION

Recognizing that tempeh has numerous benefits, particularly in terms of probiotic content, it would be preferable if awareness of tempeh consumption as a functional food is promoted. The predominant probiotic genera in tempeh are *Lactobacillus sp.*, *Lactococcus sp.*, *Weissella sp.*, *Enterococcus sp.*, and *Pediococcus sp.* Due to the presence of probiotic bacteria, tempeh consumption can improve digestive health, reduce insulin resistance, HbA1C, serum glucose, total cholesterol, triglycerides, free fatty acids, insulin, LDL, and raise HDL levels.

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