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REVIEW

A Short Review: Bioactivity of Fermented Rice Bran

Ardiansyah*

Department of Food Technology, Universitas Bakrie, Kawasan Epicentrum, Jalan HR Rasuna Said Kav C.22, Jakarta 12920, INDONESIA

Abstract: Rice bran is a by-product of the rice milling process, which refers to the processing of brown rice into polished rice. It contains a considerable amount of functional bioactive compounds. However, the utilization of these compounds is limited and calls for an effort to ferment rice bran. One of the methods that can significantly increase the added value of rice bran as well as its bioactivity is the solid-state fermentation. It can also be one of the strategies that help in the production of rice bran as a functional ingredient with higher bioactivity for health promotion.

Key words: bioactive compounds, bioactivity, fermentation, fermented rice bran, solid-state fermentation

1 Introduction

Rice is one of the most important food commodities and is the second-largest agricultural commodity cultivated worldwide[1]. World paddy production reached 769.9 million tons in 2018, while the milled rice production, mostly in Asian countries, was around 510.6 million tons[2]. In line with the population growth, the demand for rice is estimated to continue rising in the next few decades, followed by an increase in the number of by-products from the rice milling process. From 1994 to 2018, Indonesia has been the third-largest rice producer in the world. In 2019, the production of milled dry paddy rice in Indonesia was 54.60 million tons[3]. Generally, the amount of rice bran is 10% of brown rice by milling process; this implies that 5.46 million tons of rice bran were produced through rice milling. The high amounts of rice bran produced can be utilised optimally with the proper processing methods.

The rice milling process produces rice as the main product and rice husk and bran as the by-products (Fig. 1). The rice grain or paddy has an outer-part (husk) to protect or cover the inner-part of rice. The inner-part of rice consists of a bran layer and endosperm. Brown rice comprises the outer layers of pericarp, seed-coat and nucellus, the germ or embryo and the endosperm. Currently, rice bran is being widely studied owing to its potential as a functional ingredient in food products. It has a high nutritional content, including vitamins, minerals and essential amino acids (tryptophan, histidine, cysteine and arginine)[4]. Moreover, it contains bioactive compounds such as γ-oryzanol, α-tocopherol, tocotrienols, polyphenols, phytosterols, carotenoids, ferulic acid and phytosterols[5-8]. These compounds serve as antioxidants and have anti-atherosclerotic, anti-diabetic, anti-cancer and anti-inflammatory properties[9, 10].

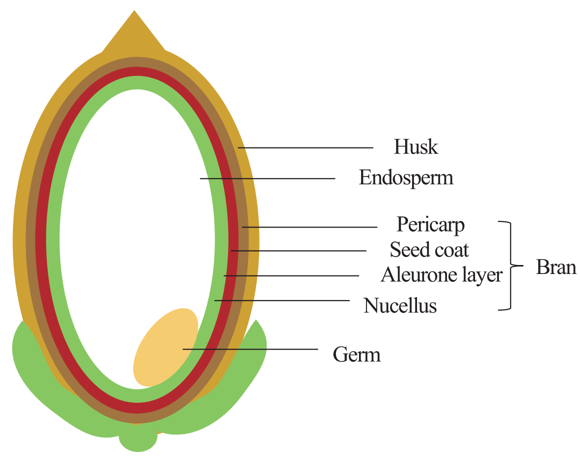

Fig. 1 Paddy structure.

There are still several obstacles in the efforts made to develop rice bran as a functional ingredient, such as the lack of public awareness about its health benefits, a few downstream industries' interest in developing rice bran and the quality of rice bran being sub-standard. In addition, rice bran contains anti-nutritional substances such as trypsin inhibitor, hemagglutinin-lecithin and phytic acid, and its instability during storage is another reason that hinders its use as a food ingredient[11, 12].

One of the methods that can be employed to increase

*Correspondence to: Ardiansyah, Department of Food Technology, Universitas Bakrie, Kawasan Epicentrum, Jalan HR Rasuna Said Kav C.22, Jakarta 12920, INDONESIA
E-mail: ardiansyah.michwan@bakrie.ac.id ORCID ID: https://orcid.org/0000-0003-2110-344X
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the added value of rice bran for further use in product development fermentation, especially solid-state fermentation (SSF). SSF is a fermentation technique that can escalate the bioactive compounds in food, such as the phenolic content, thereby contributing to antioxidant activity[13−15]. Mold, yeast and bacteria are the types of microorganisms that are often used in the SSF method. Mold species are suitable for use in SSF because they are capable of producing enzymes like amylase, pectinase, xylanase, cellulase, chitinase, protease, lipase and β-galactosidase[14]. Therefore, SSF helps to increase the bioactive compounds of plant materials. In addition, fermentation using the SSF method can improve the sensory profile of the rice bran[13].

SSF is currently used in a wide range of applications from traditional applications such as tempe fermentation in Indonesia. Recently, it has been used to develop new food ingredients like bioactive compounds. It was also a new trend regarding bioethanol and biodiesel production as new energy sources that used agricultural by-products as substrate with microbe as starter. SSF has the following advantages: (1) It is a promising method for obtaining a high yield of bioactive compounds that require less water for microorganisms' growth; (2) It can convert cheap agro-industrial by-products into products that contain various valuable compounds; (3) It can minimise microbe contaminants; (4) It is a simple processing technique and is more practical; (5) It involves high productivity; and (6) Its media conditions resemble the actual habitat[14].

This review discusses the bioactivity of fermented rice bran, which has the potential to be developed as a food ingredient. The discussion begins by defining fermented rice bran, the active compounds contained therein, both volatile and non-volatile compounds and *in vivo* examination to show fermented rice bran's bioactivities.

2 Fermentation Can Increase the Active Compounds of Rice Bran

Fermentation has been widely used to improve the quality of food. It is popular thanks to the extended storage period that it offers, which improves taste and increases the bioactive compounds and protein content of the food item[11, 16, 17]. Several studies have shown that fermented rice bran has a higher content of bioactive compounds and better functional properties than non-fermented rice bran. The increase in phenolic compounds after the fermentation process occurs due to the breakdown of complex compounds that bind to lignocellulose or polysaccharides[18, 19]. During the fermentation process, the microbes as starters produce enzymes that can hydrolyse complex compounds in the bound form into compounds in the free form[19]. Besides being able to increase the bioactive compounds and antioxidant activity, the fermentation process can improve the sensory profile of rice bran. Cempo Ireng and Inpari 30 fermented rice bran with *Rhizopus oligosporus* for 72 hours are more acceptable by the 75 naïve panellists than the benchmarks (non-fermented rice bran) because the sample had a dominant liking of both aroma and taste[20].

Compared to non-fermented rice bran, rice bran fermented with *Rhizopus oryzae* for 24 hours can increase the total phenolic compounds (TPC) up to five times and inhibit 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radicals up to 87%[21]. In addition, the TPC in fermented rice bran using *Rhizopus oryzae* for 120 hours increased from 2.4 mg/g to 5.1 mg/g[13].

The fermentation process aims to increase the nutritional content and bioactive compounds in rice bran. Several studies have been conducted to determine the effects of fermentation on the nutritional content, antioxidant activity and bioactive compounds in rice bran. The fermentation process is carried out using molds, such as *Monascus pilosus*[11], *Monascus purpureus*[22, 23], *Rhizopus oryzae*[19, 24, 25], *Aspergillus oryzae*[25], *Rhizopus oligosporus*[20, 23, 26−28], lactic acid bacteria (*Pediococcus acidilactici*, *Lactococcus lactis* and *Pediococcus pentoseous*)[29] and mushrooms (*Pleurotus sapidus*)[30].

SSF is a fermentation method effective for increasing antioxidant activity and TPC in food with solid media[31]. The mold *Rhizopus* sp. and *Aspergillus* sp. are proper cultures that can be used in the SSF method since they do not produce toxic compounds during fermentation[32]. Some of the research results regarding fermented rice bran are shown in Table 1. Some of the fermentation processes of rice bran were undertaken using cultures like *Rhizopus oryzae*, *Rhizopus oligosporus*, *Lactobacillus plantarum*, *Monascus pilosus*, *Aspergillus kawachii*, lactic acid bacteria and *Saccharomyces boulardii*.

Using lactic acid bacteria starter and *Rhizopus oryzae* in fermented rice bran produces lactic acid[33]. However, the use of *Rhizopus oryzae* is more desirable owing to the easy separation between the mold biomass and the substrate. Several studies have reported that the fermentation process in rice bran can increase the bioactive compounds. This occurs due to the production of extracellular enzymes which affect the increase in the bioactive compounds in the substrate[17]. Furthermore, the microorganisms used as starters in the fermentation process will synthesise compounds and activate metabolic pathways to adapt to the substrate[34].

Fermented rice bran using *Rhizopus oryzae* increases the ash, fibre, protein, amino acids, phospholipids and the total phenolic content. The increase in ash in fermented rice bran is due to the synthesis of mycelia[35]. Another study showed that the increase in the fibre content is due to the intrinsic production of chitin[17] which is one of the compounds of the hyphal cell wall on *Rhizopus oryzae*[36].

Table 1 Research results of fermented rice bran.

Rice cultivars	Fermentation time (h)	Starter (microbes)	Results	References
Neptune, Wells, Red Wells	24	*Saccharomyces boulardii*	Increase in bioactive compounds and decrease in lymphocyte B cell	5)
Polished rice (Yongin)	240	*Monascus pilosus*	Increase in total flavonoid	11)
Polished rice (IRGA)	96	*Rhizopus oryzae*	・Increase in phospholipid and unsaturated fatty acid ・Reduce total lipid and saturated fat	15)
Polished rice (IRGA)	96	*Rhizopus oryzae*	・Increase in ash content, dietary fiber, protein, and amino acid. ・Decrease in water content, lipid, and phytic acid	17)
Polished rice (IRGA)	120	*Rhizopus oryzae*	Increase in total phenolic content	19)
Inpari 30 and Cempo Ireng	48, 72, and 96	*Rhizopus oligosporus*, *Rhizopus oryzae* and *mixture*	Increase in total phenolic content and antioxidant activity	20)
Polished rice (IRGA)	24	*Rhizopus oryzae*	・Increase in ash content, dietary fiber, and protein content ・Decrease in lipid content	21)
Polished rice	288	*Rhizopus oligosporus* (strain F0020), *Monascus purpureus* (strain F0061) and mixture	Increase in total phenolic content and antioxidant activity	23)
Inpari 30	72	*Rhizopus oligosporus*	Increase in total phenolic content and antioxidant activity	28)
Polished rice	96	*Rhizopus oryzae* (CCT 7506)	Increase in dietary fiber, ash content, protein, lipid and total phenolic content	35)
Polished rice	44 24	a. *Aspergillus kawachii* b. Lactic acid bacteria (*Lactobacillus brevis, Lactobacillus rhamnosus, Enterococcus faecium*)	Increase in dietary fiber, lipid content, and total phenolic content	38)

Rhizopus oryzae also produces phytase that hydrolyses complex proteins leading to an increase in dissolved protein[36]. Phytic acid degradation by *Rhizopus oligosporus* can increase the content of minerals, such as iron, magnesium and zinc, which are bound to phytates[37]. The presence of phytase also accelerates the hydrolysis of phytic acid, thereby affecting the decrease in its content[17]. This further leads to the enhancement of phenolic compounds because of the degradation of lignocellulose by the enzymes in *Rhizopus oligosporus*[20]. The increase in phenolic compounds also occurs in fermented rice bran with the use of *Rhizopus oligosporus* and *Aspergillus kawachii* combined with lactic acid bacteria (*Lactobacillus brevis*, *Lactobacillus rhamnosus*, *Enterococcus faecium*)[28, 38]. Several studies have also shown a decrease in moisture, lipid and phytic acid levels. An increase in the temperature during fermentation causes a decrease in water content[17]. The lipids are used by fungi to form mycelia, resulting in decreased lipid levels[36].

Rhizopus oligosporus is the main mold and is widely used as a starter in making tempe in Indonesia. Studies on fermenting rice bran with *Rhizopus oligosporus* have been reported by several researchers[23, 28]. The research revealed a similar increase in phenolic compounds in fermented rice bran, which occurs due to the activity of hydrolytic enzymes of fungi such as β-glucosidase[25]; these enzymes can increase the hydroxyl molecule, which can result in a rise in the amount of free phenolic compounds in the rice bran[39]. The use of mixed cultures (*Rhizopus oligosporus*, *Rhizopus oryzae* and other mixtures) in the fermenting of rice bran has also been reported. Fermenting rice bran using the *Rhizopus oligosporus* starter produced the highest DPPH radical scavenging activity, with a fermentation time of 96 hours on Inpari 30 cultivar[20].

3 Volatile Compounds of Rice Bran

Volatile compounds play a role in the formation of aroma in food products. They give either a pleasant or unpleasant aroma. They can form along the food chain, starting after harvesting, and occur throughout post-harvest handling, distribution and storage. The heating treatment can result in the loss of volatile compounds due to their volatility. Several previous studies have discussed the volatile compounds found in rice and rice bran. The compounds that have been identified include alcohol, alkanes, ketones and aldehydes as shown in Table 2.

Our group has identified and compared the volatile compounds of fermented and unfermented Inpari 30 and Cempo Ireng rice bran[20]. The extraction of volatile compounds was carried out using the headspace solid-phase microextraction method and analysed using the Gas Chromatography-Mass Spectroscopy (GC-MS) instrument. The analysis showed that there were 57 volatile compounds, including alcohol (23%), aldehyde (19%), acid (11%), ketones and esters (9%), ester (7%), terpenes and benzene (5%), furans and lactones (3%) and pyridine, as well as pyrazine and thiazole (2%). The formation of volatile compounds happens as a result of the lipid degradation reaction during fermentation and the Maillard reaction due to the sterilisation process. Most of the volatile compounds in rice bran under fermentation treatment originate from the lipid degradation reactions. In Inpari 30 cultivar, they were 3-methyl-3-butenol, 2,3-butandienol, benzylalcohol, glycerine, methyl hexadecanoate, (E)-9-methyl octadecanoate, (Z,Z)-9,12-methyl octadecadienoate, 1R-α-pinene, caryophyllene, 2-methoxyphenol and 3-methyl pyridine. However, in fermented Cempo Ireng rice bran cultivar, the volatile compounds were dominated by 4-methyl-3-pentenol, benzylalcohol, glycerine, methyl hexadecanoate, ethylbenzene and caryophyllene.

The fermentation resulted in the rice bran having sweet, creamy, fatty, smoky and green aromas. Smoky and green aromas are thought to trigger the rancid aroma in rice bran due to the lipid degradation by enzymes during the fermentation process. In non-fermented rice bran, the volatile compounds are mostly formed by the Maillard reaction which is influenced by the sterilisation process. In the fermented Inpari 30 rice bran cultivar, the volatile compounds that are thought to be dominant include 2-furanmethanol, nonanal, methyl tetradecanoate, phenol and 2-methoxy-4-vinylphenol. Meanwhile, 2-furanmethanol, hexanal, naphthalene, 1R-α-pinene and 2-methoxy-4-vinylphenol are the volatile compounds in fermented Cempo Ireng rice bran. These compounds are thought to form a burnt, nutty and fatty smell. In the non-fermented rice bran, hexanal and nonanal compounds were also found, obtained from the lipid degradation reaction which is thought to produce a rancid aroma. Apart from that, other research[43] state that 4-vinylphenol is the main component that causes the unpleasant odour. The difference in the volatile compounds of several rice varieties, such as Inpari 30 and Cempo Ireng, emerges from the differences in the varieties, planting locations, nutritional contents and bioactivities in the rice bran.

Table 2 Volatile compounds in polished (white) rice cultivar.

Group volatile compounds	Compounds
Alcohols	*n*-Methanol, *n*-Ethanol, *n*-Butanol, *n*-Propanol, *n*-Pentanol, *n*-Hexanol, 1-Octen-3-ol, *n*-Nonanol, *n*-Octanol, Benzyl alcohol, 3-methyl-1-butanol, Linalooloxide, *n*-Heptanol, Linalool, Furfuryl alcohol, 2-phenethyl alcohol, 1-Dodecanol
Alkanes	*n*-Heptadecane, *n*-Oktadecane, *n*-Heneicosane, *n*-Tetracosane, *n*-Tetradecane, *n*-Decane, *n*-Undecane, *n*-Dodecane, *n*-Tridecane, *n*-Pentadecane, *n*-Hexadecane, *n*-Nonadecane, *n*-Eicosane, *n*-Dococane, *n*-Cyclohexane, *n*-Pentacosane, *n*-Hexacosane, *n*-Heptacosane, *n*-Hentriacontane
Ketones	6-Methyl-5-hepten-2-one, 2-Decanone, 6,10,14-Trimetil-2 Pentadecanone, Aceton, 3-Pentena-2-on, 2-Heptanone, 6-Methyl-3,5-heptadien-2-one, 3-Octanone, 2-Octanone, 2-Nonanone, 3-Octena-2-on, Isophrone, 2-Undecanone, 4-Methylacetophenone, Geranylacetone, β-Ionone, 2-Heptadecanone, 2-Oktadecanone, 6,10-Dimethyl-5,9-Undecadienane-2-on
Aldehydes	3-Methyl-1-butanal, *n*-Pentanal, *n*-Hexsanal, *n*-Nonanal, Benzaldehyde, Ethanal, Propanal, Isobutanal, Isopentanal, *n*-Heptanal, *trans*-2-Hexanal, *n*-Octanal, *trans*-2-Heptenal, *trans*-2-Octenal, 3-Furfural, 2-Furfural, *n*-Decanal, *trans*-2-Nonenal, 5-Methylfurfural, Phenylacetaldehyde, *trans*-2-Decenal, Deca-2,4-diena-1-al, 2-Phenyl-2-butenal

References: [40–42]

Almost the same components—aldehydes, alcohols, alkenes and ketones—were also found in red rice and black rice bran cultivars (Table 3). The β-ocimene component in red rice bran is known to have an aroma like damp clothes[44]. Meanwhile, myristic acid compounds are known to carry a waxy and fatty aroma[45], and the compounds 6,10,14 trimethyl-2-pentadecane are known to have an aroma of oil, celery and wood[46].

The guaiacol component is reported to be the main cause of the aroma of black rice. In black rice bran, the nonanal compound is known to have a citrusy, green and fatty aroma[47]. Meanwhile, caproic acid and pelargonic acid have a fatty, cheesy and waxy aroma[48, 49].

4 Non-volatile Compounds of Rice Bran

Non-volatile compounds of rice bran have been reported[50] on the Calrose, Dixiebelle and Neptune rice varieties that grow in the south-eastern part of California, United States. In this study, 465 metabolites were found, consisting of amino acids (126), carbohydrates (35), vitamins and cofactors (28), energy (11), lipids (137), nucleotides (40), peptides (28), secondary metabolites (55) and xenobiotics (8). The antioxidant compounds of rice bran include amino acids (4-guanidinobutanoate and taurine), vitamins and cofactors (tocopherols and tocotrienols) and secondary metabolites (ergothioneine and quinates)[50] which can potentially be used as antioxidants to inhibit chronic diseases and infections. Other studies have shown an increase in metabolite diversification in fermented rice bran when using *Saccharomyces boulardii*. The use of specific rice varieties and fermentation treatment on rice bran affects the amount and type of active compounds produced[5, 17, 51]. Several studies related to the identification of non-volatile compounds in rice bran are presented in Table 4.

Table 3 Volatile compounds in red and black rice bran cultivars.

Rice cultivars	Volatile compounds
Red rice	Myristic acid, Nonanal, (E)-β-ocimene, 6, 10, 14 Trimethyl-2-pentadecanone, Hexanal, Octanal, 2-Methylnaphtelene, Benzaldehyde, 2-Heptanon, 1-Octen-3-ol, *n*-Hexanol, Heptanal, *n*-Heptanol, 2-Pentylfuran, (2E)-octenal, *n*-octanol, (2E)-nonenal, Decanal, (2E)-decanal, (2E,4E)-decadienal, (2E)-undecanal, Geranylacetone, Methyl linoleat, Methyl oleat
Black rice	Myristic acid, Nonanal, Caproic acid, pentadecanal, Pelargonic acid, Guaiacol, Hexanal, Isovaleric acid, *n*-Hexanol, Enantic acid, p-menthan-3-one, Caprilic acid, 2-Hydroxy-6-methylbenzaldehyde, (2E,4E)-nonadienal, *n*-Tetradecane, Geranylacetone, *n*-Pentadecane, *n*-Hexadecane, Tetradecanal, *n*-Heptadecane, Methyl hexadecanoate, Palmitic acid, Ethyl hexadecanoate

Reference: [43]

Table 4 Non-volatile compounds of rice bran.

Rice cultivars	Non-volatile compounds	References
Neptune, Wells, and Red Wells	Galactose, Palmitic acid, α-Linoleic acid, Disaccharide, Xylitol, Glucitol, Alanine, Phosphoric acid, D-Fructose, Sorbitol, and 1, 2, 3-Propane tricarboxylate	5)
Calrose, Dixiebelle, and Neptune	• Amino acid: tryptophan, leusine, isoleusine, valine, fenilalanine, tirosine, poliamine, guanidine, and acetamido • Vitamin and cofactor: ascorbate, aldarate, glucorate, and teoronate • Metabolite seconder: quinate, ergotionein, benzoate, piperidine, tartrate, and α-amirine	50)
Basmati 217, Basmati 370, Gambiaka, Shwetasoke, DM 16, Kaho Gaew, Dorado, Sawa Mahsuli, Chennula, Njavara, Calrose, RBT 300, Jasmine 85, IAC 600, LTH, SHZ-2, and Rang Jey	Amino acid (Aspartate, Serine); Fatty acid; Oxylipins; Phospholipid; Carbohydrate; Tocopherol; Nucleotide; and Benzoate	51)
Riceberry	Sterol: 24-Methylene-ergosta-5-en-3B-ol, 24-Methylene-ergosta-7-en-3B-ol, fucosterol, gramisterol, campesterol, stigmasterol, and β-sitosterol Triterpenoid: Cycloeucalenol. 24-methylenecycloartanol	52)
Inpari 30 and Cempo Ireng	Adenosine	57)

The compounds in Thai Riceberry bran are classified into sterol and terpenoid groups[52]. The identified sterol groups include fecosterol, gramisterol, stigmasterol and campesterol. Fecosterol, commonly found in seaweed, is also found in rice bran and functions as an antioxidant compound[53]. Gramisterol can be extracted from the rice varieties of Riceberry and exhibits anti-cancer effects against acute myeloid leukemia[54], whereas stigmasterol has the ability to bind chondrocyte membranes and has anti-inflammatory and anti-catabolic effects[55]. Campesterol is a type of phytosterol that is widely available in plants, and phytosterol decreases the levels of low-density lipoprotein (LDL) cholesterol[56].

Non-volatile compounds in fermented rice bran using *Rhizopus oligosporus* in Inpari 30 and Cempo Ireng rice bran varieties have also been reported[57]. Fermentation was carried out for 72 hours at room temperature of 30℃ with SSF. The analysis of non-volatile compounds was carried out using the ultra-performance liquid chromatography-tandem mass spectrometer (UPLC-MS/MS) and electrospray ionisation (ESI) mass spectrometry in positive ion mode. There were 72 compounds identified and categorised into secondary metabolites (50%), lipids (22%), amino acids (11%), vitamins and cofactors (10%), peptides (4%), nucleotides (1%) and carbohydrates (1%). Fermentation in Inpari 30 and Cempo Ireng rice bran produces new compounds from the metabolism of tyrosine, phenylalanine, pentatonic acid, dipeptides and sphingolipids and terpenoids. The analysis also showed that adenosine was the most dominant non-volatile compound in the two types of rice bran cultivars.

5 *In vivo* Study of Fermented Rice Bran

The parameters that are widely tested in the *in vivo* study of fermented rice bran are total cholesterol (TC), triglycerides (TG), aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum blood sugar levels and blood pressure. Fermented rice bran is a good source of antioxidants owing to its bioactive compounds such as phenolic compounds, flavonoids, carotenoids and anthocyanins. Many of these bioactive compounds are known to be useful as functional ingredients to prevent various chronic diseases.

The studies *in vivo* on fermented rice bran are presented in Table 5. The hepatoprotective effect on the administration of 0.4% w/w fermented rice bran orally in induced mice carbon tetrachloride (CCl_4)[58]. The results of these studies indicate that fermented rice bran can prevent the incidence of liver damage caused by CCl_4 by increasing the antioxidant activity and decreasing AST and ALT. Another study showed the same results, i.e., a decrease in AST and ALT in the group of mice given fermented rice bran[59].

AST has been widely used as a marker to measure liver damage[58]. TNF-α, IL-6 and IL-1β are pro-inflammatory cytokines that can cause colonic tissue damage and ulceration of the large intestine if present in excessive amounts[60]. The supplementation of fermented rice bran can protect the C57BL/6N mice from ulcerative colitis by decreasing TNF-α, IL-6 and IL-1β, increasing the body weight and stool consistency and reducing intestinal bleeding due to a rise in short-chain fatty acids (SCFA) and tryptamine[59]. Another benefit of fermented rice bran is its anti-inflammatory effect which is achieved by reducing pro-inflammatory cytokines. The ovalbumin (OVA) model showed that fermented rice bran extract reduced TNF-α, interferon (IFN-γ), IL-6 and IL-10 in mice[61]. Another study states that fermented rice bran extract can prevent atopic dermatitis by reducing T cells $CD8^+$ and cells $Gr\text{-}1^+/CD11b^+$ B and inhibiting the expression of cytokine mRNA (IL-5 and IL-13)[62].

Fermented rice bran has been reported to lower blood pressure when administered to stroke-prone spontaneously hypertensive rats (SHRSP)[28, 38, 57]. Both studies reported that the oral administration of fermented rice bran can reduce systolic blood pressure (sBP), improve blood sugar levels, reduce insulin resistance and increase nitric oxide (NO) in the blood[28, 57]. Furthermore, fermented rice bran can effectively lower blood pressure due to an increase in the inhibitory activity of the angiotensin-converting enzyme (ACE) in serum[38].

TC, TG, LDL cholesterol and high-density lipoprotein (HDL) cholesterol are an important part of the lipid fraction in the human body. The anti-hypercholesterolemic effect of fermented rice bran has also been reported[63]. Rice bran compounds such as γ-oryzanol can lower the cholesterol levels in the blood, lower the LDL cholesterol, and increase the HDL cholesterol. Mice orally administrated with fermented rice bran showed a decrease in TC, TG and LDL and increased blood HDL cholesterol[38, 59, 63]. Several possible mechanisms can occur in the improvement of lipid fractions in the blood, such as a decrease in lipid and cholesterol absorption as well as cholesterol synthesis and an increase in cholesterol secretion, HDL synthesis or antioxidant activity[63].

6 Conclusions and Perspectives

Fermentation using the SSF technique is an alternative method that can be used to increase the number of active compounds in rice bran as a by-product of the rice milling process. The biochemical reactions that occur during the fermentation process lead to changes in the nature and characteristics of the rice bran. SSF can increase the TPC of rice bran. The volatile and non-volatile compounds present in the rice bran contribute to its aroma and flavour,

Table 5 *In vivo* studies of fermented rice bran.

Rice bran	Starter (microbes)	Animals	Treatment	Results	References
Fermented rice bran (Inpari 30)	*Rhizopus oligosporus*	SHRSP/Izumo, male	40 mg/kg body weight	Systolic blood pressure, blood glucose, and HOMA index ↓ Plasma NO ↑	28)
Fermented rice bran	*Aspergillus kawachii* and *Lactobacillus brevis, Lactobacillus rhamnosus,* and *Enterococcus faecium*	SHRSP/Izumo, male	2 g/kg body weight	Systolic blood pressure, diastolic blood, blood glucose, TC, LDL-C, and HOMA index ↓ ACE inhibition ↑ Serum TG ↓ p-AMPK, p-AMPKα, and HDL-C ↑	38)
Fermented rice bran	*Bacillus* sp., *Bacillus subtilis, Bacillus sonolensis, Bacillus sirculans*	ICR mice, male	0.4% body weight	Serum ALT, AST, ALP, and TC ↓ Serum TG ↑ Serum LDH ↓	58)
Fermented rice bran	*Bacillus subtilis*	Sprague Dawley rats, male	1.5% and 3% body weight	ALT, AST, and ALP ↓ Serum TG ↓ Liver TG ↓	59)
Fermented rice bran	*Aspergillus kawachii* and *Lactobacillus brevis, Lactobacillus rhamnosus,* and *Enterococcus faecium*	C57B1/6N mice, male	10% body weight	Intestine myeloperoxidase, intestine TBARS, TNF-α, IL-1β, and IL-6 ↓ Short chain fatty acid and tryptamine ↑	60)
Fermented rice bran extract	*Issatchenkia orientalis*	BALB/c mice, female	1.5 and 3 g/kg body weight	TNF-α, IL-10, and IL-6 ↓ IFN-γ ↓	61)
Fermented rice bran	*Lactobacillus rhamnosus* and *Pichia deserticola*	NC/Nga mice, male	300 mg/kg body weight	IgE ↓ CD4+, CD8+, and Gr-1/CD11b+ ↓	62)
Fermented rice bran extract	*Rhizopus oligosporus*	Sprague Dawley rats, male	1102.5 and 2205 mg/kg BW/day	Serum glucose, TC, TG, and serum LDL-C ↓ Serum HDL-C ↑	63)

Note: ↑ = increasing; ↓ = decreasing

which are formed during the fermentation process, and can improve the sensory quality of the rice bran. The increase in the number of active compounds in the rice bran is accompanied by a rise in bioactivity, which has been proven in the *in vivo* studies.

SSF is a simple technique for producing bioactive compounds in rice bran. This technique is economical because the materials used are agro-industrial by-products. Additionally, this technique is environment-friendly since it reduces the number of industrial by-products disposed into the environment. SSF can be used as an alternative method to improve the functional properties of rice bran as a food ingredient for health promotion in the future.

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