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Rice Brans, Rice Bran Oils, and Rice Hulls: Composition, Food and Industrial Uses, and Bioactivities in Humans, Animals, and Cells

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ABSTRACT: Rice plants produce bioactive rice brans and hulls that have been reported to have numerous health-promoting effects in cells, animals, and humans. The main objective of this review is to consolidate and integrate the widely scattered information on the composition and the antioxidative, anti-inflammatory, and immunostimulating effects of rice brans from different rice cultivars, rice bran oils derived from rice brans, rice hulls, liquid rice hull smoke derived from rice hulls, and some of their bioactive compounds. As part of this effort, this paper also presents brief summaries on the preparation of health-promoting foods including bread, corn flakes, frankfurters, ice cream, noodles, pasta, tortillas, and zero-*trans*-fat shortening as well as industrial products such bioethanol and biodiesel fuels. Also covered are antibiotic, antiallergic, anticarcinogenic, antidiabetic, cardiovascular, allelochemical, and other beneficial effects and the mechanisms of the bioactivities. The results show that food-compatible and safe formulations with desirable nutritional and biological properties can be used to develop new multifunctional foods as well as bioethanol and biodiesel fuel. The overlapping aspects are expected to contribute to a better understanding of the potential impact of the described health-promoting potential of the rice-derived brans, oils, and hulls in food and medicine. Such an understanding will enhance nutrition and health and benefit the agricultural and industrial economies.

KEYWORDS: *rice brans, rice bran oils, rice hulls, liquid rice hull smoke, composition, food uses, functional food, industrial uses, allelochemical effects, antibiotic activities, immunostimulating effects, anti-inflammatory effects, antiallergic effects, hypoallergenic, anticarcinogenic effects, anticholesterol effects, antidiabetic properties, human studies, animal studies, cell studies, food safety, human health*

INTRODUCTION

Rice (*Oryza sativa* L.) is a major source of nourishment for the world's population, especially in Asia. World production of rice is estimated at around 680 million tons, equivalent to that of wheat.[1] Byproducts of rice processing are rice bran and the agricultural "waste" product, rice hulls, which protect rice seeds during growth, accounting for 20% of the rice crop.[2] Rice bran serves as a source of widely studied rice bran oil and numerous individual bioactive compounds, many of which have been shown to exhibit beneficial effects in cells, animals, and humans. This accounts for the extensive literature on the multifaceted aspects of rice bran, oils, and hulls as indicated by ~3600 citations in the Scopus database for rice bran that include numerous reviews. Because published reviews[3−6] are generally focused on particular aspects, there is a need for a comprehensive review that encompasses food and industrial uses and the relationship of composition to bioactivities. This overview therefore surveys and interprets our present knowledge of the chemistry and antioxidative, antiallergenic, anticarcinogenic, anticholesterol, antidiabetic, and antimicrobial activities of rice brans, rice bran oils, and rice hulls in cells, animals, and humans. Further research is suggested for some of these categories. The described findings are not only of fundamental interest that might help our understanding of the production and biological functions of rice-derived brans, oils, and hulls but also have practical implications for agriculture and industry that could lead to better foods and improved human health. Table 1 shows the categories of bioactive rice bran compounds, and Figure 1 illustrates the structures of selected bioactive compounds.

RICE BRANS

Rice bran, a part of the rice kernel that contains pericarp, aleurone, and subaleurone fractions, is a byproduct of rice milling. It is estimated that the world annual production of rice bran amounts to 76 million tons.[7] Rice brans, oils, and hulls contain a large number of bioactive compounds, with pigmented brans containing many more bioactive compounds than do white brans. Here, we will present brief overviews of selected recent studies on the distribution of these compounds among the rice-derived products.

Composition. Compared with other solvents, treatment of rice bran with 50% (v/v) acetone showed high extraction efficiency of the protein and total phenolic contents as well as the highest 1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity.[7] Related studies with 40% acetone[8] and with food-grade ethanol[9] reported similar results. Laokuldilok et al.[10] reported that brans contained the following bioactive compounds (μg/g): (a) in normal bran, anthocyanins, 0; phenolic acids, 2101; α-tocopherol, 71; γ-oryzanol, 3681; total, 5853; (b) the corresponding values in red bran were 188, 1526, 16, 1859, and 3589, respectively; and (c) the corresponding

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Table 1. Bioactive Compounds of Rice Brans

phenolic and cinnamic acids[10,12,199]	anthocyanins, flavonoids[8,12,13,15,129,130,200]	steroidal compounds[113,201,202]	polymeric carbohydrates[102,203−205]	proteins[24,25,31]
caffeic acid	anthocyanin monomers, dimers, and polymers	acylated steryl glucosides	arabinoxylan	various
coumaric acid	apigenin	cycloartenol ferulate	glucans	
catechins	cyanidin glucoside	campesterol ferulate	hemicellulose	
ferulic acid	cyanidin rutinoside	24-methylenecycloartenol ferulate		
gallic acid	epicatechins	γ-oryzanol		
hydroxybenzoic acid	eriodtyol	β-sitosterol ferulate		
methoxycinnamic acid	hermnetins	tocopherols		
sinapic acid	hesperetin	tocotrienol		
syringic acid	isorhamnetins			
vanillic acid	luteolin			
	peonidin glucoside			
	tricin			

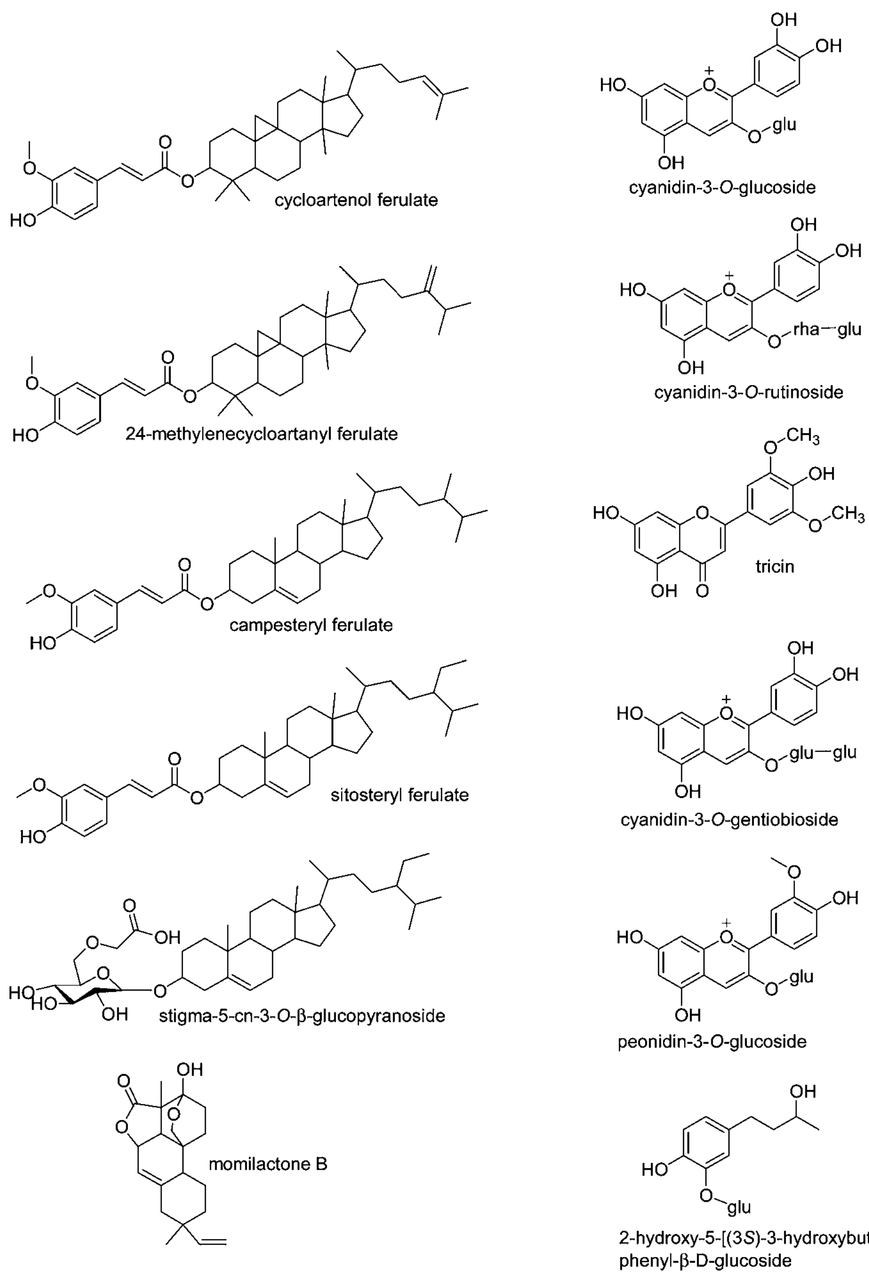

Figure 1. Structures of selected bioactive rice bran compounds.

values in black bran were 2562, 3289, 24, 4057, and 9932, respectively. Other black brans evaluated had lower values. The anthocyanin content were 179 μg/g cyanidin-3-glucoside and 9 μg/g peonidin glucoside for red bran, and the corresponding values for black bran were 2316.7 and 245.7 μg/g, respectively. This study also reported that most of the phenolic compounds were bound phenolic acids, with ferulic acid being the most abundant simple phenolic compound, and that black bran contained higher amounts of gallic, hydroxybenzoic, and protocatechuic acids than did red and normal brans. The authors conclude that the high antioxidant activity of black bran can be attributed to the high anthocyanin, phenolic acid, and γ-oryzanol contents. The more diverse γ-oryzanol composition of North American wild rice (*Zizania palustris*) (1352 μg/g) was about twice that of regular brown rice (688 μg/g).[11] Chen et al.[12] determined the phenolic and cinnamic acid, anthocyanin, proanthocyanidin, and polymeric anthocyanin contents of three brown, purple, and red rice brans isolated from different rice varieties using HPLC-PDA with the aid of 27 standards of known structure and matching unknown peaks to a spectral library of known compounds. A cancer cell inhibiting red bran fraction contained about 40 bioactive compounds.

Using HPLC with a photodiode array detector combined with an electrospray ionization tandem mass spectrometer, Sriseadka et al.[13] identified the following 11 flavonoids in Thai black rice varieties: quercetin-3-*O*-glucoside, quercetin-3-*O*-rutinoside, isorhamnetin, isorhamnetin-3-*O*-glucoside, isorhamnetin-3-*O*-acetylglucoside, isorhamnetin-7-*O*-rutinoside, taxifolin-7-*O*-glucoside, 5,3′,4′,5′-tetrahydroxyflavanone-7-*O*-glucoside, 5,6,3′,4′,5′-pentahydroxyflavone-7-*O*-glucoside, and myricetin-7-*O*-glucoside. It is not known, however, how many of these compounds would be retained in the bran from the evaluated whole rice varieties. Rice bran is also a palatable source of fiber for canine and feline nutrition.[14]

Antioxidative Activities in Relation to Composition. The antioxidative properties of individual and bran components are important for the beneficial properties described below. Here, we will briefly mention efforts to define quantitatively the antioxidative properties of brans in relation to composition. Zhang et al.[15] examined phenolic profiles and antioxidative activities of black rice bran from 12 commercial varieties of black rice. The free, bound, and total phenolic content of the black rice bran samples ranged (in mg gallic acid equiv/100 g DW) from 2086 to 7043; from 221.2 to 382.7, and from 2365 to 7367, respectively. The average values of free, bound, and total phenolic content of black rice bran were 8, 1.5, and 6 times greater than those of white bran, respectively. The free, bound, and total flavonoid contents of black rice brans ranged (in mg of catechin equiv/100 g DW) from 3462 to 12061, from 126.7 to 386.9, and from 3596 to 12448, respectively. These values were 7.4, 1.9, and 6.7 higher than those of white rice bran, respectively. The free, bound, and total anthocyanin contents of black rice brans (in mg of cyaidin-3-glucoside equiv/100 g DW) ranged from 1227 to 5096, from 4.89 to 8.23, and from 1231 to 5101, respectively. The content of cyanidin-3-glucoside, cyanidin-3-rutinoside, and peonidin-3-glucoside of black brans ranged (in mg/100 g DW) from 736.6 to 2557, from 22.70 to 96.62, and from 100.7 to 534.2, respectively. The free, bound, and total antioxidant activity (in μmol gallic acid equiv/g DW) ranged from 180 to 476.9, from 79.48 to 47.91, and from 537.5 to 1876, respectively. These values were more than 8, 1.5, and 6 times higher than those of white bran, respectively. The total antioxidant activity correlated to the content of total phenolics, flavonoids, anthocyanins, and the three glucosides mentioned above. Tricin isolated from rice bran was found to be a strong free radical scavenger.[16] Compared with a lipophilic tocols extract of black rice bran, a hydrophilic anthocyanin extract was more effective in inhibiting cholesterol than fatty acid oxidation.[17]

Related studies on antioxidative properties are described by Tabaraki and Natghi,[9] and Chiou et al.[7] for white rice brans; by Nam et al.,[18,19] Okai and Higashi-Okai,[20] Laokuldilok et al.,[10] Jun et al.,[8] Islam et al.,[3] and Chen et al.[12] for pigmented rice brans; and by Aguilar-Garcia et al.[21] for rice brans with different antioxidant capacity assays.

These results show that the phenolics are mainly present in the free form, that there are significant differences in both phytochemical content and antioxidant activity among the different black bran varieties, and that black brans differ significantly in composition and antioxidant effects from those of white rice brans. These aspects need to be taken into consideration in designing studies on food and medical uses of pigmented and white rice brans. It seems that black rice bran has the potential to be used as a functional ingredient and natural colorant for food and pharmaceutical uses.

Food Uses. Several studies attempted to evaluate rice brans as potential food ingredients designed to improve quality and nutrition. These include the following observations.

A rice bran protein formulation can provide nourishment to preschoolers.[22] The protein with a caloric value of 416 kcal/100 g and an in vitro digestibility of 80.9−84.45% had good acceptability during a short-term infant-feeding trial. Because the nutritional quality of plant proteins in animals and humans varies widely,[23] these findings suggest that inexpensive rice bran proteins could contribute to food security. Rice bran has been used in food as full-fat bran, defatted bran, bran oil, and protein concentrates.[24] Rice bran contains about 10−15% of high-quality proteins, reviewed in Fabian and Ju.[25] These authors note that, although rice bran proteins seem to be unavailable commercially, the unique hypoallergenic and anticancer properties make the bran proteins superior to cereal proteins. Supplementation of feed with rice bran seems to improve milk production and fatty acid composition of goat milk[26] and nutrition of tilapia fish.[27] Kong et al.[28] evaluated texture and antioxidative properties of wheat-based noodles with added levels (2, 6, 10, and 15%) of black rice bran. Compared with control noodles, the noodles had a lower cohesiveness and higher content of polyphenolics, flavonoids, and anthocyanins and higher antioxidative activity. The authors suggest that black rice bran can be an excellent ingredient to increase the nutritional value an antioxidative properties of noodles. Pasta supplemented with rice bran was highly acceptable with respect to quality for up to 4 months of storage.[29] Lima et al.[30] examined the effect of defatted and full-fat rice brans from long-, medium-, and short-grain rice on bread quality. Replacement of wheat flour with 10 and 20% bran affected bread volume, with the greatest increase observed with the medium-grain bran, presumably owing to lower fiber and higher starch contents among the three varieties. Texture profile analysis of breads showed no significant differences in cohesiveness and springiness and increased hardiness, chewiness, and gumminess. Overall, full-fat bran produced better textural bread properties than did defatted bran. Because rice bran is a rich source of dietary fiber and minerals, Sairam et al.[31] examined the effect of incorporation of three levels (5, 10, and 15%) of commercial defatted rice bran on bread quality.

Sensory evaluation showed that bread with 5 and 10% bran was found to be acceptable and that bread with 15% bran was acceptable with bread improvers. Dietary fiber content, antioxidative activity, and shelf life increase with increased bran levels. These results suggest rice bran can serve as a functional ingredient for high-fiber breads with improved antioxidant potential and storage stability.

The enzyme polyphenol oxidase (PPO) catalyzes the enzymatic browning of potatoes, as discussed in detail elsewhere.[32] The following were found to be optimum conditions for the inhibition of PPO and potato browning: extraction ratio of 1:3 (rice bran/water, w/v) at pH 6.5, for 30 min at 40 °C. Higher temperatures and times resulted in reduced PPO activity and phenolic content of the extract.[33]

Álvarez et al.[34] found that addition of 2.5% rice bran in a vegetable oil emulsion to frankfurters improved their textural consistency and reduced gelling capacity, suggesting interactions of the rice bran with the meat protein matrix and fat globules. The authors suggest rice bran and other plant-derived ingredients can modify frankfurter formulations for improved nutrition and textural quality. Related studies found that replacing 10% of fat content of frankfurters with a total fat content of 30% (control) with rice bran fiber and vegetable oils did not affect the sensory properties of the frankfurters.[35] Supplementation of corn flour with rice bran flour seems to improve the organoleptic properties of corn flakes and tortilla chips.[36]

Different parts of the rice plant can concentrate iodine from the soil.[37] Iodine is an essential animal and human element that is needed for the in vivo synthesis of the thyroid hormone thyroxine, which is an important factor in thyroid function. The mean concentration of iodine in the entire plant was 20 mg/kg DW; the highest concentration of iodine was in the root (53 mg/kg) and the lowest in polished rice (0.034 mg/kg). Rice bran contained 0.61 mg/kg and rice hull, 2 mg/kg. The authors suggest that knowledge of iodine content of plant food can also help estimate exposure to radioactive iodine from nuclear facilities.

Industrial Applications. Here, we will briefly examine the potential of rice brans to serve as scavengers of toxic compounds and as raw materials for the production of bioethanol and biodiesel fuels.

An investigation of the capacity of rice and wheat brans to remove the potentially toxic textile dyes Malachite Green and Methylene Blue from contaminated water found that the absorption of the dyes by the brans was a physical process that was influenced by pH and increased with contact time.[38,39] The use of rice bran to remove textile and other pollutants from the environment merits further study.

Watanabe et al.[40] achieved bioethanol production by rice washing drainage and rice bran derived from a rinse-free process of rice manufacture. The highest ethanol production (3.0−3.4%) was achieved by ultrasonic pretreatment and adding 30 mg/100 mL of protease M and 3 mg/100 mL lipase to the rice-derived products. The authors of the bioethanol publication suggest that the two rice formulations provide a source of carbohydrate for the bioethanol production. Srilatha et al.[41] developed a process for biodiesel synthesis from rice bran fatty acids. Under optimum conditions, about 92% of the fatty acids were transformed to the biodiesel formulation. The authors suggest that modified tungstophosphoric acids are efficient solid acid catalysts for the synthesis of biodiesel from rice brans with high fatty acid content. The process was optimized by El Boulifili et al.[42] Zhang et al.[43] described a one-step process for the production of biodiesel from rice bran oil, and Moqsud et al.[44] developed a microbial fuel cell (MFC) process for the generation of electricity from rice bran and other agricultural products.

The cited studies suggest that rice brans and bran-derived products have the potential to improve the quality and nutrition of food and serve as raw materials for the production of industrial products.

Antibiotic Activities. Rice bran extracts inhibited the growth of the following bacteria isolated from patients suffering diarrheal disease: *Vibrio cholerae*, *Vibrio vulnificus*, *Salmonella* spp., *Shigella* spp., *Escherichia coli*, and *Staphylococcus aureus*.[45] The extracts were most effective against *V. cholerae* strain O139 with a minimum inhibitory concentration (MIC) value of 0.976 mg/mL, suggesting that rice bran extracts might contribute to the treatment of diarrheal disease.

Modified arabinoxylan rice bran at 1 μg/mL enhanced the phagocytosis by neutrophils of *E. coli* pathogenic bacteria in vitro but did not affect the growth of 31 strains of bacteria in the absence of the phagocyte cells, suggesting that the rice bran product might be effective in the treatment of infections in elderly and immunocompromised patients.[46,47] Whether the bran formulations are also effective against antibiotic-resistant pathogens merits further study.

Because many viruses show an affinity for polysaccharides at the surface of target cells, Ghosh et al.[48] successfully evaluated the ability of sulfated glucans prepared from a commercial rice bran preparation to inhibit the entry of cytomegaloviruses into primary human fibroblasts, suggesting that the sulfated glucans might protect against viral infections. A related study found that an arabinoxylane from rice bran inhibited the growth of HIV viruses.[49]

Piglets on a diet containing rice bran expressing porcine lactoferrin as a feed additive grew more quickly and had higher levels of biomarkers associated with the immune system than those on the control diet, suggesting that the rice bran formulation can be used as a functional additive to improve antimicrobial properties and IgG levels of early weaned piglets.[50] Adding rice bran to the feed also had a beneficial effect on postpartum reproduction in cows.[51]

The presence of rice bran in a solid-state fermentation improved the production of several antibiotics including oxytetracyline,[52] cephalosporin C,[53] and bacteriocin.[54]

Antiallergic Activities. An allergic reaction takes place when the immune system reacts to the exposure of a variety of substances (peanut proteins, soy proteins, pollen, spores) called allergens. The allergens induce the release of histamine from basophilic mast cells, which are mediators of inflammatory responses. Histamine is largely responsible for the clinical symptoms of allergic reactions, including asthma and hay fever. Manifestations of antiallergenicity include the inhibition or suppression of antigen-induced release of proinflammatory cytokines that are involved in mediating the immune response at the genetic level. Cytokines include the tumor necrosis factor alpha (TNF-α), several interleukin (IL) proteins, and intracellular calcium ions. Bellik et al.[55] review molecular mechanisms that may govern the suppression of the activation of nuclear transcription of the pro-inflammatory nuclear factor-kappa B (NF-κB) by antiallergic and anti-inflammatory phytochemicals. The following are brief summaries in chronological order of studies on the antiallergic potential of rice brans.

Nam et al.[19] compared the potential of bran extracts from one nonpigmented and five pigmented rice cultivars to inhibit the release of histamine and β-hexosaminidase in in vitro allergic reactions mediated by stimulated basophilic leukemia and rat peritoneal mast cells, widely used in studies of antiallergic effects. Black rice bran from the LK1-3-6-12-1-1 cultivar was the most effective inhibitor in a panel of chemical, biochemical, and cell assays. This cultivar merits evaluation as part of a human diet to determine whether it can prevent or protect against allergic manifestations.

An examination of the effect of cycloartenyl ferulate from rice bran oil-derived γ-oryzanol on allergic reactions in the dorsal skin of rats found that cycloartenyl ferulate captured immunoglobulin E (IgE), prevented it from binding to the allergy-related signaling receptor FceR1, and attenuated mast cell degranulation.[56,57] The results show that the rice bran ingredient suppressed biomarkers associated with skin allergy by acting as an antiallergic agent in the passive cutaneous anaphylaxis (PCA) reaction.

The commercial product arabinoxylan rice bran (MGN-3-BioBran) previously shown to be a potent biological response modifier (BRM) that activates natural killer (NK) cells, T cells, and monocytes, also activates human monocyte dendritic cells in vitro, suggesting its possible use in a dendritic cell-based vaccine against infections and cancer.[46] Similar observations were made by Cholujova et al.,[58] who found that BioBran, an enzymatically modified arabinoxylan from rice bran, is a potent enhancer of dendritic cell maturation.

Related studies showed that (a) a series of feruoyl esters of triterpene alcohols isolated from a methanol extract of edible rice bran and related known compounds exhibited anti-inflammatory activity against 12-*O*-tetradecaolylphorbol-13-actate (TPA)-induced inflammation (1 μg per ear) in mice, with a 50% inhibitory dose (ID_{50}) that ranged from 0.1 to 0.8 mg per ear;[59] (b) acid esters of oligosaccharides formed by mild acid hydrolysis of arabinoxylans from rice bran suppressed in a dose-dependent manner inflammatory mediators;[60] (c) oral administration of hydrolyzed rice bran prevented the common cold syndrome in elderly individuals via its immunomodulatory action;[61] (d) cycloartenyl ferulate from rice bran oil significantly reduced lipopolysaccharide (LPS)-induced NO production and mRNA expression of NO synthase and cyclooxygenase-2 (COX-2) and up-regulated superoxide dismutase (SOD) activity, suggesting its value for the therapy of inflammatory diseases and as an antitumor promoter;[62] (e) a stabilized rice bran extract inhibited the pro-inflammatory enzymes COX-1, COX-2, and 5-lipoxygenase (5-LOX);[63] (f) prebiotics from rice bran ameliorated inflammation in murine colitis by regulating immune cell differentiation and also significantly suppressed the growth of *Clostridium* and increased short-chain fatty acid content in colitis;[64] and (g) cycloartenyl *trans*-ferulate, a component of the bran byproduct of sake-brewing rice, inhibited mammalian DNA polymerase and suppressed inflammation in the mouse ear, suggesting its value as an anti-inflammatory agent.[65]

An investigation of the effect of oryzanol isolated from crude rice bran oil on cell-mediated and humoral immune responses in rats found that oryzanol (100 mg/kg) administered orally overcame side effects of immunosuppressive cyclophosphamide-induced myelosuppression, suggesting that this rice bran oil component could serve as an effective immunomodulatory candidate.[66] The authors suggest the need for further study to define the therapeutic effectiveness of oryzanol in the prevention of autoimmune diseases and adverse inflammatory conditions. A related study suggests that a glycoprotein fraction from rice bran shows potential as a functional therapeutic agent with immunostimulatory activity.[67]

Choi et al.[68] investigated the inhibitory effect of black rice bran (cv. LK-1-3-6-12-1-1) against a phorbol ester-induced skin edema and induced allergic contact dermatitis (ACD) in inflammatory mouse models. Intraperitoneal injection of the bran extract to TPA-treated mice significantly decreased TPA-induced inflammation (edema) and induced a marked decrease in the production of the following biomarkers associated with inflammation: TNF-α, interleukin 1β (IL-1β), interleukin 6β (IL-6β), and eicosanoid leukotriene B4 (LTB4). Feeding mice a standard diet with added 10% black rice bran also significantly suppressed DNF-induced allergic contact dermatitis on the skin of the mice. By contrast, nonpigmented brown rice bran failed to elicit similar beneficial effects.

Oral feeding of a standard diet supplemented with a water-soluble enzymatic rice bran extract restored endothelial function and vascular contractility in obese rats through the reduction of vascular inflammation and oxidative stress.[69] The authors suggest that the bran extract could be considered a candidate for functional food in the treatment of vascular complications associated with obesity.

Collectively, he cited studies suggest the potential of pigmented rice brans to be an antiallergic and anti-inflammatory food ingredient and possibly also a therapeutic agent for the prevention and treatment of diseases associated with inflammation.

Anticarcinogenic Effects. Cancer is a disease characterized by dysregulation of multiple genes resulting in a variety of adverse symptoms. Because dysregulation of inflammatory pathways that results in high levels of pro-inflammatory cytokines such as NF-κB and IL-6 are associated with various cancers, safe anti-inflammatory food ingredients that suppress the NF-κB activation and associated inflammatory pathways might alleviate cancer-related symptoms.[70] Here, we will briefly mention in chronological order selected studies designed to achieve this objective in humans, animals, and cancer cells by rice brans and bioactive compounds.[4]

A three-year study designed to evaluate the efficacy of MG-3 arabinoxylan rice bran in combination with interventional therapy (IT) to ameliorate hepatocellular carcinoma in 68 patients showed that the use of the combined treatment resulted in a lower (31.6%) recurrence of the disease than with the control (47.7%) and a higher survival in the second year of 35% compared with 6.7%, for the control.[71] The authors suggest that the combined treatment represents a new approach for the treatment of hepatocellular carcinoma and merits further study in clinical trials. Interestingly, it should also be mentioned that aflatoxin B_1 (AFB1) found in many foods is reported to be a major cause of hepatocellular carcinoma.[72,73] Will arabinoxylan protect against liver cancer caused by consumption of aflatoxin-containing food?

A randomized, placebo-controlled three-month study designed to determine the effect of MGN-3 arabinoxylan rice bran on the innate immunity of 48 multiple myeloma patients found that the MGN-3-treated individuals showed increases in natural killer (NK) cell activity and in dendritic cells (DC) in peripheral blood as well as an augmented increase in T-helper cells.[74] The authors suggest that the observed activation of innate immunity in multiple myeloma patients merits further clinical study. The rice bran polysaccharide also protected mice against adverse effects of radiation.[47]

Studies with mice revealed that various bran preparations mentioned in the titles of the cited papers inhibited breast tumors,[75] urinary bladder tumors,[76] Ehrlich carcinoma turmors,[77] colorectal carcinogenesis,[78] and head and neck carcinomas[79] and that the bran component tricin seems to be safe enough for clinical studies.[80] Related studies with rats showed that the rice brans and bioactive compounds inhibited liver,[81] oral,[82] gastric,[83] and colon[84,85] carcinogenesis.

Reported in vitro studies showed that rice brans inhibited the following cancer cell lines: endometrial,[86] leukemia,[87] breast,[88,89] breast, colon, and liver,[90] melanoma,[91] pancreatic,[92] ovarian,[93] and colorectal.[94]

We will now examine in more detail our studies on the inhibition of cancer lines and mouse tumors by pigmented brans designed to develop a better understanding of the mechanisms that govern the beneficial effects.

We investigated the effects of oral feeding of a mouse diet supplemented with 10% (w/w) pigmented black bran from the rice variety *O. sativa* cv. LK1-3-6-12-1-1 and 10% (w/w) nonpigmented brown bran from the commercial rice *O. sativa* as an internal control on the growth of transplanted tumors in mice.[68,95] Mice fed standard diets with added rice bran for 2 weeks were intracutaneously inoculated with CT-26 mouse colon cancer cells and fed the same diet for 2 additional weeks. Compared to the control diet, tumor mass was 35% lower in the black rice bran-fed group and 19% lower in the brown rice bran group. Tumor growth inhibition was associated with the following biomarkers: increases in cytolytic activity of splenic NK cells; partial restoration of nitric oxide (NO) production and phagocytosis in peritoneal macrophages; increases in released pro-inflammatory cytokines including TNF-α, IL-1β, and IL-6 from macrophages; increases in infiltration of leukocytes into the tumor; and a reduction in the number of blood vessels inside the tumor (anti-angiogenesis). Pro-angiogenic biomarkers including vascular endothelial growth factor (VEGF), COX-2, and 5-LOX were also significantly reduced in mRNA and protein expression by up to 23%. Reduced COX-2 and 5-LOX expression down-regulated VEGF and inhibited neo-angiogenesis inside the tumors.

Kim et al.[96] also investigated the effects of black rice bran and components on tumor growth in mice. Mice fed standard diets supplemented with rice bran, γ-oryzanol, Ricetrienol, ferulic acid, or phytic acid for 2 weeks were inoculated with CT-26 colon cancer cells and fed the same diet for 2 additional weeks. Tumor mass was significantly lower in the γ-oryzanol and less so in the phytic acid group. Tumor inhibition was associated with the same biomarkers mentioned above. ELISA of tumor cells confirmed reduced expression of COX-2 and 5-LOX up to 30%. Reduced COX-2 and 5-LOX expression down-regulated VEGF and inhibited neo-angiogenesis inside the tumors. The bioactivity of γ-oryzanol was similar to that of black rice bran. Overall, induction of NK activity, activation of macrophages, and inhibition of angiogenesis seem to contribute to the inhibitory mechanism of tumor regression by both black rice bran and γ-oryzanol, suggesting that this compound might be the major bioactive ingredient of black rice bran.

Because reactive oxygen species (ROS) are generated by some tumor promoters in the development of cancer and phenolic compounds can reduce ROS levels by trapping reactive free electrons, we explored the possibility that antioxidative compounds present in rice brans might be effective in blocking tumor promotion.[19] Using flow cytometry we evaluated antitumor-promoting activity of five 70% ethanol pigmented rice bran extracts by measuring the inhibition of Epstein−Barr virus early antigen activation (EBV-EA) induced by a tumor promoter. Compared to an extract from nonpigmented white cooking rice, the pigmented varieties strongly inhibited phorbol ester tumor promotion in marmoset lymphoblastoid B95-8 cells in vitro, suggesting that the inhibition of tumor promotion might contribute to the anticarcinogenic effects of pigmented brans.

These results show that induction of NK activity, activation of macrophages, increase in leukocyte infiltration, inhibition of angiogenesis, and inhibition of tumor promotion seem to contribute to the inhibitory mechanism of tumor regression by pigmented rice brans and that these brans might protect against cancer in humans.

The cited studies demonstrate the potential that rice bran and bioactive components have the potential to be used in the prevention and treatment of cancers. Whether a fibronectin-binding protein isolated from rice bran that showed cell adhesion properties to lung carcinoma cells[97] might prevent carcinogenesis merits further study.

Anticholesterol Effects. Hyperlipidemia or dyslipidemia is characterized by an elevation of plasma cholesterol and/or triglycerides or a low high-density lipoprotein (HDL) level that contributes to the development of atherosclerosis (cardiovascular and cerebral diseases associated with hardening of the arteries). Here, we briefly examine reported studies on cholesterol-lowering effects of rice brans and some bioactive components in animals and humans. Related studies with rice bran oils are covered below.

On the basis of a study with 18 healthy normocholesterolemic men, Sanders et al.[98] reported that, although consumption of a rice bran diet for 3 weeks significantly reduced plasma triglyceride concentrations, it did not affect LDL and high-density lipoprotein (HDL) cholesterol and apoprotein concentrations, suggesting that the daily consumption of 30 g of rice ban does not contribute to a reduction in plasma concentrations in man.

A 6 week randomized study with moderately hypercholesterolemic adults (n = 14) consuming stabilized rice bran reduced cholesterol and improved the LDL/HDL cholesterol in 78% of the individuals, suggesting that full-fat rice bran should be included in the diet of individuals with hyperlipidemia.[99] Oat bran elicited similar beneficial effects.

The tocotrienol-rich fraction of rice bran at 100 mg/day significantly reduced total and LDL (bad) cholesterol, apolipoprotein B, and triglycerides in 18 hypercholesterolemic human subjects compared with baseline values, suggesting that the cited amount may be an optimal dose for controlling the risk of heart disease in hypercholesterolemic humans.[100,101]

A 14 week clinical trial with 24 hypercholesterolemic men showed that β-glucan-enriched foods are more effective in lowering LDL cholesterol levels compared with rice bran-enriched foods.[102] The human studies suggest that rice bran, bioactive fractions, and components seem to reduce plasma lipids in hypercholesterolemic individuals but apparently not in individuals with normal plasma lipid profiles.

Various rice bran formulations also were found to reduce cholesterol levels in chicks,[103] hamsters,[104−107] mice,[108,109] and swine.[110]

The following in vitro studies reinforce the anticholesterol effects observed in vivo. Hu and Yu[111] investigated the use of hemicelluloses from rice bran to scavenge cholesterol and bile acids in vitro. Binding was high with hemicellulose and poor with cellulose, insoluble dietary fiber, and lignin rice bran fractions. The authors suggest that hemicelluloses from defatted rice brans have potential in the development of functional foods. Will the hemicelluloses be effective in removing cholesterol from high-cholesterol foods such as eggs?

Compared to the total extract of black rice bran, the anthocyanin extract was more effective in inhibiting (stabilizing) the oxidation of cholesterol but less effective in inhibiting fatty acid oxidation, suggesting that low-cost black rice bran is a rich source of water- and lipid-soluble antioxidants that merits use as a functional ingredient in food.[17]

Miller et al.[112,113] found that cholesterol esterases catalyzed the in vitro hydrolysis of campesteryl ferulate and β-sitosteryl ferulate to campesterol and β-sitosterol, respectively, whereas two other ferulates resisted enzyme hydrolysis, suggesting that pancreatic cholesterol esterase might be involved in metabolizing some γ-oryzanol components in vivo.

The cited studies suggest the need for further studies designed to demonstrate the cardioprotective effects of rice bran-supplemented food in humans. Combinations of rice bran with the cardioprotective tomato compound lycopene also merit study.[114]

Antidiabetic Activities. Type 2 diabetes and obesity are human diseases of epidemic proportions caused by underproduction of insulin by the pancreas and impaired insulin resistance, leading to hyperglycemia that results in impaired entry of glucose into the cells, thus hindering glucose utilization.[115] Diets high in whole grains are reported to reduce by 20−30% the risk of developing type 2 diabetes, presumably because the fiber and phytochemicals of the whole grains can ameliorate oxidative stress and inflammation.[116] Here, we present brief overviews of human and animal studies in chronological order on the beneficial effects of rice bran, rice bran fractions, and components shown to be active against diabetes.

The consumption of stabilized rice bran fractions for 60 days by insulin-dependent diabetic subjects resulted in a reduction in glycosylated hemoglobin levels (a biomarker of diabetes) and in a significant reduction in hyperglycemia and decreased daily injection of insulin and hypoglycemic drugs in about 25% of the patients.[101]

A study with 28 volunteers with type 2 diabetes randomly divided into two groups, one receiving 20 g daily of stabilized rice bran and the other placebo for 12 weeks, showed that the first group had significantly lower serum glucose, glycated hemoglobin, and lipoprotein and increased adiponectin levels than the placebo group, suggesting that rice bran might represent a functional nutrient to ameliorate glycemic and lipid anomalies in type 2 diabetes.[117]

A randomized study with type 2 diabetic subjects showed that consumption of brown rice lees, a byproduct of the manufacture of a Korean rice drink, reduced the waist size circumference.[118]

Related studies with mice[119] and rats[120−122] reinforce the cited effects in humans. An in vitro study showed that fermented rice bran strongly up-regulated the expression of adiponectin and induced insulin resistance by neutralizing free radicals in adipocytes.[123,124] γ-Oryzanol stimulates secretion of insulin by the pancreas.[125,126] Siddiqui et al.[127] proposed a mechanism that governs diabetic nephropathy and its amelioration by a tocotrienol-rich fraction (TRF) extracted from rice bran.

These results and related studies with rice bran oils and rice hull liquid smoke described below strongly suggest that inclusion of these formulations into the diet might be useful in the treatment and prevention of diabetes.

Other Beneficial Properties. Purple rice extract and its components protected against angiogenesis[128] and stress-induced retinal damage in vitro and in vivo.[129,130] A stabilized rice bran extract protected guinea pigs against mitochondrial brain dysfunction, suggesting it potential as a functional food to prevent neurodegenerative diseases.[131] Arabinoxylan rice bran protected progenitor cells in the bone marrow of whole-body irradiated mice, suggesting its potential to overcome adverse effects of radiation therapy.[47] A polysaccharide isolated from the edible *Lentinus edodes* (shiitake) liquid mycelia mushroom culture supplemented with black rice bran protected mice against induced endotoxemia.[132] Finally, topical application of entrapped rice bran compounds γ-oryzanol and ferulic and phytic acids in niosomes protected the skin of volunteers against aging.[133−135]

The cited beneficial effects of rice bran suggest that it has the potential to serve as a multifunctional, health-promoting food ingredient.

RICE BRAN OILS

Crude rice bran oil is rich in unsaturated linoleic and oleic fatty acids and bioactive compounds such as γ-oryzanol, phytosterols, tocopherols, and tocotrienols (tocols). The following observations are designed to stimulate further use of rice bran oil and some of its bioactive components as ingredients in health-promoting functional food.

Composition and Food Uses. Here, we will briefly mention selected studies on the analysis and preparation of potentially new food ingredients and reported food uses of rice bran oils.

γ-Oryzanol, a major bioactive component of rice bran oil, consists of a group of compounds containing 4-hydroxy-3-methoxycinnamic acid (ferulate) esters of cycloartenol, 24-methylenecycloartanol, β-sitosterol, and campesterol (Figure 1). Crude rice bran oil contains ∼15 g/kg of γ-oryzanol.[136] An analysis by gas chromatography−tandem mass spectrometry (GC-MS/MS) showed that the major policosanols (PCs), fatty acid alcohols of general structure $[CH_3(CH_2)_nCH_2OH]$, in rice bran oil were triacontanol, octacosanol, hexacosanol, and tetracosanol, which comprised 87.3% of the total (172.2 mg/kg oil).[137] A related study[138] reports on the distribution of policosanols, fatty aldehydes, triterpene alcohols, and oryzanols in saponified and unsaponifiable fractions of rice bran oil. Byrdwell et al.[139] described a new method for the analysis of the contents of gelcaps that contained vitamin D in rice bran oil. Another study describes the preparation of liquisolid and semisolid formulations of rice bran oil for pharmaceutical uses.[140] Liu et al.[141] used counter-current chromatography to separate triterpene alcohol ferulates from rice bran.

Because rice bran oil also contains ∼38% oleic acid and ∼34% linoleic, both long-chain fatty acids that are absorbed less efficiently than medium-chain fatty acids such as capric acid by individuals with fat absorption abnormalities, Jennings et al.[142,143] modified the fatty acid content and characterized a structured lipid by lipase-catalyzed incorporation of capric acid into rice bran oil. The authors suggest that capric acid−rice bran oil structured lipid with fewer calories and less fat storage may help prevent disease. This hypothesis needs to be tested in an animal model.

Because of the need for vegetable oil-based shortening without hydrogenation to avoid the formation of undesirable *trans* fatty acids, Reshma et al.[144] successfully evaluated lipase-catalyzed interesterification of palm stearin and rice bran oil blends for the preparation of zero *trans* fat shortening with bioactive compounds. They found that it is commercially feasible to produce nutritionally improved shortening from palm stearin and rice bran oil. A related study achieved similar results with rice bran oil produced in India.[145] Microwave heating of rice bran oil does not seem to affect the stability of oryzanol,[146] but seems to favor the formation of methyl and ethyl esters for possible use as biodiesel fuel.[147]

Protection of transesterified rice bran oils with the green tea compound epigallocatechin gallate (EGCG) against oxidation was more effective than with a rosemary antioxidant, suggesting that the interesterified fat without *trans* fatty acids could be used as a spreadable margarine stock.[148,149] It would also be of interest to evaluate the antioxidative potential of less expensive high-EGCG teas[150,151] against oxidation of rice bran oil and oil products.

An investigation of the effect of replacing bakery shortening with refined rice bran oil in bread showed that rice bran oil had a higher content of linoleic acid (35%) compared with bakery shortening (5.1%).[152] There was a statistically significant variation in the texture of breads prepared by replacing the standard shortening with 50% rice bran oil. Organoleptic properties of breads with 50% rice bran oil also vary significantly from the control. Related studies on the use of rice brans show that the brans can be used in bread and cookies but not for the production of extruded snack food[10,153] and that a rice bran wax, Oleogel, can increase the unsaturated fat content of ice cream.[154]

Anticholesterol Effects. A number of studies evaluated the effects of diets containing rice bran oil on lipoprotein concentrations in animals and humans. Here, we briefly mention selected studies in chronological order.

A study by Reena and Lokesh[155] found that feeding rats rice bran oil containing unsaturated fatty acids blended with coconut oil for 60 days reduced the atherogenic potentials of saturated fatty acid present in coconut oil. Another study found that although 5% rice bran oil in the diet decreased serum lipoprotein in rats, animals receiving 20% rice bran oil showed increased HDL.[156] Related studies in rats and mice are described by Chopra and Sambaiah,[157] Chouet al.,[158] and Jung et al.[159] and in rats by Chandrashekar et al.[160]

Because hamsters fed diets with added ferulic acid and γ-oryzanol had significantly lower aortic cholesterol ester accumulation, the cholesterol-lowering effect of rice bran oil may not be entirely explained by its composition of unsaturated fatty acids.[105] Related studies in hamsters are described by Ausman et al.[161]

An investigation of the response of rice bran oil in nonhuman primates (*Macaca fascicularis* monkeys) showed that the content of rice bran oil in the diet was the predominant factor that induced lowering of total and LDL cholesterol.[105,162]

A study with 28 men and 32 women fed a diet for 3 weeks containing concentrates from rice bran oil found that 2.1 g plant sterols/day from rice bran oil lowered total cholesterol by 5% and LDL cholesterol by 9% in normolipemic humans.[163]

Feeding mildly hypercholesterolemic men aged 38 to 64 years diets containing low (0.05 g/day) or high (0.8 g/day) levels of γ-oryzanol for 4 weeks improved the lipoprotein pattern of the subjects to a similar extent, suggesting that increasing the γ-oryzanol content of the diet does not seem to further increase the beneficial effects.[164] The authors suggest that γ-oryzanol in rice bran oil may help prevent oxidative in vitro and in vivo damage and preserve vitamin E and tocotrienol levels before consumption and during heating and frying.

Feeding hypercholesterolemic women a diet containing rice bran and other oils, individually and as mixtures, for 10 weeks resulted in reduced levels of total and LDL cholesterol, suggesting that compared with other vegetable oils a 3:1 mixture of rice bran and palm oils might further reduce the risk of atherosclerosis.[165]

A 3 month study with patients (n = 73) with hyperlipidemia consuming a blend of 80% rice bran oil and 20% safflower oil found that 82% of the subjects had LDL levels <150 mg% compared with 57% in the control group, suggesting that the blend with rice bran oil exerted a beneficial effect on LDL cholesterol levels, shifting them to the low-risk category.[166]

A randomized study with 80 mildly hypercholesterolemic individuals showed that the consumption of a phytosterol-containing spread derived from rice bran oil for 12 weeks significantly reduced total and LDL cholesterol, confirming that the spread is effective in lowering serum cholesterol when consumed as part of a normal diet.[167]

Consumption by 50 hyperlipidemic individuals of a low-calorie diet (1400 kcal energy, 17% protein, 26% fat, and 57% carbohydrate) containing rice bran oil (30 g/day) for 4 weeks resulted in significant decreases in total and LDL cholesterol and the atherogenic ratio (total/HDL cholesterol), suggesting that the rice bran oil diet can improve risk factors for cardiovascular disease.[168]

Administration of 30 mg daily of the rice bran oil component octacosanol to 10 healthy women for 4 weeks did not affect cholesterol levels but resulted in decreased neutral sterol and bile acid concentration in the feces, suggesting the test substance seems to influence cholesterol metabolism.[169]

These results show that rice bran oils and components might help alleviate cardiovascular disease in humans.

Regulation of the Immune System. Because rice bran oil is rich in linoleic acid, a precursor of n-6 fatty acid derived eicosanoids, as well as in γ-oryzanol, a compound of the unsaponifiable fraction with antioxidant properties, Sierra et al.[170] investigated the effect of the oil- and/or γ-oryzanol-enriched diets on the immune response of mice. The results show that the oil modulates the immune system by enhancing B-lymphocyte proliferation, suggesting that it might have antiallergenic properties and that although γ-oryzanol may also modulate the immune system, it is not responsible for the immunostimulation effect observed with rice bran oil.

Antidiabetic Activities. Feeding 35 patients with type 2 diabetes 250 mL of soybean oil-modified milk (18 g of soybean oil) for 5 weeks induced increased insulin resistance and serum LDL cholesterol levels significantly.[171] By contrast, consumption of 250 mL of rice bran oil-modified milk (18 g of rice bran oil) daily resulted in significant decreases in total and LDL cholesterol but not in the index of insulin resistance, suggesting that rice bran oil can improve the abnormal lipid profile in patients with type 2 diabetes.

Related studies with diabetic rats showed that diets containing the rice bran oil ingredients γ-oryzanol and γ-tocotrienol improved lipid abnormalities, reduced the athero-

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genic index, suppressed the hyperinsulinemic response, and increased fecal neutral sterol and bile acid secretion[158] and that long-term supplementation of high pigmented rice bran oil ameliorated diabetes-associated organ injuries of rats.[120] In addition to rice bran oil, numerous other food oils can be used to prevent or treat diabetes mellitus complications.[172]

The cited studies indicate that the health-promoting effects of rice bran oils complement those described for rice brans. It would be interest to compare the relative beneficial effects of the oils to those reported for brans.

■ RICE HULLS

Rice hulls consist mainly of lignin, hemicellulose, cellulose, and hydrated silica.[173] In developing nations, the hull is sometimes used as a biofuel, incinerated in boilers to produce electricity. Here, we will briefly describe the composition, industrial uses, and allelochemical and other bioactive aspects of rice hull formulations and the recently developed rice hull liquid smoke.

Composition. Analysis of the hulls showed that they contain (in %) crude protein, 2.33; crude fat, 0.29; crude fiber, 40.84; ash, 18.71; moisture, 6.18; cellulose, 35.62; hemicellulose, 11.96; lignin, 15.39; acid detergent fiber, 67.74; and neutral detergent fiber, 79.70.[174−176] These results show that the hulls are a complex lignocellulosic material with high lignin and mineral contents.

Industrial Uses. Fermentation of a rice hull hydrolysate by recombinant *E. coli* strain FBR 5 produced 0.43 g of ethanol per gram of available sugars, suggesting that the hulls have the potential to serve as a low-cost feedstock for the production of ethanol.[177] Rice hulls are a potentially low-cost adsorbent for the removal of potentially toxic heavy metals and dyes.[178]

An acid hydrolysate of rice hull waste was used as a raw material to scale up ethanol production.[179,180] The solution and precipitation of lignocellulosic components of rice hulls in ionic media reduce the silicon content of the product.[181] Far-infrared radiation released bound phenolic compounds in rice hulls and enhanced the antioxidant activities of the treated hulls.[182] A rice hull hydrolysate was used for the production of microbial lipids as a potential feedstock for biodiesel production.[183] A process for the production of lignocellulolytic cellulases and xylanase enzymes from *Aspergillus heteromorphus* is based on solid-state fermentation of microwave-alkali pretreatment of rice hulls and straw.[184] Rice hulls were used to remove radioactive cesium from aqueous solutions.[185]

Allelochemical Effects. Allelochemicals are compounds that protect plants against phytopathogens. Soil amended with tricin-rich rice hull reduced the risk of developing rice seedling rot disease caused by soilborne pathogenic fungi, suggesting that tricin and the tricin isomer aurone are lead compounds for the discovery of new fungicides.[186] One of four new compounds (1-phenyl-2-hydroxy-3,7-dimethyl-11-aldehydic-tetradecane-2-β-D-glucopyranoside) isolated from rice hulls strongly inhibited the growth of duckweed (*Lemna paucicostata* Hegelm 381).[187] In a related study, Chung et al.[188] isolated additional compounds from a methanolic extract of rice hulls, one of which (cholest-11-en-3β,6β,7α,22β-tetraol-24-en-3β-palmitoleate) was effective in controlling the growth of algae and weeds that are harmful to water-logged rice. A study by Souza et al.[189] showed that rice hulls added to soil containing organic pollutants accelerated the bioremediation process. Naggia et al.[190] isolated and characterized seven secondary metabolites from the fungus *Aspergillus flavipes* MM2 that grows on rice hulls and that were found to possess antimicrobial properties. In addition to the anticarcinogenic properties mentioned above, momilactones A and B from rice hulls may also serve as potential natural herbicides for weed control in paddy fields, thus reducing our dependence on synthetic herbicides.[191] Activated carbon produced from rice hulls can be used to adsorb NO_x emission for future deep-space missions.[192]

Inhibition of Cytotoxicity. A methanol extract of rice hulls was cytotoxic against human cancer cells in vitro (IC_{50} = 0.5 μg/mL). Feeding rats a diet fortified with the extract (50 mg/kg body wt) for 40 weeks reduced induced clonic neoplasms.[193] These authors also isolated and characterized the compound momilactone B, which also exhibited strong antitumor activity. Later studies confirmed the anticancer effect of momilactone B against human lymphoma and breast cancer cells,[194,195] suggesting that the rice hull extract and momilactone B might be candidates for therapy of human colon and other cancers. Methanolic extracts of far-infrared irradiated rice hells were found to possess significant scavenging activity of free electrons in ROS, metal-chelating activity, and a protective effect against oxidative DNA damage in human lymphocytes.[196] Acid and alkali degradation products from rice hull lignins exhibited antioxidant activity in a DPPH radical scavenging assay.[173] Incorporation of rice hulls reduced the pathogenic bacteria count of poultry litter substrates.[197]

These results show that rice hulls can serve as a source for the production of value-added industrial products and as a source of bioactive compounds for human health.

■ RICE HULL LIQUID SMOKE

There has been considerable interest in the use of silica, the main residue from the widely used pyrolysis of rice hulls, in building materials as strengtheners and as environmental and industrial adsorbents.[2] Another byproduct of the combustion of rice hulls is the smoke that is generated. There is interest in utilizing this smoke as a new source of liquid smoke flavorings, the wood-derived versions of which are now widely used in foods. Liquid smoke has gained widespread acceptance in the food industry, replacing traditional smoking practices for use as flavors and preservatives. Liquid smoke preparations are easier to apply and provide more consistent results than traditional smoking. In the United States, liquid smoke has been granted generally recognized as safe (GRAS) status as a natural flavoring.[198]

To help stimulate interest in the potential food and health-promoting uses of liquid smoke prepared from the pyrolysis of rice hulls, we investigated the composition of antioxidative, antiallergic, and anti-inflammatory effects of the extract in chemical and cell assays and in a mouse model and determined in vivo molecular biomarkers associated with the observed beneficial effects. The new liquid rice hull smoke extract with a smoky aroma and sugar-like odor prepared by pyrolysis of rice hulls followed by liquefaction of the resulting smoke contained 161 compounds characterized by GC-MS.[174] Below, we describe in some detail reported studies on the bioactivities of the liquid rice hull smoke.

Anti-inflammatory and Antiallergic Effects. Antioxidative, antiallergic, and anti-inflammatory activities of a new liquid rice hull (husk) smoke extract prepared by pyrolysis of rice hulls followed by liquefaction of the resulting smoke were assessed in vitro and in vivo.[174] At pH 5, the liquid smoke extract inhibited DPPH free radicals and suppressed NO and β-hexosaminidase releases from lipopolysaccharide (LPS)-

induced RAW264.7 mouse macrophage leukemia cells and ionophore A23187-stimulated RBL-2H3 rat basophilic cells, respectively. In addition, TPA was applied to the ears of CD-1 mice to induce inflammation (edema), which was accompanied with increases in a series of biomarkers. Topical application of 1% of the liquid rice hull extract significantly reduced the expression of the following biomarkers associated with the TPA-induced inflammation: TNF-α, IL-1β, IL-6, leukotriene B_4 (LTB_4), prostaglandin E_2 (PGE_2), and myeloperoxidase (MPO). These in vitro and in vivo findings demonstrate the potential value of rice hull smoke extract to serve as a potentially new anti-inflammatory rice hull-derived biomaterial for the treatment and prevention of inflammation-associated disorders. Overall, these results demonstrated that the extract from rice hull smoke had high inhibitory activities in all of the chemical/cellular/molecular in vitro and in vivo tests designed to define antioxidative, antiallergic, and anti-inflammatory activities.

Antibacterial Effects. The liquid hull smoke was also tested for bactericidal activity against the foodborne pathogen *Salmonella* Typhimurium.[175] The minimum inhibitory concentration (MIC) value was 0.822% (v/v). The in vivo antibacterial activity (1.0%, v/v) was also examined in a *Salmonella*-infected Balb/c mouse model. Mice infected with a sublethal dose of the pathogens were administered intraperitoneally a 1.0% solution of the hull extract at four 12 h intervals during the 48 h experimental period. The results showed that smoke extract inhibited bacterial growth by 59.4, 51.4, 39.6, and 28.3% compared to 78.7, 64.6, 59.2, and 43.2% inhibition with the medicinal antibiotic vancomycin (20 mg/mL). Consecutive administrations at 12 h intervals elicited the most effective antibacterial effect of 75.0% and 85.5% growth reduction of the bacteria by the liquid smoke and vancomycin, respectively. The combination of rice hull smoke extract and vancomycin acted synergistically against the pathogen.

The inclusion of the liquid smoke (1.0% v/w) as part of a standard mouse diet fed for 2 weeks decreased mortality of 10 mice infected with lethal doses of the *Salmonella* and protected the liver tissues against *Salmonella*-induced pathological necrosis lesions. These beneficial results suggest that hull liquid smoke can complement wood-derived smoke as antimicrobial and flavor formulations for application to human foods and animal feeds.

Antidiabetic Effects. Two studies described the protective effect of a liquid rice hull smoke against type 2 diabetes induced by a high-fat diet administered to mice.[115,176] Dietary administration of 0.5 or 1% of the liquid smoke for 7 weeks resulted in significantly reduced blood glucose and triglyceride and cholesterol concentrations, higher serum insulin levels, and improved glucose tolerance compared with the control group of mice fed high a high-fat diet. Oral liquid smoke intake increased HDL (good) cholesterol levels and decreased LDL (bad) cholesterol levels. The hypoglycemic effect was accompanied by changes in enzyme activities and cognate gene expression. Among the glucose metabolism regulating genes evaluated, hepatic glucokinase (GCK), the glucose transporters GLUT2 and GLUT4, and peroxisome proliferator activated receptor-γ (PPAR-γ) were up-regulated, whereas glucose-6-phosphatase (G6 Pase) and phosphoenolpyruvate carboxykinase (PEPCK) were down-regulated in the liver of the mice. These changes resulted in restoring glucose-regulating molecule activities to normal control levels.

Histopathology showed that a high-fat diet intake also induced liver necrosis and damage of the Langerhans islet in the pancreas, whereas the dietary administration of the liquid smoke restored necrotic damage to normal levels and restored the reduced insulin-producing β-cell population of the pancreas associated with a high-fat diet intake to nondiabetic normal control levels.

The protective effect against type 2 diabetes in mice can be attributed to the blockage of oxidative stress-induced damage of the β-cells of the pancreas and improved metabolism of glucose in the liver. The results suggest that functional food supplemented with rice hull liquid smoke might protect food against microbial contamination and has the potential to protect against infectious disease, allergies, and cancer and in the management of diabetes. These aspects merit further study.

In summary, the results of the cited studies show that various rice bran formulations, especially pigmented brans, rice bran oils, and rice hull liquid smoke and some of their bioactive components, might contribute to the prevention and therapy of several chronic human diseases, including allergy, cancer, diabetes, infections, and cardiovascular disease. Because pigmented, especially black, brans have a more diverse content and higher amounts of bioactive compounds than brans derived from white and brown rice cultivars, the emphasis of future studies should be to define their chemopreventive and other beneficial effects in humans. In addition, possible synergism of combinations of rice brans and other bioactive food compounds and extracts that have been shown to exhibit beneficial in vivo effects also merit study. Such dietary combinations in which the individual components might exert their effect by different mechanisms might act as multifunctional foods and might make it possible to use lower amounts of each component.

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Notes

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■ ABBREVIATIONS USED

ACD, allergic contact dermatitis; BRM, biological response modifier; COX-2, cyclooxygenase-2; DC, dendritic cells; DNF, dinitrofluorobenzene; DPPH, 1-diphenyl-2-picrylhydrazyl radical; DW, dry weight; EBV-EA, Epstein−Barr virus early antigen activation; ELISA, enzyme-linked immunosorbent assay; G6 Pase, glucose-6-phosphatase; GCK, hepatic glucokinase; GC, gas chromatography; GLUT2 and 4, glucose transporters 2 and 4; GRAS, generally recognized as safe; HDL, high-density lipoprotein; HPLC-PDA, high-performance liquid chromatography with photodiode array detection; IC_{50}, ID_{50}, inhibitory concentration or dose that kills 50% of the cells; IgE, immunoglobulin E; IL-1β, interleukin 1β; IL-6β, interleukin 6β; IT, interventional therapy; LDL, low-density lipoprotein; 5-LOX, 5-lipoxygenase; LPS, lipopolysaccharide;

LTB4, eicosanoid leukotriene B4; MFC, microbial fuel cell; MIC, minimum inhibitory concentration; MPO, myeloperoxidase; MS, mass spectrometry; MTT, tetrazolium cell viability assay; NF-κB, nuclear factor κB; NK, natural killer cells; ORAC, oxygen value absorbance antioxidant capacity; PC, policosanols; PCA, passive cutaneous anaphylaxis; PEPCK, phosphoenolpyruvate carboxykinase; PGE2, prostaglandin E2; PPO, polyphenol oxidase; PPAR-γ, peroxisome proliferator activated receptor-γ; ROS, reactive oxygen species; SOD, superoxide dismutase; TNF-α, tumor necrosis fact α; TPA, 12-*O*-tetradecaolylphorbol-13-acetate; TRF, tocotrienol-rich fraction; VEGF, vascular endothelial growth factor

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