Pharmacogn. Rev.
A multifaceted peer reviewed journal in the field of Pharmacognosy and Natural Products
www.phcogrev.com | www.phcog.net

A Comprehensive Review on Functional Properties of Fermented Rice Bran

Bhagavathi Sundaram Sivamaruthi, Periyanaina Kesika, Chaiyavat Chaiyasut

Innovation Center for Holistic Health, Nutraceuticals and Cosmeceuticals, Faculty of Pharmacy, Chiang Mai University, Chiang Mai, Thailand

ABSTRACT

A predominant by-product of rice processing is rice bran (RB). The phytochemical composition of the RB varied among the cultivars. RB is rich in oil, phenolic compounds, polysaccharides, proteins, and micronutrients along with more than 100 known antioxidants and bioactive phytonutrients. The crude and purified RB extracts were used in pharmacological, cosmeceuticals, and food industries. Fermentation process improved the phytochemical constituents and enhanced the bioactivity of RB. The fermented RB (FRB) has been reported for the enhanced antioxidant, anti-cancer, and anti-inflammatory bowel diseases, anti-diabetes activities, etc., FRB is used as potent animal feed, especially in poultry industries. RB bioactive principles were studied for their potential application in anti-aging treatments, and cosmetics. The current manuscript summarizes the changes in the phytochemical content of RB during the fermentation process and functional property of FRB.

Key words: Antioxidants, fermented rice bran, phytochemicals, rice bran

INTRODUCTION

Fermentation, a chemical process mediated by microbes that break down substances, is one of the ancient methods to preserve food with more than 6000 years of history.[1] Fermentation is the critical process for making bread, cheese, and alcoholic beverages, etc., In addition to preservation, fermentation process enhances the availability of nutrients, texture, taste, and increases the flavor of foods. The microbes involved in fermentation produces inhibitory compounds, such as organic acids, ethanol, short-chain fatty acids (SCFAs), and bacteriocins, which prevent the growth of contaminating microorganisms.[2] Several studies have focused on the health benefits of fermented foods, especially on gastrointestinal tract health and nutrient absorption. Recent studies proved that the supplementation of fermented foods improved the health status of type 2 diabetes, impaired glucose metabolism, obesity, irritable bowel syndrome, hyperlipidemia, hypertension, osteoporosis, etc.[3-9]

One of the amplest and treasured byproducts of rice processing is rice bran (RB). RB is governing natural source for several phytochemicals with pharmacological importance. RB is rich in oil, phenolic compounds, polysaccharides, proteins, and micronutrients along with more than hundreds of known antioxidants and bioactive phytonutrients, such as γ-oryzanol, B Vitamins, tocotrienols, minerals, phytosterols, polyphenols, and trace minerals including zinc, selenium, magnesium, omega-3 fatty acids, and Vitamin E. Several studies have been proved that the phytochemicals in RB could enhance the immune system.[10] The current review paper summarizes the changes in the phytochemical content of RB during the fermentation process and functional property of fermented RB (FRB).

CHANGES IN THE COMPOSITION OF RICE BRAN

RB accounts for 5%–8% of the total weight of rice grain. RB contains 11%–13% of crude protein, ~11.5% of fibers, and about ~20% of the oil.[11,12] The RB oil contains fatty acids, waxes, monoacylglycerols, diacylglycerols, triacylglycerols, triterpene alcohols, tocotrienols, tocopherols, and sterols. About 31%–33% linoleic, 37%–42% oleic, and 21%–26% of palmitic acids are present in RB oil.[11,13]

Rhizopus oryzae mediated solid state fermentation altered the lipid content of RB. About 9% of the reduction in lipid content was recorded after 120 h of fermentation while phospholipids were found to be increased. There was no significant alternation in linoleic, oleic, and palmitic acids. About 20% reduction was observed in saturated fatty acids while unsaturated fatty acids were increased up to 5%.[13] Another report proved that fermentation of RB with *R. oryzae* CTT 7560 enhanced the total phenolic compounds and free radical scavenging property. The protein recovery from RB was also increased after fermentation.[14] *R. oryzae* CTT 1217, strain isolated from RB, has been used for the solid-state fermentation of RB and the phytochemical changes and antioxidant property were evaluated. The results showed that the fermentation of RB by *R. oryzae* CTT 1217 improved the total phenolic compounds, and free radical scavenging ability. Methanol and aqueous extract of FRB also showed the antioxidant property.[15] The total phenolic content of RB was found to be increased after *Monascus purpureus* and *Rhizopus oligosporus* mediated fermentation. The phenolic acids such as 4-hydroxybenzoic,

Correspondence:
Dr. Bhagavathi Sundaram Sivamaruthi,
Innovation Center for Holistic Health, Nutraceuticals and Cosmeceuticals,
Faculty of Pharmacy, Chiang Mai University, Chiang Mai 50200, Thailand.
E-mail: sivasgene@gmail.com

Access this article online

Quick Response Code:	
	Website: www.phcogrev.com
	DOI: 10.4103/phrev.phrev_11_18

Cite this article as: Sivamaruthi BS, Kesika P, Chaiyasut C. A comprehensive review on functional properties of fermented rice bran. Phcog Rev 2018;12:218-24.

caffeic, syringic, ferulic, vanillic, and sinapic acids were increased in the methanol extract of FRB. The antioxidant capacity of RB has also been enhanced by fungal fermentation.[16] *M. purpureus* strain F0061 mediated fermentation has not significantly altered the total phenolic content, whereas antioxidant capacity was increased considerably. The phenolic acids such as caffeic, syringic, ferulic, vanillic, and sinapic acids were increased dramatically after the fermentation of RB with *M. purpureus*.[17]

Separate fermentation of RB with *Aspergillus oryzae* and *R. oligosporus* enhanced the total phenolic content from 1.66 ± 0.61 to 7.96 ± 0.18, and 7.22 ± 0.28 mg gallic acid equivalent/g of the sample, respectively. *A. oryzae* mediated fermentation increased the concentration of caffeic, syringic, ferulic, protocatechuic, and sinapic acids in RB after 12 days of fermentation. Similarly, *R. oligosporus* mediated fermentation increased the level of 4-hydroxybenzoic and caffeic acids in RB. Both, *A. oryzae* and *R. oligosporus* mediated fermentation of RB showed greater antioxidant capacity in ferric reducing/antioxidant power (FRAP) assay.[18] *R. oryzae* mediated fermentation decreased the reducing sugars (60%), and phytic acid (50%), fat (40%) content of RB while increasing the proteins (40%) and fibers (50%) content.[19] Jung *et al.*[20] evaluated the changes in total phenolic content, β-glucan, and γ-oryzanol, of FRB of 21 different Korean rice varieties, and found that fermented (*Lentinula edodes* mediated fermentation) RB of the cultivar Haedam showed increased total phenolic content with bioactivity improvement. Migwang RB exhibited the highest γ-oryzanol content after fermentation with *L. edodes.*

Lactic acid bacteria (*Lactococcus lactis, Pediococcus pentoseous*, and *Pediococcus acidilactici*) mediated solid state fermentation of RB improved α-tocopherol content. *P. acidilactici* mediated simultaneous saccharification and fermentation (SSF) of RB increased the γ-oryzanol content. The total phenolic content of FRB was also altered compared to unFRB, and ferulic acid concentration was found to be increased in *P. acidilactici* mediated SSF of RB. During fermentation, increased level of organic acids was observed due to lactic acid bacteria mediated fermentation. Authors also observed the improvement in the antioxidant capacity of RB after fermentation for 48 h.[21] Heat-stabilized defatted RB (HSDRB) has been reported as a possible source of bioactive phenolic compounds with several claimed health benefits. The fermentation of HSDRB by *Bacillus subtilis* subspecies *subtilis* release 26.8 mg (ferulic acid equivalents/g of sample) of phenolic compounds. About 96 h of fermentation process significantly improved the total phenolic content ((-)-epicatechin, caffeic, syringic, ferulic, gentistic, sinapic, benzoic, and *p*-courmaric acids) and free radical scavenging activity.[22]

Preussia aemulans mediated fermentation of RB displayed a significant increase in nucleoside, protein, amino acid, and phenolic contents.[23] Fermentation of RB with *M. pilosus* KCCM60084 increased the total flavonoid content up to 4.58-fold.[24]

Gas chromatography-mass spectrometry analysis revealed that galactose, palmitic acid, and α-linoleic acid content was reduced, and xylitol, alanine, phosphoric acid, and 1,2,3-propanetricarboxylic acid content were increased in *Saccharomyces boulardii* FRB of Neptune rice cultivars (PI 655959), while glucitol was detected only after fermentation. Likely, palmitic acid was detected in the RB of Red Wells cultivar after the fermentation by *S. boulardii.* The results indicated that the fermentation process could introduce new active principle in the FRB, which could enhance the protective nature of the RB phytochemicals.[25] Yeast fermentation improved protein content (up to 6.77%), and total amino acid content of the RB (cultivar MR 219).[26] However, *Saccharomyces cerevisiae* mediated fermentation did not significantly alter the phytochemical content of Thai black RB, whereas the free radical scavenging activity was augmented slightly.[27] Thus, the significant positive changes in chemical composition RB desperately depends on the strain used for fermentation.

The phenolic acids such as gallic, protocatechuic, chlorogenic, *p*-hydroxybenzoic, caffeic, syringic, vanillin, and ferulic acid content were found to be changed in RB after *R. oryzae* mediated fermentation. More significantly, gallic (2.6 ± 0.8–154.5 ± 6.0 mg/g of dry weight) and ferulic acid (33.3 ± 2.3–764.7 ± 32.0 mg/g of dry weight) content was found to be increased after 120 h of fermentation.[28] *A. oryzae* and *R. oryzae* mediated FRB showed an increase in ferulic acid (43.2 ± 4.9 μg/ml), and organic acid, especially citric acid (214.6 ± 12.1 mg/g) content.[29]

FUNCTIONAL PROPERTIES OF FERMENTED RICE BRAN

Antioxidant property

Grifola frondosa mediated fermented defatted RB water extract (GFDRBE) (1 mg/ml) exhibited a significant increase in hydroxyl radical scavenging activity, which is comparable to ascorbic acid (positive control). Nine days fermented extract displayed reduced effective concentration (EC_{50}) value of 0.31 mg/ml when compared to unfermented samples (EC_{50} = 0.38 mg/ml). About 87.85% of 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging ratio was attained at 2.0 mg/ml of GFDRBE whereas unfermented sample exhibited only 56.2% of DPPH scavenging activity. Similarly, the EC_{50} value of GFDRBE (0.6 mg/ml) in DPPH was significantly reduced when compared to unfermented sample (1.17 mg/ml). Nitric oxide (NO) production was also significantly decreased by GFDRBE at low concentration (50–100 μg/ml) while increasing the NO production at high concentration (200–400 μg/ml) of GFDRBE. The concentration-dependent regulation of NO production by GFDRBE could be used to activate the macrophages or to neutralize the over production of NO.[30]

R. oryzae FRB showed <50% of inhibition of DPPH free radical at the concentration of 0.1 mg/ml. The EC_{50} value of the FRB extract (250 ± 4 mg of antioxidant per gram of DPPH) was slightly similar to the value of ferulic acid (235 ± 4 mg of antioxidant per gram of DPPH) and un FRB extract (213 ± 10 mg of antioxidant per gram of DPPH), whereas the EC_{50} values were lower than the reported EC_{50} values for white RB extract, onion, and cardamom extracts. Whereas, *R. oryzae* FRB exhibited potent peroxidase enzyme inhibition activity.[28]

M. purpureus, R. oligosporus, M. purpureus + *R. oligosporus* FRB showed a significant increase in antioxidant activity (FRAP assay). The water extract of unfermented, *M. purpureus, R. oligosporus, M. purpureus* + *R. oligosporus* FRB showed the antioxidant activity of 30.22 ± 9.57, 61.21 ± 4.50, 116.33 ± 4.74, and 144.03 ± 10.12 mg ascorbic acid equivalent (AAE) per gram of sample, respectively. The methanol extract of unfermented, *M. purpureus, R. oligosporus, M. purpureus* + *R. oligosporus* FRB showed the antioxidant activity of 30.93 ± 3.80, 80.68 ± 1.07, 61.44 ± 0.98, and 74.75 ± 1.18 mg AAE/g sample, respectively. Whereas, the percentage of radical scavenging activities (DPPH) of water and methanol extracts of FRB was not altered significantly.[16]

An active radical scavenging property on the DPPH radical was observed in *P. acidilactici* FRB. The DPPH radical scavenging activity of RB was reported to be 82.6% after fermentation with *P. acidilactici*, whereas, RB fermented with *P. pentoseous* and *L. lactis* exhibited 71.5% and 77.2% of activity, respectively.[21]

A mixture of RB, *Actinidia deliciosa* (kiwifruit) and *Laminaria Japonica* (seaweed) were fermented by effective microbes showed an incredible increase in antioxidant activity determined by FRAP assay.[31] The fermentation of RB with *R. oryzae* exhibited 87% of DPPH radical scavenging property.[14] The solid-state fermentation of RB with *M. pilosus* KCCM60084 showed 38%, 80%, and 60% increase in ABTS + radical scavenging activity, iron chelating activity, and reducing power, respectively.[24]

RB fermented with *R. oryzae* CTT 1217 has been kinetically analyzed for the improvement of the antioxidant property. 96 h FRB exhibited about 50% of DPPH radical scavenging activity after 15 min of reaction. The methanol extract of FRB was incubated with olive oil to determine the peroxidase property. About 60% of peroxidase inhibition was observed after 21 days of incubation, whereas 30 days of incubation showed only 34%.[15]

Naturally FRB protein concentrate (NFRBPC), yeast-FRB protein concentrate (YFRBPC), and unFRB concentrate (UFRBPC) exhibited 55.29%, 58.62%, and 47.14% of DPPH radical scavenging activity, respectively. The ferric reducing ability of NFRBPC, YFRBPC, and UFRBPC were 0.58, 0.73, and 0.41 mmol Trolox equivalent per gram of sample, respectively.[26]

Jung *et al*.[20] reported the changes in the antioxidant capacity of *L. edodes* mediated FRB of 21 different rice cultivars of Korea. FRB of cultivars Segyejinmi, Chindeul, Seolgaeng, Sunpum, Heonpum, Haedam, Chujum, Wolbaek, O. sativa cv. Haepum, Danmi, Goami2, Dasan1, Misomi, Ilpum, Migwang, Jungsaenggold, and Haiami displayed improvement in DPPH radical scavenging activity and the FRB of all 21 Korean cultivars exhibited increased oxygen radical absorbance capacity.

B. subtilis fermented HSDRB showed an increase in antioxidant activity after 96 h of the fermentation process when compared to that of the unfermented control sample. Authors claimed that the improvement of antioxidant activity was attributed to an enzyme produced by the fermenting organism. Oxidative inhibition rate was reduced sharply during the 1st 50 h of fermentation.[22]

The aqueous extract of *Issatchenkia orientalis* MFST1 mediated FRB was reported to be effective against high glucose and hydrogen peroxide-induced oxidative stress in 3T3-L1 adipocytes. FRB exposure significantly suppressed the reactive oxygen species formation and induced adiponectin and peroxisome proliferator-activated receptor gamma expression. The results revealed that FRB exposure diminishes the oxidative stress-induced insulin resistance.[32]

ANTI-CANCER AND ANTI-INFLAMMATORY BOWEL DISEASES PROPERTIES

A series of studies on the anti-cancer property of brown rice and RB fermented by *A. oryzae* has been published. *A. oryzae* mediated fermented brown rice, and RB (AFBRRB) significantly suppressed the azoxymethane mediated aberrant crypt foci formation in the rat. About 5% of AFBRRB reduced the incidence and inhibit the cell proliferation in colon adenocarcinomas.[33] AFBRRB has also been reported for the protective effect against diethylnitrosamine and phenobarbital induced hepatocarcinogenesis in male F344 rats.[34] N-nitrosomethylbenzylamine-induced esophageal tumorigenesis development was inhibited by AFBRRB supplementation. The incidence and multiplicity of dysplasia were significantly decreased by AFBRRB (10%) supplementation.[35] Another study with AFBRRB revealed that the protective effects of AFBRRB against inflammation-related carcinogenesis in mice were through inhibition of inflammatory cell infiltration.[36] N-nitrosobis (2-oxopropyl) amine-induced pancreatic tumorigenesis in hamsters has also been suppressed by AFBRRB (10%) supplementation via reduction of proliferation rate of tumor cells.[37] The anti-carcinogenesis effect of AFBRRB was demonstrated using transgenic rat for adenocarcinoma of the prostate (TRAP). TRAP model was fed with AFBRRB for 15 weeks. AFBRRB supplementation reduced the rate of adenocarcinoma in the lateral prostate, and also reduced the development of prostate carcinogenesis. It is observed that the AFBRRB supplementation induces the cell death and inhibit the proliferation of cells. The suppression of tumor growth depends on the phospho-adenosine monophosphate-activated kinase regulation by AFBRRB.[38] The chemoprotective effect of AFBRRB through the suppression of cell proliferation was reported against 4-nitroquinoline 1-oxide-induced oral carcinogenesis,[39] N-methyl-N'-nitro-N-nitrosoguanidine-induced gastric carcinogenesis,[40] and regulation of inflammatory system was reported against azoxymethane-induced colorectal carcinogenesis[41] in rat models. The aqueous extract of AFBRRB powder was evaluated for its anti-cancer activity in human acute lymphoblastic leukemia Jurkat cells. AFBRRB extract reduced the viability of leukemia, which is attributed to DNA fragmentation. The cleavage of caspase-8,-9, and-3 was accelerated by AFBRRB extract exposure and also reduced the B-cell lymphoma-2 (Bcl-2) expression while inducing the Death receptor-5 (DR5), Fas (tumor necrosis factor receptor) and pro-apoptotic protein (tBid) expression. The results suggested that AFBRRB extract activates the death receptor-mediated pathway to suppress the multiplication of human acute lymphoblastic leukemia cells.[42]

A. oryzae, L. rhamnosus, and *S. cerevisiae* mediated FRB, and its aqueous extract FRB extract (FRBE) were evaluated for melanoma inhibition property. Fermentation process reduces the cytotoxicity of RB. FRBE suppressed the α-melanocyte stimulating hormone-induced melanin synthesis in B16F1 cells and also reduced the intracellular tyrosinase activity. Microphthalmia-associated transcription factor expression was significantly diminished by FRBE. Thereby, FRBE suppresses the development of melanoma.[43] Exo-biopolymer isolated from *Lentinus edodes* FRB showed anti-cancer activity in B16/Bl6 melanoma transplanted mice via natural killer cell activation.[44]

RB was fermented by *S. cerevisiae* Misaki-1 and *L. plantarum* Sanriki-SU8 for 2 days at 30°C, and then FRB was subjected to aqueous extraction. The protective effect of FRB extract was evaluated using sodium sulfate-induced inflammatory bowel disease model mice. The spleen enlargement, structure of the crypt, and submucosa of colon tissues were reduced in FRB extract treated group when compared to control. The fermentation process improved the anti-inflammatory property of RB. Heating process diminishes the bioactivity of FRB extract.[45]

The anti-colitis property of *Aspergillus kawachii, L. brevis*, *L. rhamnosus*, and *Enterococcus faecium* FRB was assessed using dextran sodium sulfate-induced colitis mice model. Colitis-induced mice were supplemented with FRB, and the changes in body mass, disease activity index (DAI), histopathology score, myeloperoxidase (MPO) activity, the expression pattern of cytokine and chemokines, and the production of SCFAs and mucin were evaluated. FRB supplementation improved the weight gaining process and reduced the DAI. The total inflammation, crypt cell damage, epithelial loss, and infiltration of inflammatory cells was significantly reduced in FRB supplemented mice when compared to that of the control, and raw RB supplemented group. MPO activity and thiobarbituric acid reactive substance were reduced on FRB treatment in colitis-induced mice. The mRNA analysis revealed that FRB supplementation suppresses the expression of pro-inflammatory cytokines (*Tnf-α, Il-6,* and *Il-1 β*), chemokines (*Ccl2* and *Cxcl1*), and its receptor gene (*Cxcr3*). The feces SCFAs level was increased in FRB treated group.[46]

ANTI-DIABETIC PROPERTY

Lim and Lee[47] prepared *Bacillus* sp. KS-25, *B. circulans* KS-80, *B. licheniformis* KS-30, *B. sonorensis* KS-33, and *B. subtilis* KS-29 fermented materials (FM) that mainly contains RB, soybean powder, and the anti-diabetic property of FM was evaluated in type 2 diabetes mice model. The experimental animals fed with FM for 10 weeks showed a reduction in serum glucose, triglyceride, and HbA1c level. The glucose uptake was raised up to 60% after the treatment using ethanol extract of FM in C2C12 cells, and also activates insulin signaling process by

Table 1: Other functional properties of fermented rice bran

Interventions and dose	Microbes used for fermentation	Observed results	General claimed property	Reference
EM-YU (fermented mixture of RB, seaweed, and kiwifruit)	Effective microbes (strains details not available)	Fermented RB broth showed antibacterial activity against *P. aeruginosa* PAO1, and *E. coli* O157:H7 and exhibited tyrosinase inhibition activities. Ethyl acetate extract of EM-YU showed anti-biofilm activity against *E. coli* O157:H7	Antibacterial, tyrosinase inhibition, and anti-biofilm property	[31]
FCSRE (a fermented mixture of rice bran, coffee bean, and soybean aqueous extracts), Guardox™; 2 g per kg body weight per day for 12 weeks	*B. subtilis* Natto	Inhibit the formation of thiobarbituric acid reacting substance. The results suggested that FCSRE could prevent atherosclerosis	Anti-atherogenic effects	[57]
Aqueous extracts of FRB; 1.5 and 3 g/kg at day 7 and 21.	*Issatchenkia orientalis* MFST1	Inhibit the release of β-hexosaminidase, and suppressed the systemic allergic reaction *in vitro* Levels of IL-6, IL-10, IFN-γ, and TNF-α were suppressed in FRB supplemented ovalbumin-sensitized mice model. FRB supplementation showed anti-allergic activity by inhibiting the release of histamine and suppressing the production of the pro-inflammatory cytokine	Anti-allergic property	[58]
Hot water extract of FRB	*S. cerevisiae*	GOT, GPT, total cholesterol, glucose, LDH levels were reduced after FRB intervention. FRB supplementation extended the swimming time	Anti-stress, and Anti-fatigue	[59,60]
FRB extract with plants (*A. gigantis* Radix, *A. princeps*, *C. sinensis*, and *C. officinale*)	*L. rhamnosus, P. deserticola*	FRB withdrew collagen-induced platelet aggregation and attenuates the formation of thrombus FRB blocked the intracellular calcium mobilization and inhibits the stimuli-responsive kinase 1/2, p38-mitogen-activated protein kinases and c-Jun N-terminal kinase phosphorylation	Anti-thrombotic activity	[61]
FRB; 0.4% of FRB in normal diet for 8 weeks.	*Bacillus* sp. (KCTC11351BP), *B. circulans* (KCTC11355BP), *B. sonolensis* (KCTC11354BP), and *B. subtilis* (KCTC11352BP)	Eight weeks of FRB intervention reduced aspartate aminotransferase, alanine aminotransferase, triglycerides, total cholesterol levels, and increased glutathione in tetrachloride induced hepatotoxic mice FRB suppressed the liver fibrosis	Hepatoprotective property	[62]
FRB with *A. princeps*, *A. gigantis*, *C. sinensis*, and *C. officinale*	*L. rhamnosus* and *P. deserticola*	Reduced the skin lesions in 1-chloro-2,4-dinitrobenzene-induced atopic dermatitis and serum IgE, and WBC count. FRB treatment significantly nullified the toxin-induced consequences of atopic dermatitis	Prevents atopic dermatitis	[63]
FRB; 100 mg per kg for 5 days	*L. plantarum* NCIMB 8826	FRB supplementation showed 30% toxic incidence, 10% of mortality, and 40% of gastrointestinal mucosal pathology, while nonfermented RB showed 50%, 30%, and 50% of incidence, death, and mucosal pathology, respectively	Chemoprotective effect on doxorubicin-induced toxicity. Aid therapy for cancer treatment.	[64]
Fermented black rice bran	*B. subtilis* KU3	68.07% and 71.65% of cytotoxicity were observed against HeLa and MCF-7 cells, respectively	Cytotoxic activities	[65]
FRB; 5%-10% of FRB in diet	*A. oryzae*	The incidence of hepatitis was reduced. Survival period of the rat was extended No significant changes in serum Cu level	Protects liver from acute hepatitis	[66]
A mixture of FRB and *S. cerevisiae*; 20 g per kg per day for 7 days	*S. cerevisiae*, *Bacillus* spp	Activates the macrophage and regulate IL-6 production, and increase the proliferation of bone marrow cells	Immune enhancer	[67]
FRB (Rice bran exo-biopolymer, RBEP); Six capsules per day for 8 weeks to healthy human subjects	*Lentinus edodes*	Increased the production of IFN-γ NK cell activity and TNF-α, IL-12, IL-4, IL-10, and IL-2 levels were not affected by FRB intervention	Immune enhancer	[68]

Contd...

Table 1: Contd...

Interventions and dose	Microbes used for fermentation	Observed results	General claimed property	Reference
FRB supplementation (21 g per day for two weeks and then for 12 weeks intermission and again 2 weeks ingestion) to healthy human subjects	*A. oryzae*	Showed prebiotic property in healthy adults, and FRB is safe for human consumption	Prebiotic effects	[69]

P. aeruginosa=Pseudomonas aeruginosa, E. coli=Escherichia coli, B. subtilis=Bacillus subtilis, S. cerevisiae=Saccharomyces cerevisiae, L. rhamnosus Lactobacillus rhamnosus, P. deserticola, Pichia deserticola, A. oryzae=Aspergillus oryzae, S. cerevisiae=Saccharomyces cerevisiae, L. edodes, Lentinus edodes, C. officinale=Cynoglossum officinale, C. sinensis=Clonorchis sinensis, A. gigantis=Angelica gigantis, A. princeps=Artemisia princeps, TNF-α=Tumor necrosis factor, IL=Interleukin, IFN-γ=Interferon-gamma, RB=Rice bran, FRB=Fermented rice bran, GOT=Glutamic oxaloacetic transaminase, GPT=Glutamic pyruvic transaminase, LDH=Lactic acid dehydrogenase, WBC=White blood cells

phosphorylating Akt (glucose transporter modulator). FM extract does not affect the insulin-independent signaling process while suppressing the negative signaling to the insulin pathway. The results suggested that FM extract increase glucose uptake through the activation of PI3kinase/Akt pathways.

RB was fermented with *A. kawachii,* and a blend of lactic acid bacteria (*L. brevis, L. rhamnosus*, and *E. faecium*) and the FRB was supplemented to stroke-prone spontaneously hypertensive SHRSP/Izm rats. The oral administration of 5% FRB for 4 weeks reduced the systolic and diastolic blood pressure and enhanced the serum adiponectin level. Besides, FRB intervention amended serum insulin levels, insulin sensitivity, glucose tolerance, and lipid profiles. The results suggested that the dietary supplementation of FRB may reduce hypertension and complications of metabolic syndrome.[48]

A. oryzae fermented soybean, brown rice, brown rice and RB paste, and brown rice-red ginseng marc was investigated for the influence of glucose metabolism in high-fat diet mice model. The high fat-induced hyperglycemic condition was reduced with the supplementation of fermented paste. The hepatic glucose-regulating enzyme activities were altered by the fermented paste. Even though fermented brown rice and RB showed anti-hyperglycemic property, the fermented brown rice-red ginseng marc exhibited improved hypoglycemic and antioxidative activities.[49]

COSMETICS

RB was fermented with *A. oryzae, R. oryzae,* and *R. oligosporus* separately. Then the fermented samples were extracted with an aqueous solution. The phytochemical content and enzyme inhibitory activity of the fermented extracts were evaluated. Tyrosinase (tyrosinase inhibition prevents the hyperpigmentation in the skin) and elastase inhibition activities (helps to claim the anti-aging property of the extract) were examined to assess the skincare properties of extracts. *A. oryzae* FRB showed about 56, and 60% of tyrosinase, and elastase inhibition, respectively. Researchers appealed that the FRB could be a potent cosmeceutical ingredient for skincare products.[18,29]

RB fermented with *S. cerevisiae,* and *L. rhamnosus* has been studied for anti-photoaging properties. FRB showed inhibition of melanin synthesis in B16F1 melanoma cells. Ultraviolet (UV)-B irradiated human fibroblasts were exposed to different concentration of FRB and found that FRB supplementation increase the type I collagen synthesis, reduced the matrix metalloproteinase-1 expression, and inhibited the IL-1α production. The results suggested that the FRB could protect the UV-B mediated skin damages.[50]

ANIMAL FEED

The naturally FRB was microbiologically evaluated, and the active strains, *R. oligosporus*, and *S. cerevisiae* were selected for specific fermentation. The fermentation of RB has enhanced the nutritional value, especially protein content, and digestibility of fiber. The FRB has been claimed as a health feed for the rabbit.[51]

RB fermented with *A. niger* for 72 h was enriched with dry matter, crude protein, organic matter, and nitrogen retention, which can be used as poultry feed.[52] RB used in phytase production has been extracted, and the crude used RB was supplemented to the broiler chickens, and the impacts were evaluated. Chicken fed with RB does not show any significant difference in body mass, growth rate, and feed intake. The supplementation of by-product (used RB) of phytase production did not cause any adverse effects to broiler chicken, and it can be used as an alternative feed for poultry.[53] *Bacillus amyloliquefaciens* mediated fermentation of RB with humic substances condensed crude fiber content of RB, and one-day-old chicks were fed with different concentrations (0%–20%) of FRB along with the normal feed. Supplementation of FRB (15%) in the regular diet for chicks improved the feed conversion ratio, and weight gain, significantly.[54]

Hot water extract of *S. cerevisiae* and *Bacillus* sp. mediated FRB was supplemented as feed additives to rats and found that the FRB supplementation improved the immune system and reduced the stress level.[55] Supplementation of FRB improved the total free amino acid content, taste, flavor, aroma, and juiciness of the pork.[56]

OTHER FUNCTIONAL PROPERTIES

FRB prepared with various microbial action were reported for several health promoting and chemoprotective properties such as anti-atherogenic,[57] anti-allergic,[58] anti-stress, anti-fatigue,[59,60] anti-thrombotic,[61] hepatoprotective,[62] antibacterial, anti-biofilm, tyrosinase inhibition,[31] prevents atopic dermatitis,[63] chemoprotective on doxorubicin-induced toxicity,[64] cytotoxic activities on cancer cells,[65] protects liver from acute hepatitis,[66] and immune enhancer.[67,68] FRB has also been reported as a potent prebiotic.[69] Detailed information on the preparation of FRB, intervention, and observed results are listed in Table 1.

CONCLUSION AND FUTURE PROSPECTUS

The fermentation processes improved the phytochemical content and bioactivity of RB, especially the improvement in the antioxidant property. The microbes used in the fermentation process played a critical role in the quality enhancement of RB. *Bacillus* strain (*B. subtilis* KU3) isolated from Kimchi, a traditional Korean food, decreased the anthocyanin and phenolic content of RB after fermentation. Moreover, DPPH radical scavenging activity and FRAP were reduced in FRB compared to non-FRB.[65] Isolation and identification of compelling starter culture would extend the use of FRB. Further, in-depth studies are required to extract and characterize the active principles from the FRB that may provide the valuable active candidates for pharmacological and cosmetic applications.

Acknowledgment

Authors gratefully acknowledges the Faculty of Pharmacy and Chiang Mai University, Chiang Mai, Thailand. BSS wish to acknowledge the CMU Postdoctoral Fellowship (Ref: No. 6592 (11)/1379, dated 26 February 2018), Chiang Mai University, Chiang Mai, Thailand.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. McGovern PE, Zhang J, Tang J, Zhang Z, Hall GR, Moreau RA, *et al*. Fermented beverages of pre- and proto-historic China. Proc Natl Acad Sci U S A 2004;101:17593-8.
2. Ivey M, Massel M, Phister TG. Microbial interactions in food fermentations. Annu Rev Food Sci Technol 2013;4:141-62.
3. Chen M, Sun Q, Giovannucci E, Mozaffarian D, Manson JE, Willett WC, *et al*. Dairy consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. BMC Med 2014;12:215.
4. An SY, Lee MS, Jeon JY, Ha ES, Kim TH, Yoon JY, *et al*. Beneficial effects of fresh and fermented kimchi in prediabetic individuals. Ann Nutr Metab 2013;63:111-9.
5. Byun MS, Yu OK, Cha YS, Park TS. Korean traditional chungkookjang improves body composition, lipid profiles and atherogenic indices in overweight/obese subjects: A double-blind, randomized, crossover, placebo-controlled clinical trial. Eur J Clin Nutr 2016;70:1116-22.
6. Laatikainen R, Koskenpato J, Hongisto SM, Loponen J, Poussa T, Hillilä M, *et al*. Randomised clinical trial: Low-FODMAP rye bread vs. regular rye bread to relieve the symptoms of irritable bowel syndrome. Aliment Pharmacol Ther 2016;44:460-70.
7. Lim JH, Jung ES, Choi EK, Jeong DY, Jo SW, Jin JH, *et al*. Supplementation with *Aspergillus oryzae*-fermented kochujang lowers serum cholesterol in subjects with hyperlipidemia. Clin Nutr 2015;34:383-7.
8. Fekete ÁA, Givens DI, Lovegrove JA. Casein-derived lactotripeptides reduce systolic and diastolic blood pressure in a meta-analysis of randomised clinical trials. Nutrients 2015;7:659-81.
9. Tu MY, Chen HL, Tung YT, Kao CC, Hu FC, Chen CM, *et al*. Short-term effects of kefir-fermented milk consumption on bone mineral density and bone metabolism in a randomized clinical trial of osteoporotic patients. PLoS One 2015;10:e0144231.
10. Park HY, Lee KW, Choi HD. Rice bran constituents: Immunomodulatory and therapeutic activities. Food Funct 2017;8:935-43.
11. Lemos MR, Souza-Soares LA. Rice and its byproducts in Southern Brazil. Vetor. Rev Ciênc Exatas Engenharias 2000;10:21-36.
12. da Silva MA, Sanches C, Amante ER. Prevention of hydrolytic rancidity in rice bran. J Food Eng 2006;75:487-91.
13. Oliveira Mdos S, Feddern V, Kupski L, Cipolatti EP, Badiale-Furlong E, de Souza-Soares LA, *et al*. Changes in lipid, fatty acids and phospholipids composition of whole rice bran after solid-state fungal fermentation. Bioresour Technol 2011;102:8335-8.
14. Kupski L, Cipolatti E, da Rocha M, Oliveira MD, Souza-Soares LD, Badiale-Furlong E. Solid-state fermentation for the enrichment and extraction of proteins and antioxidant compounds in rice bran by *Rhizopus oryzae*. Braz Arch Biol Technol 2012;55:937-42.
15. Oliveira MD, Cipolatti EP, Furlong EB, Soares LD. Phenolic compounds and antioxidant activity in fermented rice (*Oryza sativa*) bran. Cienc Tecnol Aliment Camp 2012;32:531-7.
16. Abd Razak DL, Rashid NY, Jamaluddin A, Sharifudin SA, Long K. Enhancement of phenolic acid content and antioxidant activity of rice bran fermented with *Rhizopus oligosporus* and *Monascus purpureus*. Biocatal Agric Biotechnol 2015;4:33-8.
17. Jamaluddin A, Razak DL, Rashid NY, Sharifudin SA, Kahar AA, Saad AZ, *et al*. Effects of solid state fermentation by *Monascus purpureus* on phenolic content and biological activities of coconut testa and rice bran. J Teknologi 2016;78:23-8.
18. Abd Razak DL, Jamaluddin A, Rashid NY, Sharifudin SA, Long K. Comparative study of antioxidant activities, cosmeceutical properties and phenolic acids composition of fermented rice bran and coconut testa. J Teknologi 2016;78:29-34.
19. Oliveira MD, Feddern V, Kupski L, Cipolatti EP, Badiale-Furlong E, de Souza-Soares LA. Physico-chemical characterization of fermented rice bran biomass. CyTA J Food 2010;8:229-36.
20. Jung TD, Shin GH, Kim JM, Choi SI, Lee JH, Lee SJ, *et al*. Comparative analysis of γ-oryzanol, β-glucan, total phenolic content and antioxidant activity in fermented rice bran of different varieties. Nutrients 2017;9. pii: E571.
21. Abd Rashid NY, Razak DL, Jamaluddin A, Sharifudin SA, Long K. Bioactive compounds and antioxidant activity of rice bran fermented with lactic acid bacteria. Malays J Microbiol 2015;11:156-62.
22. Webber DM, Hettiarachchy NS, Li R, Horax R, Theivendran S. Phenolic profile and antioxidant activity of extracts prepared from fermented heat-stabilized defatted rice bran. J Food Sci 2014;79:H2383-91.
23. Li Y, Meng S, Shi M, Hu X, Yang Y, Zhang Z. Bioactivity evaluation of crude polysaccharide from rice bran fermented by *Preussia aemulans* and the changes in its nutritional contents. J Food Biochem 2016;40:664-72.
24. Cheng J, Choi B, Yang SH, Suh J. Effect of fermentation on the antioxidant activity of rice bran by *Monascus pilosus* KCCM60084. J Appl Biol Chem 2016;59:57-62.
25. Ryan EP, Heuberger AL, Weir TL, Barnett B, Broeckling CD, Prenni JE, *et al*. Rice bran fermented with *Saccharomyces boulardii* generates novel metabolite profiles with bioactivity. J Agric Food Chem 2011;59:1862-70.
26. Chinma CE, Ilowefah M, Shammugasamy B, Ramakrishnan Y, Muhammad K. Chemical, antioxidant, functional and thermal properties of rice bran proteins after yeast and natural fermentations. Int J Food Sci Technol 2014;49:2204-13.
27. Chaiyasut C, Pengkumsri N, Sirilun S, Peerajan S, Khongtan S, Sivamaruthi BS, *et al*. Assessment of changes in the content of anthocyanins, phenolic acids, and antioxidant property of *Saccharomyces cerevisiae* mediated fermented black rice bran. AMB Express 2017;7:114.
28. Schmidt CG, Gonçalves LM, Prietto L, Hackbart HS, Furlong EB. Antioxidant activity and enzyme inhibition of phenolic acids from fermented rice bran with fungus *Rizhopus oryzae*. Food Chem 2014;46:371-7.
29. Abd Razak DL, Rashid NY, Jamaluddin A, Sharifudin SA, Kahar AA, Long K. Cosmeceutical potentials and bioactive compounds of rice bran fermented with single and mix culture of *Aspergillus oryzae* and *Rhizopus oryzae*. J Saudi Soc Agric Sci 2017;16:127-34.
30. Liu Q, Cao X, Zhuang X, Han W, Guo W, Xiong J, *et al*. Rice bran polysaccharides and oligosaccharides modified by *Grifola frondosa* fermentation: Antioxidant activities and effects on the production of NO. Food Chem 2017;223:49-53.
31. Li Z, Lee J, Cho MH. Antioxidant, antibacterial, tyrosinase inhibitory, and biofilm inhibitory activities of fermented rice bran broth with effective microorganisms. Biotechnol Bioprocess Eng 2010;15:139-44.
32. Kim D, Han GD. Ameliorating effects of fermented rice bran extract on oxidative stress induced by high glucose and hydrogen peroxide in 3T3-L1 adipocytes. Plant Foods Hum Nutr 2011;66:285-90.
33. Katyama M, Yoshimi N, Yamada Y, Sakata K, Kuno T, Yoshida K, *et al*. Preventive effect of fermented brown rice and rice bran against colon carcinogenesis in male F344 rats. Oncol Rep 2002;9:817-22.
34. Katayama M, Sugie S, Yoshimi N, Yamada Y, Sakata K, Qiao Z, *et al*. Preventive effect of fermented brown rice and rice bran on diethylnitrosoamine and phenobarbital-induced hepatocarcinogenesis in male F344 rats. Oncol Rep 2003;10:875-80.
35. Kuno T, Hirose Y, Hata K, Kato K, Qiang SH, Kitaori N, *et al*. Preventive effect of fermented brown rice and rice bran on N-nitrosomethylbenzylamine-induced esophageal tumorigenesis in rats. Int J Oncol 2004;25:1809-15.
36. Onuma K, Kanda Y, Suzuki Ikeda S, Sakaki R, Nonomura T, Kobayashi M, *et al*. Fermented brown rice and rice bran with *Aspergillus oryzae* (FBRA) prevents inflammation-related carcinogenesis in mice, through inhibition of inflammatory cell infiltration. Nutrients 2015;7:10237-50.
37. Kuno T, Takahashi S, Tomita H, Hisamatsu K, Hara A, Hirata A, *et al*. Preventive effects of fermented brown rice and rice bran against N-nitrosobis (2-oxopropyl) amine-induced pancreatic tumorigenesis in male hamsters. Oncol Lett 2015;10:3377-84.
38. Kuno T, Nagano A, Mori Y, Kato H, Nagayasu Y, Naiki-Ito A, *et al*. Preventive effects of fermented brown rice and rice bran against prostate carcinogenesis in TRAP rats. Nutrients 2016;8. pii: E421.

39. Long NK, Makita H, Yamashita T, Toida M, Kato K, Hatakeyama D, *et al.* Chemopreventive effect of fermented brown rice and rice bran on 4-nitroquinoline 1-oxide-induced oral carcinogenesis in rats. Oncol Rep 2007;17:879-85.
40. Tomita H, Kuno T, Yamada Y, Oyama T, Asano N, Miyazaki Y, *et al.* Preventive effect of fermented brown rice and rice bran on N-methyl-N'-nitro-N-nitrosoguanidine-induced gastric carcinogenesis in rats. Oncol Rep 2008;19:11-5.
41. Phutthaphadoong S, Yamada Y, Hirata A, Tomita H, Hara A, Limtrakul P, *et al.* Chemopreventive effect of fermented brown rice and rice bran (FBRA) on the inflammation-related colorectal carcinogenesis in ApcMin/+ mice. Oncol Rep 2010;23:53-9.
42. Horie Y, Nemoto H, Itoh M, Kosaka H, Morita K. Fermented brown rice extract causes apoptotic death of human acute lymphoblastic leukemia cells via death receptor pathway. Appl Biochem. Biotechnol 2016;178:1599-611.
43. Chung SY, Seo YK, Park JM, Seo MJ, Park JK, Kim JW, *et al.* Fermented rice bran downregulates MITF expression and leads to inhibition of alpha-MSH-induced melanogenesis in B16F1 melanoma. Biosci Biotechnol Biochem 2009;73:1704-10.
44. Kim HY, Kim JH, Yang SB, Hong SG, Lee SA, Hwang SJ, *et al.* A polysaccharide extracted from rice bran fermented with *Lentinus edodes* enhances natural killer cell activity and exhibits anticancer effects. J Med Food 2007;10:25-31.
45. Kondo S, Kuda T, Nemoto M, Usami Y, Takahashi H, Kimura B. Protective effects of rice bran fermented by *Saccharomyces cerevisiae* Misaki-1 and *Lactobacillus plantarum* Sanriki-SU8 in dextran sodium sulphate-induced inflammatory bowel disease model mice. Food Biosci 2016;16:44-9.
46. Islam J, Koseki T, Watanabe K, Ardiansyah, Budijanto S, Oikawa A, *et al.* Dietary supplementation of fermented rice bran effectively alleviates dextran sodium sulfate-induced colitis in mice. Nutrients 2017;9. pii: E747.
47. Lim S, Lee B. Anti-diabetic effect of material fermented using rice bran and soybean as the main ingredient by *Bacillus* sp. J Korean Soc Appl Biol Chem 2010;53:222-9.
48. Alauddin M, Shirakawa H, Koseki T, Kijima N, Ardiansyah, Budijanto S, *et al.* Fermented rice bran supplementation mitigates metabolic syndrome in stroke-prone spontaneously hypertensive rats. BMC Complement Altern Med 2016;16:442.
49. Chung SI, Rico CW, Kang MY. Comparative study on the hypoglycemic and antioxidative effects of fermented paste (doenjang) prepared from soybean and brown rice mixed with rice bran or red ginseng marc in mice fed with high fat diet. Nutrients 2014;6:4610-24.
50. Seo Y, Jung S, Song K, Park J, Park C. Anti-photoaging effect of fermented rice bran extract on UV-induced normal skin fibroblasts. Eur Food Res Technol 2010;231:163-9.
51. Oduguwa OO, Edema MO, Ayeni AO. Physico-chemical and microbiological analyses of fermented corn cob, rice bran and cowpea husk for use in composite rabbit feed. Bioresour Technol 2008;99:1816-20.
52. Hardini D. The nutrient evaluation of fermented rice bran as poultry feed. Int J Poult Sci 2010;9:152-4.
53. Mu KS, Kasim AB, Ideris A, Saad CR. Effect of fermented rice bran, bio-converted byproduct on performance of broiler chickens. J Anim Vet Adv 2011;10:2990-5.
54. Supriyati, Haryati T, Susanti T, Susana IW. Nutritional value of rice bran fermented by *Bacillus amyloliquefaciens* and humic substances and its utilization as a feed ingredient for broiler chickens. Asian Australas J Anim Sci 2015;28:231-8.
55. Koh JH, Yu KW, Suh HJ. Biological activities of *Saccharomyces cerevisiae* and fermented rice bran as feed additives. Lett Appl Microbiol 2002;35:47-51.
56. Kim D, Fan JP, Choi D, Park H, Han GD. Effects of fermented rice bran addition on the quality of improvement of Pork. Korean J Food Sci Tecnhol 2007;39:608-13.
57. Naito M, Wu X, Lin J, Kimura A, Kodama M, Takada A, *et al.* Anti-atherogenic effects of fermented fresh coffee bean, soybean and rice bran extracts. Food Sci Technol Res 2003;9:170-5.
58. Fan JP, Choi KM, Han GD. Inhibitory effects of water extracts of fermented rice bran on allergic response. Food Sci Biotechnol 2010;19:1573-8.
59. Kim KM, Yu KW, Kang DH, Koh JH, Hong BS, Suh HJ. Anti-stress and anti-fatigue effect of fermented rice bran. Biosci Biotechnol Biochem 2001;65:2294-6.
60. Kim KM, Yu KW, Kang DH, Suh HJ. Anti-stress and anti-fatigue effect of fermented rice bran. Phytother Res 2002;16:700-2.
61. Jeon BR, Ji HD, Kim SJ, Lee CH. Anti-thrombotic activity of fermented rice bran extract with several oriental plants *in vitro* and *in vivo*. Korean J Vet Res 2016;55:233-40.
62. Park S, Lee S, Nam Y, Yi S, Seo M, Lim S. Hepatoprotective effect of fermented rice bran against carbon tetrachloride-induced toxicity in mice. Food Sci Biotechnol 2014;23:165-71.
63. Saba E, Lee CH, Jeong DH, Lee K, Kim T, Roh S, *et al.* Fermented rice bran prevents atopic dermatitis in DNCB-treated NC/Nga mice. J Biomed Res 2016;30:334-43.
64. Lee KH, Rhee K, Cho CH. The chemoprotective effect of fermented rice bran on doxorubicin induced toxicity in the rat. Nat Prod Sci 2014;20:29-32.
65. Yoon HJ, Lee KA, Lee JH, Jin HJ, Kim HJ, Kim K, *et al.* Effect of fermentation by *Bacillus subtilis* on antioxidant and cytotoxic activities of black rice bran. Int J Food Sci Technol 2015;50:612-8.
66. Shibata T, Nagayasu H, Kitajo H, Arisue M, Yamashita T, Hatakeyama D, *et al.* Inhibitory effects of fermented brown rice and rice bran on the development of acute hepatitis in Long-Evans cinnamon rats. Oncol Rep 2006;15:869-74.
67. Koh JH, Suh HJ. Immune enhancing effect by orally-administered mixture of *Saccharomyces cerevisiae* and fermented rice bran. J Microbiol Biotechnol 2005;13:196-201.
68. Choi JY, Paik DJ, Kwon DY, Park Y. Dietary supplementation with rice bran fermented with *Lentinus edodes* increases interferon-γ activity without causing adverse effects: A randomized, double-blind, placebo-controlled, parallel-group study. Nutr J 2014;13:35.
69. Nemoto H, Ikata K, Arimochi H, Iwasaki T, Ohnishi Y, Kuwahara T, *et al.* Effects of fermented brown rice on the intestinal environments in healthy adult. J Med Invest 2011;58:235-45.