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Rice Bran as a Functional Food: An Overview of the Conversion of Rice Bran into a Superfood/Functional Food

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Abstract

Rice bran is a byproduct of the rice milling process; it constitutes 10% of rice, with a potential global production of 48 million tons per year. The major portion of this is used as animal feed or discarded as waste material. However, rice bran is attracting attention from researchers because it is widely available, cheap and rich in nutrients such as protein, fat, carbohydrates, bioactive compounds and dietary fiber. Many food-processing techniques that have improved rice bran resources have been pioneered, such as enzyme treatment and fermentation. We have been investigating the functional role of rice bran since 2003. Our experiments revealed that rice bran and its active compounds, such as γ-oryzanol, tocopherol, tocotrienol, adenosine and ferulic acid, play a role as a functional food. In this review, we summarize how rice bran is a super food and functional food to illustrate the global interest in rice bran and its functional aspects and medicinal qualities. We also describe the techniques to prepare functional bran and the composition and health benefits of functional bran, which may encourage entrepreneurs to produce rice bran-based food on a large scale and meet the global demand for super foods and functional foods.

Keywords: functional bran, bioactive compounds, adenosine, ferulic acid, γ-oryzanol

1. Introduction

Throughout the history of human civilization, food has been developed to provide nutrition and sustain health. In this regard, the development of "functional foods" is gaining momentum,

because consumers in developing and developed countries wish to maintain better health [1]. The concept of a "functional food" originated in the 1980s in Japan, from where it migrated to Europe and the United States [2]. In general, a functional food is a modified food that improves health and well-being beyond the effects of the nutrients it contains. Generally, foods can be made functional foods by increasing the concentration of, adding, or improving the bioavailability of particular components. Food is considered functional when it can be established that it enhances body function or reduces the risk of diseases [3].

Functional foods have recently emerged as convenient, inexpensive and promising candidates to prevent chronic health problems. Rice bran, a byproduct of the rice milling process, is derived from the outer layer of the rice grain; it contains a number of nutrients and biologically active compounds. Rice bran is often processed using stabilization, fractionation, enzymatic treatment, or fermentation. This treated rice bran is called functional bran. The identification of the bioactive components contained in rice bran has reinforced its status as a functional food.

Experiments have revealed that enzyme-treated or ethanol-extracted rice bran (6% of the diet for 8 weeks) improves blood pressure (BP), the lipid profile and glucose metabolism. Furthermore, adenosine supplementation (10 mg/kg body weight), an active component of functional bran, improved metabolic syndrome in stroke-prone spontaneously hypertensive rats (SHRSPs) [4]. In addition, ferulic acid (FA) supplementation (9.5 mg/kg body weight), another active compound in functional bran (0.19 mg/100 g of rice bran), improves BP and the lipid profile [5]. Thus, the aim of this review was to analyze the evidence of rice bran as a functional food as well as the global interest in rice bran.

2. Compositional distinctiveness of rice bran

The composition of rice bran differs with the variety of rice, geographical conditions and processing methods. Rice bran, the outer layer of the rice grain, accounts for 8–10% of the total weight of the grain; however, it contains most of the nutrients: carbohydrates (34–62%), lipids (15–20%), protein (11–15%), crude fiber (7–11%) and ash (7–10%). In particular, rice lipids and bioactive components are concentrated in rice bran [6, 7]. Fatty acids such as palmitate (21–26%), linoleate (31–33%) and oleate (37–42%) are predominant in rice bran. In addition, due to its high content of polyunsaturated fatty acids, rice bran is considered a healthy food [7, 8]. Significant quantities of bioactive compounds such as γ-oryzanol, tocotrienol, tocopherol and α-sitosterol as well as dietary fibers such as α-glucan, pectin and gum have been found in rice bran [9, 10]. Specifically, γ-oryzanol, the main antioxidant present in rice bran, has a 10-times higher antioxidant activity than tocopherol, while tocotrienol has 40–60 times greater antioxidant activity than tocopherol. However, the proportions of these phytochemicals vary with the type of rice cultivar [11]. In addition, rice bran contains 4-hydroxy-3-methoxycinnamic acid (FA), which has photoprotective and antioxidative effects [12–14].

The health information website SelfNutritionData (http://nutritiondata.self.com) reports that one cup of crude rice bran provides 88 calories and that 28 g of rice bran contains 5.8 g of fat, 1.2 g of which is saturated and 4.2 g of healthy unsaturated fatty acids. According to Walter

Willett, a nutritionist from Harvard University (https://www.hsph.harvard.edu/walter-willett), heart health is directly related to the ratio of unsaturated to saturated fatty acids in the diet. In addition, one cup of rice bran delivers 13.9 g of carbohydrate and 3.7 g of protein, which is 7% of our daily requirement and a single serving of rice bran delivers more than half of our daily nutritional requirements of thiamine, niacin and pyridoxine.

3. Rice bran as functional bran

3.1. Fermentation

Owing to its disease-preventing properties, rice bran is popular in the food industry. Interestingly, the antidiabetic and antidyslipidemic activities of rice bran have been reported in different animal model experiments [15–17]. Furthermore, the active components in processed rice bran promote health; indeed, the processing itself adds value to the rice bran [18, 19]. Such treated rice bran may protect against metabolic syndrome by attenuating hypertension, dyslipidemia and insulin resistance; it is a candidate functional food because it prevents oxidative stress in rat and mouse models [20–23]. To create a more applicable and functional bran, several fermentation processes have been used to enhance its nutritional value. Rice bran fermented using *Saccharomyces cerevisiae* has anti-stress and anti-fatigue effects. Furthermore, the polysaccharide extracts of rice bran fermented using *Lentinus edodes* showed an anti-cancer effect and they prevented defective immune responses; the water extracts of the same fermented rice bran had an anti-photoaging effect [24, 25]. Moreover, brown rice fermented using *Aspergillus oryzae* has a suppressive effect on dextran sulfate sodium-induced ulcerative colitis and it inhibits inflammation-mediated cell infiltration [26, 27]. Rice bran extract fermented using *Lactobacillus plantarum* improves functional recovery and reduces cognitive impairment after ischemic brain injury in a rat model [28, 29]. Fermentation using different microbes can increase the levels of bioactive compounds as well as the availability of functional food. For instance, fermentation using *Rhizopus oryzae* increases the protein content of rice bran (43%); it also increases the levels of phenolic compounds, which have high antioxidant activity, by breaking down lignin in the substrate cell wall [30].

3.2. Compositional improvement as functional bran

Rice bran is processed to inactivate lipases and other nutritional inhibitors such as field fungi, bacteria and insects, to reduce their toxicity without damage to the protein quality of rice bran. The rice bran must be stabilized using suitable techniques while bran layers are removed from the endosperm during milling. Specifically, to achieve proper stabilization, each individual bran particle must have the same moisture content, depending on the time and temperature. Furthermore, to inactivate the enzymes in the rice bran that are responsible for rancidity, different stabilization methods are used. Among these, microwave energy offers an alternative energy source for stabilization [30–32]. Next, stabilization fractionation is performed. This is an important step in industrial processing; it involves the conversion of rice bran into various parts that contain more desirable than undesirable components. Subsequently, the different

fractions are centrifuged to separate the insoluble fiber fraction—called rice bran fiber—from the aqueous dispersible fraction—called rice bran soluble. The mixture of both insoluble and soluble extracts is called rice bran balance. Using different technologies, the bran is fully stabilized and the oil is removed. The resultant food-grade, defatted rice bran is temporarily stored in food grade silos until it can be used in edible applications. Bleaching of the edible oil typically leaves minor flavor and odor compounds that must be removed by steam distillation before the oil is used. Steam distillation is the final step in the processing of edible oil, whereby any off-flavor and residual free fatty acids left in the oil are removed.

We produced two types of rice bran fraction: Driselase® fraction (DF) and ethanol fraction (EF). To process the rice bran, 500 g bran was agitated in 1.0 L of 70% ethanol for 2 h; this yielded two fractions: the solid and filtered fractions. The DF was derived from the solid fraction. Driselase® is a commercial plant cell wall-degrading enzyme mixture containing cellulase, xylanase and laminarinase; however, it is esterase free. The solid fraction of rice bran was dried at room temperature and then suspended in 10 mM acetate buffer (500 mL) containing Driselase (0.2 mg/L) from *Basidiomycetes* spp. The bran was treated in this manner overnight at 37°C; the suspension was then filtered and finally lyophilized. As a result, Driselase-treated rice bran had increased quantities of bioactive components that improve glucose and lipid metabolism in the SHRSPs—a genetic animal model of metabolic syndrome [33, 34].

## 4. Extraction, isolation and identification of the active components in rice bran

Different conventional methods are used to extract the bioactive compounds from plant materials. Of these, solvent, supercritical fluid, microwave-assisted and ultrasonic-assisted extraction are notable. Microwave-assisted extraction and ultrasound-assisted methods are used to detect antioxidant and anticancer bioactive components in the plant extracts [35, 36]. Imsanguan et al. described conventional solvent extraction, with different modifications at different temperatures (32–60°C), using 100 ml hexane at a rotating speed of 200 rpm for 24 h to extract γ-oryzanol from rice bran [37]. However, this conventional technique does not fully remove toxic solvent residues from the final product; for this reason, Herrero et al. used the prominent technique of supercritical fluid extraction, which offers better extraction and purification of bioactive compounds [38]. Zigoneanu et al. described antioxidant extraction from rice bran oil using microwave-assisted extraction, which uses electromagnetic radiation in the range of 0.3–300 GHz [39].

We developed the DF method to identify active components in the rice bran. As already described, the DF was derived from the solid fraction and chromatographed onto a silica gel column. One fraction derived from the methanol eluate was further fractionated using an octadecylsilane (ODS) column. The active fraction was obtained from the methanol/water (20–70%) eluate and separated by high-performance liquid chromatography (HPLC) using an ODS column. The BP-lowering activity of each fraction was examined using a single oral adminis-tration to male, 14-week old SHRSPs; we found that gavage of a certain fraction at 40 mg/kg

body weight decreased BP significantly 1, 2, 4 and 6 h after administration. The chemical structure of this fraction was determined using fast atom-bombardmentmass spectrometry, as well as NMR analyses; we then identified adenosine as the active compound [4].

γ-Oryzanol was initially acknowledged as a single component when it was extracted from rice bran oil. Subsequently, 10 fractions were isolated using reverse-phase HPLC and their structures were determined using gas chromatography-mass spectrometry. Cycloartenyl ferulate, 24-methylenecycloartanyl ferulate and campesteryl ferulate were identified as the major components of γ-oryzanol [40–42].

Phenolic compounds were identified in the rice bran using sequential fractionation and subfractionation using Sephadex LH-20 chromatography with 40% acetone. The total phenolic content was highest in the subfraction portion and the major phenolic acid was identified as FA (178.3 µg/mg) using HPLC and liquid chromatography-electrospray ionization-tandem mass spectrometry analyses [43, 44]. The chemical structure of the active components of rice bran is illustrated in **Figure 1**.

Adenosine

Cycloartenyl ferulate

24-Methylenecycloartanyl ferulate

Campesteryl ferulate
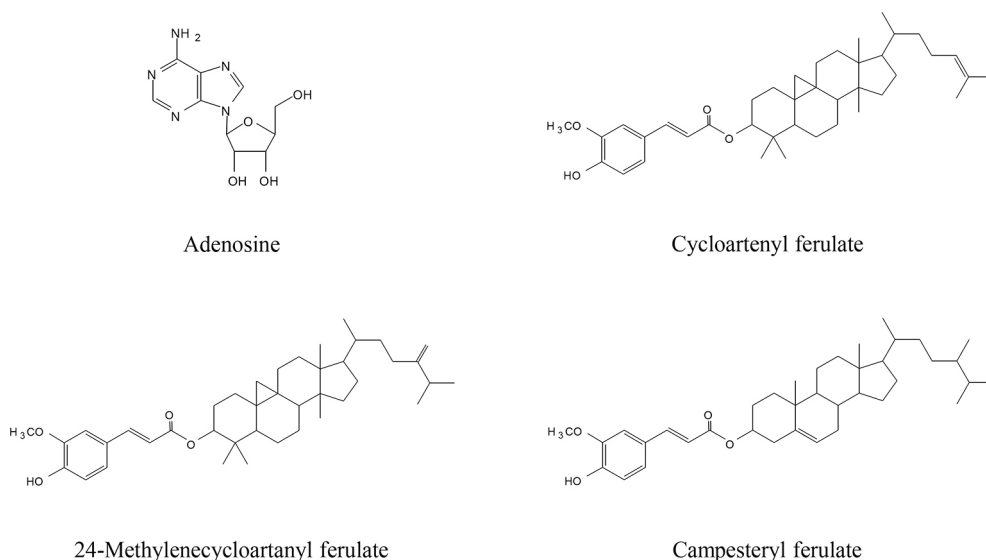
Figure 1. Chemical structure of bioactive components of rice bran.

5. Role of bioactive components

5.1. Hypertensive aspects

The following factors increase the risk of diet-related disorders such as obesity, cancer and cardiovascular disease (CVD): consumption of fewer plant-based foods, changing dietary

patterns, increased consumption of Westernized food and socioeconomic conditions. High BP, one manifestation of CVD, continues to be a major cause of morbidity and death and one public health strategy is dietary management of high BP. Studies have shown that a 5-mm Hg decrease in BP is related to a 16% decrease in CVD [45]. The risk factors for CVD are higher plasma cholesterol levels, lower high-density lipoprotein (HDL) levels and higher low-density lipoprotein (LDL) levels. Several bioactive compounds from rice bran that have been identified and used may reduce the risk of CVD. For instance, angiotensin-converting enzyme (ACE) inhibitors reduce BP via the renin-angiotensin system and FA has plasma ACE-inhibitory activity. In this regard, Ardiansyah et al. showed that food supplementation using FA reduces high BP by inhibiting plasma ACE activity [5]. Later, the novel compound adenosine, isolated from the DF fraction, was also found to have BP-lowering activity. Specifically, single-dose or long-term orally administered adenosine may reduce BP in the spontaneous hypertension of the SHRSP model [4]. Administered adenosine increases plasma nitric oxide levels, which in turn increase vasodilation. Adenosine also causes potent vasodilation by activating adenosine receptors (A2) on vascular smooth muscle; moreover, it stimulates K+ATP channels, resulting in the hyperpolarization of smooth muscle [4].

The risk of CVD is elevated in conditions of oxidative stress. Urinary 8-hydroxydeoxyguanosine (8-OHdG) serves as a sensitive biomarker of oxidative stress resulting in genetic damage. FA significantly reduces urinary 8-OHdG levels; thus, it can reduce CVD risk factors [4, 5].

Diets containing cholesterol-lowering phytochemicals and antioxidants can prevent the progression of atherosclerotic lesions. Experiments have demonstrated that γ-oryzanol possesses potent anti-atherogenic and antioxidant activity. Furthermore, in a rat model of two-kidney, one-clip renovascular hypertension, Boonla et al. described the vasorelaxant and antihypertensive effects of peptides derived from rice bran protein hydrolysates [46]. **Table 1** describes the anti-hypertensive roles of various bioactive components of rice bran.

5.2. Metabolic disorder aspects

Metabolic disorders consist of metabolism-related diseases, including hyperglycemia, hypercholesterolemia, hypertriglyceridemia and insulin resistance; they accompany type 2 diabetes mellitus, obesity and CVD. Rice bran and its various active components, prevents or ameliorates metabolic disorders. Specifically, a rice bran enzymatic extract-supplemented diet can prevent the adipose and macrophage changes associated with diet-induced obesity in mice [54]. In addition, the antihyperlipidemic effects (lower cholesterol and triglyceride levels) of α-tocopherol have been investigated in F344 rats fed a Western diet [55]. Pigmented rice, which contains anthocyanins and proanthocyanidins concentrated in the bran layer, stimulates glucose uptake by 3T3-L1 adipocytes—a key function in glucose homeostasis. Specifically, basal glucose uptake is increased two to three fold, while mRNA levels of both GLUT1 and GLUT4 are upregulated [56]. γ-Oryzanol and FA ester with phytosterols—both of which are abundant in rice bran—prevent high-fat and high-fructose diet (HFFD)-induced metabolic syndrome [57]. In addition, only γ-oryzanol treatment is more effective than FA in significantly decreasing the liver index and hepatic triglyceride content. Decreased serum C-reactive protein and IL-6 levels and increased serum adiponectin concentration confirmed that FA and γ-

oryzanol can be used as dietary supplements to alleviate the deleterious effects of HFFD [57]. Adenosine, in particular, effectively mitigates metabolic syndrome in SHRSP [50]. Specifically, single-dose and long-term oral administration of adenosine improves hyperlipidemia and hyperinsulinemia; it also regulates body weight gain and food intake. Studies have shown that enhanced plasma adiponectin levels alleviate hyperinsulinemia and that dietary adenosine can elevate plasma adiponectin and increase insulin sensitivity. Adenosine administration for 3 weeks downregulates mRNA levels of glucose-6-phosphatase, a gene encoding the rate-controlling enzyme of hepatic gluconeogenesis. Adenosine also plays an important role in regulating hepatic mRNA expression of genes involved in β-oxidation, fatty acid synthesis and AMP-activated protein kinase [4, 50]. In conclusion, various active components of rice bran ameliorate metabolic-related diseases.

Rice bran component	Species	Dose	Effect	Ref
Adenosine	Rat	10 mg/L drinking water	↓ Blood pressure Blood ↓ TC, LDL-C, TG, FFA, glucose, insulin, leptin, ↑ HDL-C, adiponectin Liver ↓ TC, TG	[4]
Ferulic acid	Rat	9.5 mg/kg BW	↓ Blood pressure Blood ↓ TC, TG, ACE activity	[5]
Peptides-derived from rice bran protein	Rat	50–100 mg/kg BW	↓ Blood pressure Blood ↓ ACE activity, ↑ NO Thoracic aorta ↑ eNOS, ↓ p47[phox] NADPH oxidase subunit	[46]
γ-Oryzanol	Rat	0.5–2% diet	Blood ↓ TC, LDL-C, HDL-C, VLDL-C Liver ↓ cholesterol esters, TG	[47]
γ-Oryzanol	Rat	10 mg/kg BW/day	Blood ↓ TC, PL, TG, FFA, free cholesterol	[48]
γ-Oryzanol	Rat	1% diet	Blood ↓ TC, LDL-C, VLDL-C, TG, PL, ↑ HDL-C	[49]
Adenosine 5′-monophosphate	Rat	87.5 mg/kg diet	↓ Blood pressure Blood ↓ TG, glucose, insulin, ↑ HDL-C, adiponectin Liver ↓ TC, TG	[50]
γ-Oryzanol	Human	300 mg/day	Blood ↓ TC, LDL-C, TG, lipid peroxides, ↑ HDL-C	[51]
Tocotrienol	Human	200 mg/day	Blood ↓ TC, LDL-C, Apo B, platelet aggregation	[52]
Rice bran oil	Human	50 g/day	Blood ↓ TC, LDL-C, TG	[53]

ACE, angiotensin-converting enzyme; ApoB, apolipoprotein B; BW, body weight; FFA, non-esterified fatty acid; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; PL, phospholipid; TC, total cholesterol; TG, triglycerides; VLDL-C, very low density lipoprotein cholesterol; eNOS, endothelial nitric oxide synthase.

Table 1. Summary of bioactive components and their prospective effects on blood pressure and metabolic parameters in different species.

5.3. Anti-cancer aspects

Dietary factors have a significant effect on the risk of cancer. Only 5–10% of all cancer is heredity; all other incidents are directly or indirectly correlated with lifestyle and dietary habits. If dietary supplements are used appropriately, they may reduce the incidence of cancers

in humans by as much as 30% [58, 59]. Phytic acid extracted from rice bran has anticancer activity against hepatocellular carcinoma (HepG2) cells, wherein apoptotic activity was evaluated by expression analysis of apoptosis-regulatory genes (i.e., p53, Bcl-2, Bax, Caspase-3 and -9) [60]. Similarly, δ-tocotrienol (δ-T3) is reportedly useful as an anticancer agent against human colorectal adenocarcinoma (DLD-1) cells under both normoxic and hypoxic conditions. *In vivo*, oral administration of rice bran tocotrienol (mainly γ-T3; 10 mg/mouse/day) significantly inhibited tumor growth in nude mice [61]. Tumor cells produce reactive oxygen species, which damage cellular integrity. Cycloartenyl ferulate, a major component of γ-oryzanol, successfully inhibits proliferation in the colorectal adenocarcinoma SW480 cell line because of its antioxidant activity [62].

5.4. General health-promoting aspects

Rice bran itself has health benefits, while rice bran oil and isolated active components have immune stimulatory effects. Rice bran that is rich in phytosterols, γ-oryzanol and compounds with antioxidant properties may modulate the immune system. In addition, rice bran has several generalized health-promoting characteristics. For example, rice bran supplementation enhances gut health by encouraging the growth and colonization of *Lactobacillus rhamnosus* and it provides effective protection against human rotavirus diarrhea in pigs by modulating gut permeability [63].

Long-term supplementation has a positive impact on survival, cognition and brain mitochondrial function, which may delay Alzheimer's disease [64]. Rice bran supplements can also be used as ergogenic supplements by body builders and athletes [65] and they may mitigate menopausal symptoms such as hot flashes, as well as bone loss in older women who suffer from osteoporosis [66]. Rice bran can be regarded as a source of plant-derived active compounds and as an alternative to expensive vitamin sources from animals. For instance, different colored rice bran has micronutrients, including a rich reserve of β-carotene, which can be converted to vitamin A [67]. **Table 2** describes the role of various bioactive components of rice bran for general health.

Rice bran component	Health aspects	Dose	Effect	Ref
Rice bran	HRV induced diarrhea prevention in gnotobiotic pigs	10%	↑ Intestinal IFN-γ and total IgA levels	[63]
γ-Oryzanol	Brain aging in NMRI mice	4 g/kg diet for 6 months	↑ Mitochondrial proteins	[64]
γ-Oryzanol	Human health growth	500 mg/day	↑ Muscular strength (bench press and squat) and vertical jump power	[65]
γ-Oryzanol	Postmenoposal osteoporosis in rats	0.3% crystalized oryzanol	↑ Estrogen, Bone mineral	[66]

HRV, human rota virus; IFN-γ, interferon gamma; IgA, immunoglobulin A.

Table 2. Summary of bioactive components and their prospective effect on generalized health aspects.

6. Conclusion

Previously, rice bran was only used in animal feed or discarded as waste. However, now it is treated as a potential source for the preparation of nutraceuticals. In this review, the therapeutic role of rice bran itself and of its bioactive and novel components has been described briefly from different clinical points of view. We noted that rice bran has various health benefits in terms of disease prevention and that it can be used to treat humans and experimental animals with no side effects. Owing to its significant nutritive and therapeutic value, rice bran may enhance well-being and health, as well as reduce the risk of disease, providing health benefits and improving quality of life. Thus, rice bran can be considered a super food and/or functional food. However, the true potential of functional bran could be developed using new biotechnological methods.

In conclusion, there is a strong demand for the enrichment of functional bran components in different diet-based approaches that mitigate lifestyle-related disorders. Entrepreneurs should be encouraged to consider rice bran as a major source of bioactive components for the developments of super foods.

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