

Review

*Corresponding author

Shaw Watanabe, MD, PhD

President

Life Science Promoting Association

25-3-1004, Daikyo-cho, Shinjuku-ku

Tokyo 160-0015, Japan

E-mail: watashaw@lifescience.or.jp

Volume 2 : Issue 2

Article Ref. #: 1000AFTNSOJ2129

Article History

Received: July 14th, 2016

Accepted: July 20th, 2016

Published: July 22nd, 2016

Citation

Watanabe S, Hirakawa A, Nishijima C, et al. Food as medicine: The new concept of "medical rice". *Adv Food Technol Nutr Sci Open J*. 2016; 2(2): 38-50. doi: [10.17140/AFTNSOJ-2-129](https://doi.org/10.17140/AFTNSOJ-2-129)

Copyright

©2016 Watanabe S. This is an open access article distributed under the Creative Commons Attribution 4.0 International License (CC BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Food as Medicine: The New Concept of "Medical Rice"

Shaw Watanabe, MD, PhD^{1*}; Azusa Hirakawa, BS¹; Chiharu Nishijima, BS²; Ken'ichi Ohtsubo, PhD³; Kozo Nakamura, PhD⁴; Shigeru Beppu, PhD⁵; Patcharee Tungtrakul, PhD⁶; Sun Jian Quin, MD⁷; E-Siong Tee, MD⁸; Takuo Tsuno, PhD⁹; Hajime Ohigashi, PhD¹⁰

¹Lifescience Promoting Association, Tokyo, Japan

²Kagawa Nutrition University, Sakado, Japan

³Niigata University, Niigata, Japan

⁴Department of Agriculture, Shinshu University, Matsumoto, Japan

⁵Forica Foods Co. Ltd., Niigata, Japan

⁶Institute of Food Research and Product Development, Kasetsart University, Bangkok, Thailand

⁷Clinical Nutrition Center, Huadong Hospital, Fudan University, Shanghai, China

⁸Nutrition Society of Malaysia, Petaling Jaya, Malaysia

⁹Tsuno Rice Fine Chemical Co., Ltd., Wakayama, Japan

¹⁰Kyoto University and Human Health Foundation, Kyoto, Japan

ABSTRACT

In many countries, rice contributes to health by supplying dietary energy, proteins and fat. Many different species of rice have been developed in Japan and other rice producing countries. Some varieties are expected to prevent various diseases, or to be used for dietary therapy. The health effects of brown rice are empirically well known, and accumulating evidence about the physiological and pharmacological activity of rice bran strongly supports the use of brown rice in the dietary therapy. These could be categorized in the new concept, "medical rice". For example: medical rice for diabetes (glycemic index<55), medical rice for chronic kidney disease (CKD) (protein<1/20), medical rice for mental health (high gamma-aminobutylic acid or γ -aminobutylic acid (GABA), gamma oryzanol (γ -oryzanol) and/or ferulic acid), and medical rice for cancer prevention (high antioxidant capacity). Organic cultivation is necessary to avoid toxic substances from fertilizers and insecticides. In response to the enormous increase of medical costs in many countries, encouragement of healthy longevity by changes of dietary habits is mandatory. Functional food labeling has started in 2015 in Japan, so the proper food labeling of medical rice could help people who want to control and/or improve their health status.

KEYWORDS: Brown rice; Rice bran; Rice ingredients; Glycemic index; Low protein rice; Gamma-aminobutylic acid or γ -aminobutylic acid (GABA); γ -oryzanol; Ferulic acid; Phytate.

ABBREVIATIONS: CKD: Chronic Kidney Disease; GABA: Gamma-aminobutylic acid or γ -aminobutylic acid; γ -oryzanol: Gamma Oryzanol; LDL: Low-density lipoprotein; HbA1c: Glycated hemoglobin; BMI: Body Mass Index; DRI: Dietary Reference Intake; MHLW: Ministry of Health, Labour and Welfare; EPA: Eicosapentaenoic acid; DHA: Docosahexaenoic acid; FTLD: Frontotemporal lobar degeneration; RCT: Randomized Clinical Trials; HDL: High-density lipoproteins; HPLC-UV: High-performance liquid chromatography-ultraviolet; TD2: Type-2 diabetes; BRAVO: Branch Retinal Vein Occlusion; MDRD: Modification of Diet in Renal Disease; WHO: World Health Organization; IGF-1: Insulin Like Growth Factor 1; POMS: Profile of Mood States; TMD: Total Mood Disorders.

INTRODUCTION

Rice is the main staple food for approximately 70 percent of the world's population, principally living in ten areas of the Asia-Pacific region.¹ In many countries, rice contributes to health

by supplying dietary energy, proteins and fat. It accounts for more than 50% of the diet in Bangladesh, Myanmar, Lao PDR, VietNam and Indonesia.² In this regards, the nutritional aspects of rice should be re-evaluated, especially the integrated composition of functional ingredients.

BROWN RICE AND HEALTH

Until the late 19th century, Japanese traditional meals were composed of unpolished brown rice and barley as staple food, *miso* (fermented soy) soup and side dishes cooked with vegetables, soybean products, and various varieties of roots.³ In the Meiji era (1868-1905), polished rice became popular, and beri-beri increased to epidemic proportions until vitamin B1 was found in rice bran. After the World War II, polished rice, meat, eggs, and dairy products became the major food items composing main and side dishes. Consequently, new dietary habits largely account for the high prevalence of the metabolic syndrome and other lifestyle related chronic diseases.⁴

On the other hand, there is a traditional way of eating in Japan. Macrobiotic is one of the school of dietary therapy founded by Sagen Ishizaka, Kenzo Futaki, and Yukikazu Sakurazawa (George Ohsawa).³ Whole grains and whole foods have been emphasized as central to macrobiotic diet.⁵⁻⁷ Locally-produced and organically grown, and minimally processed foods are also recommended. Macrobiotic meals are practically plant-based: seasonal vegetables, beans, and sea vegetables with brown rice as staple food.⁸ Recently a variety of rice species have been harvested, and they are expected to contain various ingredients, in addition to the ordinary nutrients.^{8,9}

NUTRITIONAL ASPECTS OF BROWN RICE

According to our research, macrobiotic practitioners consume more magnesium, iron, vitamin E, vitamins B and dietary fibers,

although their energy intake is less than that for average Japanese. Their body mass index (BMI), blood pressure and low-density lipoprotein (LDL) cholesterol levels are often found to be low, while glycated hemoglobin (HbA1c) remained within normal levels. Even when analyzed in comparison with other vegetarian dietary data, daily nutritional values were higher in those who ate rice more frequently than noodles, and even higher in brown rice than white rice.¹⁰ The macrobiotic dietary habit of eating brown rice seemed to contribute to their healthy state. The consumption of small fish, in the shape of whole food, for macrobiotic practitioners supplemented vitamin B12, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

Using sample meals, we investigated whether or not macrobiotic meals (we say *genmai-shoku*) could fulfill nutritional requirement.¹¹ In the radar charts displayed in Figure 1, central circle (in blue) represent the dose of Dietary Reference Intake (DRI) 2010 recommended by the Ministry of Health, Labour and Welfare, (MHLW) Japan. The outer green lines represent the relative intake doses from *genmai-shoku* (Figure 1). Sample meals of *genmai-shoku* provided enough energy, fat and protein, and several times more minerals and vitamins than required.

In addition to the functional effects of ingredients in brown rice, the frequency of mastication influences the brain function. In Japan, fast foods with soft texture have recently become popular for younger generation. The mastication frequency has been decreasing in proportion. The brown rice increases the chewing number of times than a meat or fish dishes.¹² National Health and Nutrition Survey, Labour and Welfare (2010) showed it was only 800 times per American meal compared to the 30,000 times by *genmai* meal. Longer eating time acts to prevent fast eating, which would be lead to obesity, and relaxes stress.

So, brown rice could be called the “medical rice for

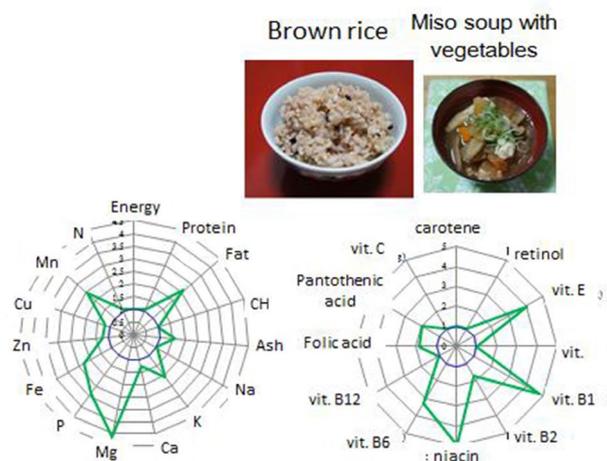


Figure 1: *Kenji-shoku*: Japanese traditional meal with brown rice and miso soup. The macrobiotic meals (*genmai-shoku* in Japanese) could fulfill the nutritional requirement by making the sample meal. Center blue circle is a recommended dose of DRI 2010 by the Ministry of Health, Labour and Welfare (MHLW). Outer green line is a relative intake dose by *genmai-shoku*. The meal fulfills the energy and protein, and several times more minerals and vitamins than required.

health". The effects of eating brown rice have been gaining attention for preventing and treating not only beri-beri and constipation, but also other chronic diseases. Organic rice can remove arsenic and other toxic chemicals ingested from fertilizers and/or insecticides.⁸

FUNCTIONAL INGREDIENTS IN RICE BRAN

Compared with white rice, whole brown rice, is rich in vitamins, minerals, dietary fibers and various functional chemicals (Tables 1A, 1B and 1C).^{9,13} About 8.52 million metric tons of brown rice are produced every year in Japan. Rice bran makes about 10% of unprocessed rice by weight, and contains 18-22% oil, of which up to 5% of unsaponifiable dark oil (Figure 2). Rice bran can be used in a variety of applications such as food, animal feed and fertilizer, but most of the rice bran is discarded at present.

Recently, much attention has been paid to rice bran, because of various pharmacological properties of its ingredients,

like anti-oxidation. A current study further clarified the properties of many functional ingredients in rice bran.^{13,15} A current study has further clarified the properties of many functional ingredients in rice bran¹⁵ It is separated to gum, wax, dark oil and scum by different boiling temperature for further extraction of a number of chemicals (Figure 2). The biological activities of each factor have been clarified by many *in vivo* and *in vitro* experiments. Human data by randomized clinical trials (RCT) are also accumulating.¹⁶

(1) Lipophilic Ingredients

The nutritional benefits of rice bran oil are well known.¹⁵⁻¹⁷ γ -oryzanol and tocotrienol are considered to be the active ingredients in the oil.¹⁸ The pharmacological effects are: a decrease in total and LDL cholesterol, an increase in high-density lipoproteins (HDL) cholesterol, a decrease in triacylglycerol and ApoB, and the inhibition of platelet aggregation. γ -oryzanol is contained in the non-saponifiable fraction of rice bran. γ -oryzanol is

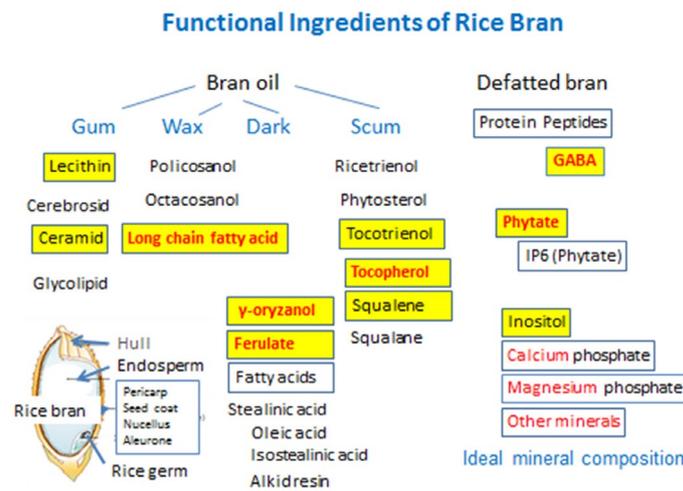


Figure 2: Ingredients in rice bran. Brown rice is produced in amounts of about 8.52 million metric tons (MT) a year in Japan. This means that 0.8 million MT of rice bran are produced annually, because rice bran makes 8 to 10% of the brown rice. Rice bran is used in a variety of applications such as food, animal feed and fertilizer, but most of the rice bran is discarded at present. Recently much attention has been paid to rice bran, because it has been reported that the ingredients of rice bran show various interesting properties, such as anti-oxidation and lowering of serum lipid levels.

Constituent	Rice part		
	Whole	Polished	Bran
Energy content (J)	1520-1610	1460-1560	1670-1990
Energy content (kcal)	363-385	349-373	399-476
Crude protein (g)	7.1-8.3	6.3-7.1	11.3-14.9
Crude fat (g)	1.6-2.8	0.3	15.0-19.7
Available carbohydrate (g)	73-87	77-89	34-62
Total dietary fiber (g)	2.9-4.0	0.9-2.3	17-29
Water-insoluble fiber (g)	2.0	0.5	15-27
Sugar (g)	1.4	0.2-0.5	0.8-5.5
Phytic acid (g)	0.4-0.9	0.1-0.2	3.0-7.4
Phenolic (g catechin)	0.01-0.02	0.01-0.02	0.01-0.02

Table 1A: Nutrient composition of brown rice, milled rice and rice bran at 14% moisture content.¹⁴

Minor components	Crude rice bran oil (%)	Refined rice bran oil (%)
Free fatty acids	6-10	0.04-0.08
Phytosterol	2.9	1.8
gamma-oryzanol	1.6-1.8	0.2-0.8
Total tocopherol	0.078	0.062
tocopherols	0.021 (27.3% of tocols)	0.020 (32.4% of tocols)
tocotrienols	0.057 (72.6% of tocols)	0.042 (67.6% of tocols)
Rice bran wax	2-3	0

Table 1B: Typical minor components found in Thai rice bran oil. Thai Edible Oil Co. Ltd's Lab, 2010-2011.

	Major nutrients	Cooked rice			
		Whole brown rice	Brown rice	Polished rice	Pre-germinated rice
Major nutrients	Water (g)	14-15	60-64	61-64	60-62
	Energy (kcal)	353-357	150-204	145-154	156-160
	Protein (g)	5.7-6.8	2.8-3.7	1.8-2.4	2.4-2.6
	Fat (g)	3.2-3.3	1.2-1.7	0.2-0.3	0.8-1.0
	FFA (g)	2.26-2.81	0.72-1.21	0.23-0.29	0.5-0.57
	SFA (g)	0.58-0.71	0.2-0.3	0.09-0.11	0.16-0.17
	UFA (g)	1.68-2.1	0.52-0.9	0.14-0.2	0.35-0.4
	Carbohydrate (g)	74-76	32-35	34-35	34-35
	maltose (g)	0.3	0.05	0.05	0.05
	glucose (g)	0.2-0.3	0.05	0.05	0.05
	Dietary fiber (g)	2.2-3.1	2.1-2.5	0.3-0.6	1
Ash (g)	Ash (g)	1.1-1.3	0.5-0.7	0.1-0.2	0.3
Minerals	Ca mg	8-9	1.2-1.7	3-4	4-5
	P mg	290-300	120-150	22-24	63-69
	Fe mg	0.9-1	0.5-0.6	0.1	0.2-0.3
	K mg	220-250	100-140	16-20	53-63
	Mg mg	110-120	51-68	2-3	20-23
	Zn mg	1.9-2.2	0.8-1.3	0.6-0.7	0.8-0.9
	Cu mg	0.12-0.27	0.1-0.16	0.04-0.08	0.11-0.14
	Mn mg	2.0-2.5	1.0-1.5	0.17-0.25	0.8-0.9
Vitamins	Se mg	2.5	2.5	2.5	2.5
	vitamin B1 mg	0.32-0.46	0.11-0.22	0	0.11-0.12
	vitamin B2 mg	0.02-0.03	0.005-0.01	0.005	0.005
	vitamin B6 mg	0.36-0.41	0.17-0.32	0.007-0.008	0.054-0.094
	niacin mg	5.3-5.9	2.1-3.4	0.008-0.1	0.4-0.8
	αtocopherol mg	1.3-1.5	0.6-0.8	0	0.5-0.7
	βtocopherol mg	0.1	0	0	0
	γtocopherol mg	0.1-0.2	0	0	0
protein amino acids	θtocopherol mg	0	0	0	0
	Protein (g)	5.7-6.8	2.8-3.7	1.8-2.4	2.4-2.6
	Arg mg	445-534	201-285	149-194	185-208
	Lys	228-253	100-137	65-77	85-93
	His	139-164	92-137	41-53	53-59
	Phe	269-329	130-175	95-124	111-125
	Tyr	164-196	87-111	67-86	78-88
	Ala	325-383	144-213	105-136	134-146
	Gly	274-316	121-176	86-111	111-121
	Pro	233-284	107-158	80-105	99-116
	Glu	922-1130	413-603	321-423	400-443
	Ser	297-354	137-198	104-135	129-141
	Thr	220-240	100-148	171-219	85-93
	Asp	518-611	236-335	171-219	213-233
Tryp	53-75	19-38	17-20	22-23	
GABA Phytic acid	Cys	141-177	54-85	50-55	58-63
	GABA	3-7	4-6	<0.5	3-5
	Phytic acid	1.18-1.21	1.3-2.0	0.8-1.3	0.4-0.5

Table 1C: Various nutrients and ingredients in rice per 100 g.

bound to ferulic acid, and thus belongs to the family of ferulated sterols. γ -oryzanol exists in 4 chemical forms with similar functional activities: two are triterpene alcohol esters and the other two are sterol esters (Figure 3).^{19,20} The solubility of γ -oryzanol is only 0.06% in water, and 0.2% in 20% ethanol. The absorption of γ -oryzanol may not be optimal after oral intake of brown rice. The proportion of γ -oryzanol is 0.1% in rice bran, but it is possible to take 300 mg of γ -oryzanol by oral intake of brown rice.

Phenolic compounds are major antioxidant and radical scavenging ingredients in rice. Nakamura et al^{19,20} developed a method for the simultaneous determination of phenolic compounds in rice by high-performance liquid chromatography-ultraviolet (HPLC-UV). Eleven kinds of phenolic compounds were identified in rice: ferulic acid, caffeic acid, sinapinic acid, *p*-coumaric acid, vanillic acid, protocatechuic acid, syringic acid, hydroxybenzoic acid, chlorogenic acid, 6'-*O*-feruloylsucrose and 6'-*O*-sinapoylsucrose (Table 2). In unpolished rice,

the three most abundant ones are: 6'-*O*-feruloylsucrose, 6'-*O*-sinapoylsucrose, and ferulic acid.²⁰ With their representative concentrations of 1.09, 0.42 and 0.33 mg/100 g rice flour, they represent 84.0% by weight of the total amount of soluble phenolic compounds (2.19 mg/100 g brown rice flour). Polished rice contains only 0.28 mg of phenolic compounds/100 g rice flour.

Tocotrienol and tocopherol are lipid-soluble antioxidants, which prevent cardiovascular diseases and cancer.²¹ Squalene, an isoprenoid compound structurally similar to beta-carotene, is an intermediate metabolite in the synthesis of cholesterol. In humans, about 60 percent of dietary squalene is absorbed.

(2) Water-Soluble Ingredients

Inositol and phytic acid are water-soluble ingredients like GABA.²²⁻²⁸ Magnesium, calcium and other trace elements are

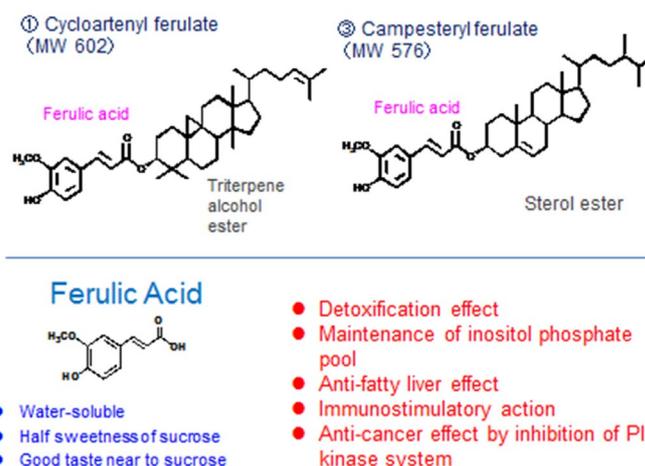


Figure 3: Gamma-oryzanol in unsaponifiable fraction of rice bran: γ -Oryzanol: Anti-stress effects, palliation of menopausal disorders and dysautonomia.

Gamma-Oryzanol being bound to a molecule known as *Ferulic Acid*; so it is essentially a term used to refer to a collection of ferulated sterols. Major γ -oryzanol has 4 types; two are triterpene alcohol ester and the other two are sterol esters. The functional activity is not different.

	Unpolished	Polished
ferulic acid	0.33	0.07
caffeic acid	0.02	0.025
sinapinic acid	0.02	0.005
<i>p</i> -coumaric acid	0.098	0.02
vanillic acid	0.072	0.032
protocatechuic acid	0.037	0.013
syringic acid	0.03	0.01
hydroxybenzoic acid	0.04	0.021
chlorogenic acid	0.033	0.028
6'- <i>O</i> -feruloylsucrose	1.089	0.026
6'- <i>O</i> -sinapoylsucrose	0.417	0.032
Total	2.186	0.282

Table 2: Contents of soluble phenolic compounds in rice (mg/100 g).

also included in this fraction.

In 2008, Maeba et al²⁶ reported an interesting clinical observation about the preventive effect of inositol on metabolic syndrome. Seventeen subjects with metabolic syndrome were given inositol *per os* for 2 weeks (5 g a day for one week and 10 g a day thereafter). The authors observed a significant decrease in total cholesterol, LDL cholesterol, small dense LDL cholesterol and apolipoprotein B (a marker of post-prandial hyperlipidemia). Waist circumference, high-sensitivity CRP and fasting blood glucose level also improved. Interestingly, a significant decrease in blood glucose level was only observed among subjects with metabolic syndrome. This may reflect higher concentrations of serum plasminogen, which is a protective factor against oxidative stress. The finding suggests that plasminogen is a key factor mediating the beneficial effect of inositol on the metabolic syndrome.

Myoinositol is a ring-shaped polyalcohol (Figure 4). It has half the sweetness of sucrose. It is an element of the vitamin B complex, although it is not a real vitamin. It is present in human colostrum, and considered to be essential for babies' growth. It is also effective for the prevention of metabolic syndrome. It has shown anti-fatty liver effect, anti-diabetic effect, improvement of metabolic syndrome, effectiveness against panic disorders and obsessive-compulsive disorders, and inhibitory effect on lung cancer in animal experiment.²⁷ The intake of large amounts of inositol (more than 10 g a day) could improve the panic syndrome.²⁸

Phytic acid is a phosphatized inositol, and has a strong chelating effect, pH adjustment effect, and antioxidant action. It is used for the prevention of discoloration and as a deodorant. *In vivo*, it is expected to have various effects, for example: detoxification, anti-fatty liver effect, immuno-stimulatory action, and anti-cancer effect by inhibition of the phosphoinositide (PI) 3-kinase system.

CONCEPT OF MEDICAL RICE

Many different kinds of rice have been developed in Japan and other rice producing countries.^{9,29} Some varieties are expected to prevent various diseases, or to be used for dietary therapy.³⁰ For example, 'super-hard' high-amylose rice could be used for diabetic patients,³¹ low-protein or low-gluten rice for patients with renal failure,^{32,33} GABA-rich large germ rice is expected to improve mental health,³⁴ and rice with high antioxidant properties would be effective for the prevention of cancer and other diseases.^{35,36} Human data are accumulating, so we believe it is time to introduce the concept of medical rice for disease prevention and treatment (Table 3).

(1) Medical Rice for Diabetes

In 2012, a meta-analysis reported an association between white rice intake and increased risk of type-2 diabetes (T2D), suggesting the need to replace white rice by brown rice in the Japanese diet.³⁷ The effects of brown rice on visceral obesity and endothelial function were shown in the Okinawa branch retinal

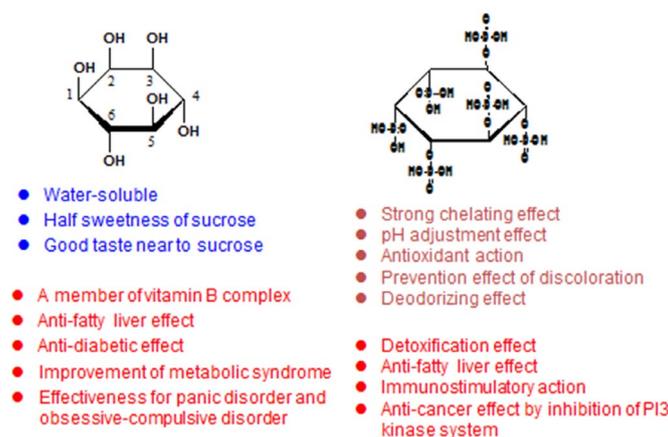


Figure 4: Inositol and phytic acid. Inositol and phytic acid are water soluble ingredients like GABA, for mental health. Magnesium, calcium and other trace elements are also present in the same fraction. Inositol is a member of vitamin B complex, although it is not a real vitamin. It is rich in human colostrum, and considered to be essential for baby's growth. It has anti-fatty liver effect, anti-diabetic effect, improvement of metabolic syndrome, effectiveness for panic disorder and obsessive-compulsive disorder. Intake of large amount of inositol, more than 10 g a day, could improve the panic syndrome.

Medical rice for health	Organic brown rice containing nutrients and functional ingredients
Medical rice for diabetes	Superhard rice or rice powder with low GI, mostly less than 50
Medical rice for kidney disease	Low protein rice containing less than 1/25 protein
Medical rice for mental health	High GABA, and/or γ-oryzanol/ferulic acids
Medical rice for cancer prevention	Brown rice with high antioxidant activity with functional ingredients

Table 3: Candidates of medical rice.

vein occlusion (BRAVO) study.³⁸ Participants were between 30 and 60-years-old males with metabolic syndrome. Brown rice reduced their post-prandial blood glucose level and insulin level. A decrease in body weight and an improvement of various biochemical abnormalities were also observed. The benefit of brown rice and brown rice with legumes for glycemic and insulinemic control were also shown by Mulan et al.³⁰

Recently, Ohtsubo et al.³⁹⁻⁴¹ succeeded in harvesting special super-hard rice, which contained a high concentration of resistant starch, due to long amylopectin chains. It showed good effect on postprandial glucose level and insulin secretion (Figure 5). However, the taste is different from ordinary *Japonica* rice. So, they next developed super-hard-rice powder after boiling. Now, the powder of super-hard rice is available for a number of new food items. For example, medical "Tomato Bread" is made of super-hard rice powder, containing resistant starch, GABA rich pre-germinated brown rice, tomato as a source of lycopene, and gelatinized rice flour for durable palatability. The size and taste is comparable to wheat bread. Tasty rice noodle is also made from this powder.^{31,40}

(2) Medical Rice for Chronic Kidney Diseases (CKD) and Renal Dysfunction.

One of the benefits of a low-protein diet is the preservation of the kidney function.⁴² Distinct mechanisms could be identified: (1)

improvement of hyperphosphatemia and hyperkalemia, (2) decrease in urinary protein, (3) improvement of subjective symptoms, (4) prevention of complication, (5) good control even after indication of hemodialysis for better survival.⁴³

The protein in rice is stored in two different types of compartment.⁴⁴ The major proteins are prolamin and glutelin. Prolamin is the alcohol soluble protein fraction remaining after salt extraction of globulin. Glutelin is the dilute-acid or dilute-alkaline soluble protein fraction after prolamin extraction. Most of the prolamin was present at the periphery in whole rice grains, implying that prolamin is removed by enzymatic digestion on polished white rice.³³

Low-protein rice is available in Japan in five different packages, depending on their different amount of protein. The rice content varies between 150 g and 180 g to reach a total content of 160 kcal (2 E-unit).⁴⁵ The lowest protein concentration is 0.1 g/pack, which is 1/25 of normal rice (Figures 6A and 6B). The palatability period is usually 7 months, but some packages have an extended storage period of 3.5 years for disaster situations.

Ideura⁴⁶ confirmed the effects of a low-protein diet on patients with chronic kidney diseases. At the threshold of renal failure of 6 mg serum creatinine/dl, low protein diet had started. With a content of 0.4-0.5 g/kg body weight, the median survival

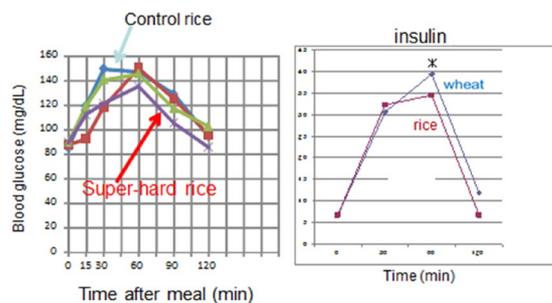


Figure 5: Postprandial blood glucose and insulin level. Super hard rice showed suppression of postprandial glucose level and insulin secretion. Super hard rice or purple rice, and new technology, such as co-extrusion with red onion germination, make it possible to fortify bio-active rice bread.

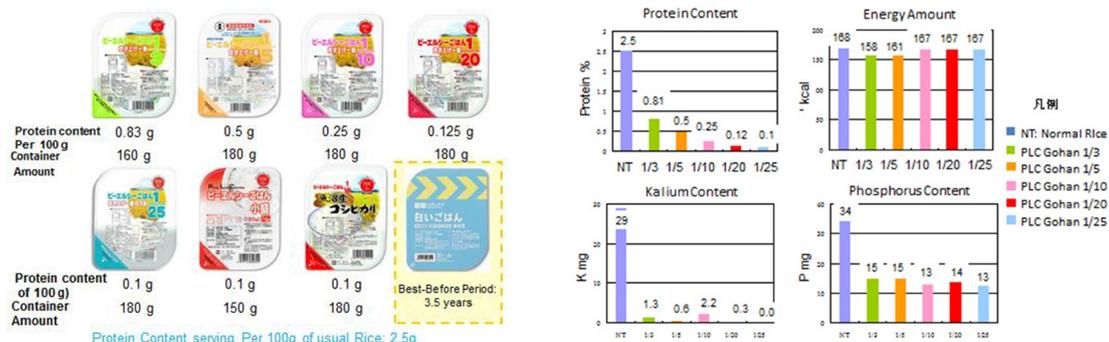


Figure 6: (a) Aseptic Package of low protein rice and (b) nutritional components of low protein rice.

A: Low protein rice.

Low protein rice is available in packed state in Japan. There are five different amount of protein rice. The rice content is 150 g to 180 g to fulfill 160 kcal (2 serving unit of Diabetic Society). Lowest protein concentration is 0.1 g, which is 1/25 of normal rice. Palatability period is usually 7 months, but some has 3.5 year best-before period as storage pack for a disaster.

B: Low protein rice.

Nutritional aspect of low protein rice is characteristic. Energy source is preserved and protein concentration is well controlled. Low potassium and phosphate concentration are additional benefits for CKD patients. If the patients continue to eat meat, the control of K and P is very difficult.

was 4 years.

With a content of 0.6 and 0.7 g/kg, no beneficial effect was observed compared with a control group (>0.8 g/kg body weight). The optimal low-protein content was 0.3 g/kg body weight. Low potassium and phosphate concentrations are additional benefits for CKD patients.

Sun et al⁴⁷ performed a preliminary study in Huadong Hospital (Shanghai, China), examining the effect of 12-weeks of low-protein rice as dietary therapy (0.6 g/kg body weight) for CKD patients. Cooked rice was provided 3 packs/day containing 1.35 g proteins and 900 kcal energy.³³ The meal plan was checked by trained research dietitians, and dietary intake and compliance were monitored through diet diaries.

Compared with baseline levels, the total dietary energy increased from 1606 kcal/d (27.9 kcal/kg bwt) to 1748 kcal (30.8 kcal/kg bwt). Dietary daily vitamin B1 intake increased from 0.34 mg to 0.78 mg, and vitamin B2 intake from 0.42 mg to 1.08 mg. Serum albumin slightly increased from 44 g/L to 46 g/L. The total serum protein concentration increased from 74 g/L to 77 g/L. Meanwhile, changes in body weight, BMI, and hemoglobin were not significant. After 12 weeks, urinary protein levels decreased from 0.4 g/d to 0.1 g/d. Urine albumin decreased from 130.8 mg/24 h to 60.8 mg/day. Twenty-four urinary protein, albumin excretion, and urinary albumin/creatinine ratio decreased by 63.7%, 55.0% and 52.0%, respectively.

Low-protein rice was well accepted by Chinese CKD patients. It is an important tool for CKD dietary therapy as it increases energy and micronutrients intake and improves the nutritional status. A long-term and large sample size RCT study is planned in Thailand to confirm the protective effects of low-protein rice on CKD progression.

The average Japanese citizen consumes 60 g protein a day, and half comes from rice. By using low-protein rice, we can reduce the protein intake by half. The amount of fish or chicken on side dishes does not need to be strictly restricted. However, if the main dish contains a large portion of beef like in the American diet, meat is the source of both protein and energy. In the well-designed multicenter Modification of Diet in Renal Disease (MDRD) study,⁴⁸ the benefit of a very low protein diet could not be shown. We analyzed their data and found the reason why MDRD study was failed.⁴⁹ The energy intake was less than 70% of the protocol, probably due to the cut of meat from main dish. So, energy deficiency could plausibly have worsened the disease.⁴⁹

Medical rice for CKD should contain enough energy source and low protein, as well as low potassium and phosphate.

(3) Medical Rice for Mental Health

As the society is aging, the number of people with impaired cognitive function becomes serious problem in the world. In Japan

the number of people with dementia is estimated to be 2 million, and World Health Organization (WHO) estimates that 47.5 million people have dementia, with 7.7 million new cases every year worldwide.⁵⁰

Large-germ brown rice and pre-germinated brown rice contain functional ingredients to prevent dementia, such as GABA, γ -oryzanol, in addition to nutritional elements such as vitamins, minerals, and dietary fibers.^{51,52} GABA and γ -oryzanol are involved in the metabolism of hypothalamic catecholamines.

γ -Oryzanol is known to have anti-stress effects, to palliate menopausal disorders and dysautonomia. Other effects have recently been reported, for example: improvement of hypertension, curative effect of Alzheimer's disease, amelioration in muscular fatigue.^{53,54} Antioxidant effect, radical eliminating action, ultraviolet absorptive action, anti-inflammatory effect, antidiabetic effect, anti-allergic effect, increase of insulin like growth factor 1 (IGF-1) and antibacterial action are also reported, but the main hope is an improvement of cognitive function.⁵²

GABA is also a candidate for mental health. Large-germ rice and pre-germinated brown rice (GBR) contain a high amount of GABA.⁵⁴ Pre-germinated brown rice was developed for easy cooking, keeping the many nutritional and functional ingredients, such as dietary fiber, vitamins and minerals, GABA, γ -oryzanol, acyl-sterol glycoside, etc. GBR contained not only GABA, but also ferulic acid.

The effect of ferulic acid mixed with *Angelica archangelica* extract on cognitive functions and behavioral and psychological symptoms of dementia have been examined by Kimura et al⁵² (Figure 7) and many symptoms were shown to improve (Table 4).

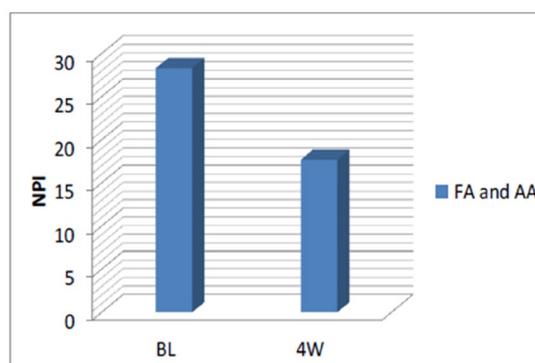


Figure 7: Mental health: Control of behavioral and psychological symptoms of dementia (BPSD). Treatment with ferulic acid extract led to reduced NPI scores in 19 (95.0%) out of 20 patients and to significantly decreased NPI scores overall ($p < 0.001$).⁵⁵

Pregnant women often become unstable in mood. In an intervention study, 41 pregnant women were randomized to take germinated rice or white rice for 14 days.⁵⁴ A psychological test profile of mood states (POMS) was done before and after the study, and salivary amylase was measured as a stress marker. POMS test measures 6 dimensions of mood, and depression,

	Baseline	Follow-up	p value*
NPI total score	28.3±9.6	17.7±9.7	<0.001
Delusions	2.2±2.7	1.3±2.1	<0.05
Hallucinations	2.8±3.4	1.1±2.1	<0.02
Agitation/aggression	4.6±3.2	2.5±1.9	<0.001
Depression/dysphoria	1.7±2.9	1.2±2.0	NS
Anxiety	1.9±2.3	1.5±2.0	<0.04
Euphoria	0.2±0.9	0.2±0.9	NS
Apathy/indifference	5.9±2.4	3.3±1.9	<0.001
Disinhibition	1.9±3.1	1.8±2.9	NS
Irritability/lability	4.0±3.2	2.3±2.0	<0.005
Aberrant behavior	3.4	2.6	<0.05

4 weeks after Feru-guard® treatment in 20 patients with frontotemporal lobar degeneration or dementia with Lewy bodies.

Table 4: Changes in neuropsychiatric inventory score.

anger-hostility, fatigue score significantly improved by brown rice eating, and total mood disorders (TMD) was nearly half of that of white rice (Figure 8).

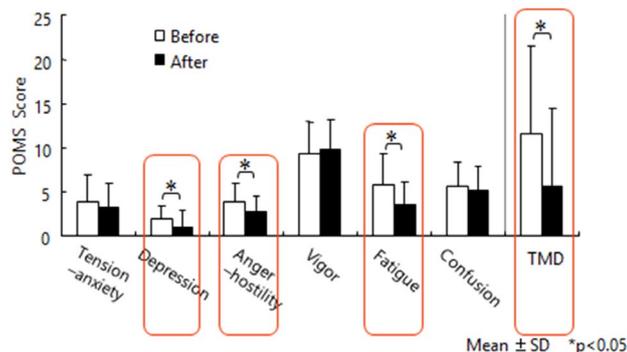


Figure 8: Mother's stress measured by POMS: Changes in POMS scores before and after dietary intervention by GABA rich rice.

Pregnant women often becomes unstable in mood. In this intervention study, 41 pregnant women were randomized to take germinated rice or white rice for 14 days. As the psychological test, POMS test was done before and after the study, and salivary amylase was measured as a stress marker. POMS test measures the 6 axes of mood, such as tension-anxiety, depression, anger-hostility, vigor, fatigue, and confusion. High score of all six, except for vigor, suggests the unfavorable mood, and high score of vigor suggests favorable mood. Higher TMD score (Total Mood Disturbance) suggests in bad mood.⁵⁶

Mothers who in took pre-germinated rice is shown by black column and those who ate white rice is shown by white column. Depression, anger-hostility, fatigue score significantly improved by brown rice eating, and TMD was nearly half of that of white rice.

In addition to their mental effects, the giant-germ rice and GBR are also useful for diabetic and hypertensive patients. In a randomized-controlled trial comparing two packs of GBR rice with white rice, 24 healthy volunteers (10 males and 14 females, aged from 27 to 47) were studied for the effect on blood pressure. The GBR group displayed a significant reduction in systolic blood pressure after 12 h of GBR intake, particularly marked after 6 minutes of physical load with an ergometer. It was also shown that the blood glucose levels and the incremental area under the curve (IAUC) were lower after taking GBR. The IAUC was 1448 mg/min/dl in GABA rich group, whereas it was

1601 mg.min/dl in white rice group.

These results demonstrate that this special pre-germinated brown rice (GABA+ferulic acid) may be effective in subjects with mild hypertension and diabetes mellitus, in addition to the mental health.

Other components of rice bran (steryl glucosides [PSG] for example) were found to be effective for coping against stress. So, medical rice for mental health is at least defined to contain high GABA and γ -Oryzanol or ferulic acid.⁵⁷

(4) Medical Rice for Cancer Prevention

In various animal experiments, Muto et al⁵⁸⁻⁶⁰ showed that fermented rice bran (FBRA) strongly prevented the incidence of colon, breast, head and neck, esophageal, and pancreatic cancers almost half. The antioxidant activity of rice bran could be considered to be a major factor.

The effects of many phytonutrients are expected to work well beyond free radical protection. Of late, an antioxidant test known as Oxidation Radical Absorbance Capacity (ORAC) has become popular⁶¹⁻⁶³ Other similar assays, such as DPPH, TRAP, TEAC etc. are available to specify the antioxidant capacity of food ingredients.

This is why consumers are often confused by different values as there is no readily available comparison method among the values obtained by different assay systems. It is proposed that the antioxidant capacity of complex supplements should be expressed in terms of standardized antioxidant units (AOU), pondering the antioxidant values obtained in aforementioned assay system.⁶⁴ Japanese intake of AOU per day is estimated more than 10000 AOU unit throughout a year.⁶⁵

Beyond the standard antioxidant vitamins, such as vitamin C and E, we should consider antioxidants found in brightly pigmented whole fruits and vegetables, mostly due to anthocyanins and proanthocyanins.⁶⁴ We measured antioxidant activities

of various rice varieties, and found that only brown rice showed antioxidant activity (Table 5). Black rice showed the highest anti-oxidant activity. Both brown rice and black rice retained the high anti-oxidant activity even after cooking.⁶⁶ Polished rice did not show antioxidant activity at all. The presence of antioxidant activity in daily meals should prevent carcinogenesis and diseases caused by free radicals.

CONCLUSION

The health effects of brown rice are empirically well known, and accumulating evidence about the physiological and pharmacological activity of rice bran strongly supports the use of brown rice in meals, although this is not popular in Japan and other countries. However, in response to the enormous increase of medical costs, the Japanese government starts to encourage

healthy longevity measures by changes of dietary habits. Functional food labeling has started in 2015, so the proper food labeling of medical rice could help people who want to control and/or improve their health status.⁴⁴ An example of food label for 'Medical Rice for Health' is shown in the figure (Figure 9).

A word in the lower part of the mark could be changed according to the purpose.

ACKNOWLEDGEMENTS

The authors deeply appreciate the participants in the East Asia Conference of Standardization of Rice Function, which was held in Kyoto from December 10 to 12, 2014. All authors attended the conference and contributed to make the entity of medical rice, providing their original data.

	ORAC_W (AOU P)	ORAC_L (AOU C)	Total
Raw brown rice	13	4	17
Raw brown rice	15	4	19
Raw brown rice	11	5	15
Cooked brown rice by pressure pan	5	3	8
Cooked brown rice by pressure pan	6	1	7
Cooked brown rice by pressure pan	6	1	7
Cooked brown rice without pressure	6	1	7
Cooked brown rice without pressure	5	1	6
Cooked brown rice without pressure	7	2	9
Pregerminated rice	1	<0.5	1.5
Pregerminated rice	2	<0.5	2.5
Cooked polished rice "kinme"	<0.5	<0.5	<0.5
Cooked polished rice "kinme"	<0.5	<0.5	<0.5
Cooked polished rice "kinme"	<0.5	<0.5	<0.5
cooked polished white rice	<0.5	<0.5	<0.5
cooked polished white rice	<0.5	<0.5	<0.5
cooked polished white rice	<0.5	<0.5	<0.5

AOU-F: Antioxidant unit by flavonoids; AOU-C: Antioxidant unit like carotenoids.

Table 5: Antioxidant activity of various rice and cooked rice.

These rice with high antioxidant activity could be categorized in the medical rice for cancer prevention.



Figure 9: Food labeling of medical rice and licensed medical rice for health.

This rice is organic brown rice, containing enough vitamins and minerals with high antioxidant ability, without any detectable herbicide or toxic heavy metals.

The authors also thank the financial support of Human Health Foundation, Toyo Rice Cooperation, Tsuno Rice Fine Chemicals Co, Ltd. Fancel Cooperation, Genmai-koso Co. Ltd, and Forica Food Co. Ltd. to open this conference. A part of this work was presented at the 9th Asia Pacific Conference on Clinical Nutrition, which was held in Kuala Lumpur, Malaysia in 2015. They also thank to Dr. Philippe Calain for his contribution to complete this manuscript.

CONFLICTS OF INTEREST

The authors do not have any conflicts of interest regarding this paper to any company.

REFERENCES

1. Vanavichit A. Facts about rice. In: Sontag J, ed. *Rice Processing: The Comprehensive Guide to Global Technology and Innovative Products*. ERLING, Germany: Verlag GmbH & Co. KG; 2014: 11-24.
2. FAOSTAT. Final 2012 data and preliminary 2013 data for 5 major commodity aggregates. Web site. <http://faostat.fao.org/site/339/default.aspx>. Accessed July 13, 2016
3. Watanabe S. *Principles of Nutritional Science*. Tokyo, Japan: Nanko-do Co. Ltd.; 2011.
4. Udagawa K, Miyoshi M, Yoshiike N. Mid-term evaluation of "Health Japan 21": Focus area for the nutrition and diet. *Asia Pac J Clin Nutr*. 2008; 17(S2): 445-452. doi: [10.6133/apjcn.2008.17.s2.08](https://doi.org/10.6133/apjcn.2008.17.s2.08)
5. Jushi M, Jack A. *The Macrobiotic Path to Total Health*. New York, USA: Ballantine Books; 2004.
6. Ishida E. *Genmai-Brown Rice for Better Health*. Tokyo, Japan: Japan Pub Inc.; 1989.
7. Kushi LH, Byers T, Doyle C, et al. American Cancer Society guidelines on nutrition and physical activity for cancer prevention: Reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin*. 2006; 56: 254-281. doi: [10.3322/canjclin.56.5.254](https://doi.org/10.3322/canjclin.56.5.254)
8. WHFoods. Brown Rice. 2012. Web site. <http://www.whfoods.com/genpage.php?tname=foodspice&dbid=128>. Accessed July 13, 2016
9. Tsukuba Agriculture Research Gallery. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 316-336.
10. Nishijima C, Nakamoto K, Kawabata T, Kagawa Y, Hirakawa A, Watanabe S. Macrobiotic lifestyle and health. *Clin Funct Nutriol*. 2014; 6(3): 144-151.
11. Watanabe S. Tailor-made nutrition "Magotachishoku". *Clin Funct Nutr*. 2010; 2: 162-167.
12. Smit HJ, Kemsley EK, Tapp HS, Henry CJK. Does prolonged chewing reduce food intake? Fletcherism revisited. *Appetite*. 2011; 57: 295-298. Web site. <http://www.ifr.ac.uk/research/publications/307/does-prolonged-chewing-reduce-food-intake-fletcherism-revisited/>. Accessed July 13, 2016
13. Ogawa S. *Rice Studies, Present and Future: In Commemoration of Second International Symposium on Rice and Disease Prevention*. Tokyo, Japan: Sankyo Pub. Co. Ltd.; 2012.
14. Juliano BO, Boulter D. Extraction and composition of rice endosperm glutenin. *Phytochemistry*. 1985; 15: 1601-1606. doi: [10.1016/S0031-9422\(00\)97436-3](https://doi.org/10.1016/S0031-9422(00)97436-3)
15. Nakagami T, Gonda H, Hashimoto H, Tsuno T. LC/MS analysis of cerebrosides in rice bran. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 225-232.
16. Watanabe S. Proceedings of the East Asia Conference on Standardization of Rice Function. Kyoto, Japan: Lifescience Promoting Organization. 2013.
17. Most MM, Tulley R, Morales S, Lefevre M. Rice bran oil, not fiber, lowers cholesterol in humans. *Am J Clin Nutr*. 2005; 81(1): 64-68. Web site. <http://ajcn.nutrition.org/content/81/1/64.long>. Accessed July 13, 2016.
18. Sugano M. Functional characteristics of rice bran oil. Shokuhin Kako Gijutu. *J Jpn Soc Food Engineering*. 2002; 22: 26-30.
19. Tian S, Nakamura K, Cui T, Kayahara HJ. High-performance liquid chromatographic determination of phenolic compounds in rice. *J Chromatogr A*. 2005; 1063(1-2): 121-128.
20. Tian S, Nakamura K, Kayahara H. Analysis of phenolic compounds in white rice, brown rice, and germinated brown rice. *J Agric Food Chem*. 2004; 52: 4808-4813. doi: [10.1021/jf049446f](https://doi.org/10.1021/jf049446f)
21. Miyazawa T, Sibata A, Nakagawa K, Phumon S. Cancer prevention by rice bran tocotrienol. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 217-224.
22. Morita N, Maeda T. Gamma-aminobutyric acid and functional materials in brown rice and pseudo-cereal during germination and their applications to food processing. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 150-161.
23. Dilworth L, Omoruyi F, Asemota H. Effects of IP6 on carbohydrate and lipid metabolism in rat model. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 150-161.

- culture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 162-143.
24. Grases F, Costa-bauza A, Prieto RM. Phytate as modulator of calcification processes in humans. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 167-177.
25. Vucenik I. IP6 and inositol in cancer prevention and therapy. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 196-208.
26. Maeba R, Hara H. Myo-Inositol and plasmalogens. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 178-188.
27. Szabo E. Myo-inositol and the prevention of lung cancer. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 189-195.
28. Benjamin J, Levine J, Fux M, Aviv A, Levy D, Belmaker RH. Double-blind, placebo-controlled, crossover trial of inositol treatment for panic disorder. *Am J Psychiatry*. 1995; 152(7): 1084-1086. doi: [10.1176/ajp.152.7.1084](https://doi.org/10.1176/ajp.152.7.1084)
29. Tungtrakul P. Innovative rice products in Thailand. Proceedings of the East Asia Conference on Standardization of Rice Function. Kyoto, Japan. 2013; 61-62.
30. Muran V, Spiegelman D, Sadha V, et al. Effect of brown rice, white rice, and brown rice with legumes on blood glucose and insulin responses in overweight Asian Indians: A randomized control trial. *Diabetes Technol Ther*. 2014; 16: 317-325. doi: [10.1089/dia.2013.0259](https://doi.org/10.1089/dia.2013.0259)
31. Ohtsubo K, Nakamura S, Tsuji K, Utsunomiya K, Masuda Y, Hasegawa M. Possibility of diabetes prevention by high amylose rice. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 109-115.
32. Kadowaki M, Watanabe R, Kubota M, Kuragai T, Masumura T. Digestibility, bioavailability, and beneficial effects of alkali-extracted rice protein. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 123-135.
33. Beppu S. Low Protein Processing Cooked Rice. Proceedings East Asia Conference on Standardization of Rice Function. Kyoto, Japan. 2014; 33-34.
34. Yokoyama WH, Ohtsubo K, Bartley G, Suzuki K. Health benefits of pre-germinated rice and recent studies of hamsters fed PGR. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 116-122.
35. Kosaka H, Nemoto H, Motojima A, et al. Antitumorigenic effect and antioxidative activity of the brown rice fermented by *aspergillus oryzae* (FBRA). In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 266.
36. Grant BL, Hamilton KK. Medical nutrition therapy for cancer prevention, treatment, and recovery. In: Mahan LK, Escot-Stump S, Raymond JL, eds. *Krause's Food and the Nutrition Care Process*. 13th ed. St. Louis, USA: Elsevier; 2012: 832-863.
37. Hu EA, Pan A, Malik V, Sun Q. White rice consumption and risk of type 2 diabetes: Meta-analysis and systematic review. *BMJ*. 2012; 344: e1454. doi: [10.1136/bmj.e1454](https://doi.org/10.1136/bmj.e1454)
38. Shimabukuro M, Masuzaki H, Rie K, et al. Effects of brown rice diet on visceral obesity and endothelial function: The BRAVO study. *British J Nut*. 2013; 111: 310-320. doi: [10.1017/S0007114513002432](https://doi.org/10.1017/S0007114513002432)
39. Nakamura S, Satoh H, Ohtsubo K. Characteristics of pregelatinized ae mutant rice flours prepared by boiling after pre-roasting. *J Agric Food Chem*. 2011; 59(19): 10665-10676. doi: [10.1021/jf200973x](https://doi.org/10.1021/jf200973x)
40. Nakamura S, Satoh H, Ohtsubo K. Palatable and bio-functional wheat/rice bread from pre-germinated brown rice of super hard cultivar, EM10. *Biosci Biotechnol Biochem*. 2010; 74(6): 1164-1117. doi: [10.1271/bbb.90850](https://doi.org/10.1271/bbb.90850)
41. Nakamura S, Ohtsubo K. Acceleration of germination of super-hard rice cultivar EM10 by soaking with red onion. *Biosci Biotechnol Biochem*. 2011; 75(3): 572-574. doi: [10.1271/bbb.100621](https://doi.org/10.1271/bbb.100621)
42. Kopple JD, Massry SG. *Nutritional Management of Renal Disease*. Baltimore, Maryland, USA: Williams & Wilkins; 1997.
43. Watanabe S. *Recipe of Low Protein Diet to keep Kidney Function*. Tokyo, Japan: Shufu-no-tomo-sha; 2010.
44. Masumura T, Saito Y. Structure and function of rice seed protein. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future*. Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 144-149.
45. Hirakawa A, Watanabe S, Melby M. Comprehensive food labeling for obesity control. *Adv Obes Weight Manag Cont*. 2016; 4(3): 00088. doi: [10.15406/aowmc.2016.04.00088](https://doi.org/10.15406/aowmc.2016.04.00088)
46. Mizuno S. A secondary analysis of ideura data of low protein diet practice for progressive chronic kidney disease patients. *Clin Funct Nutriol*. 2009; 1(5): 242-245.
47. Sun J-Q, Wang Y. Effects of low-protein rice on nutrition status and renal function in patients with chronic kidney disease: A pilot study. *Proceedings East Asia Conference on Standard-*

- ization of Rice Function. 2014; 49-50.
48. Kopple JE, Levey A, Greene T, et al. Effect of dietary protein restriction on nutritional status in the modification of diet in renal disease study. *Kidney Int.* 1997; 52: 778-791. doi: [10.1038/ki.1997.395](https://doi.org/10.1038/ki.1997.395)
49. Watanabe S. Evaluation of modification of diet in renal disease (MDRD) Study. *Clin Funct Nutriol.* 2009; 1(5): 238-241.
50. WHO. Dementia: Fact Sheet. 2016. Web site. <http://www.who.int/mediacentre/factsheets/fs362/en/>. Accessed July 13, 2016
51. Tahira T. Prevention of dementia by improving life style. *Clin Funct Nutriol.* 2012; 4(6): 296-301.
52. Kimura T. Ferulic acid and angelica archangelica extract in dementia: Effects upon cognitive efunctions and behavioral and psychologic symptoms of dementia. *Proceedings East Asia Conference on Standardization of Rice Function.* 2014; 75.
53. Bui TN, Nguyen do H, Tran QB, et al. Pre-germinated brown rice reduced both blood glucose concentration and body weight in Vietnamese women with impaired glucose tolerance. *Proceedings East Asia Conference on Standardization of Rice Function.* 2014; 45-46.
54. Shoichi I, Yukihiro I. *Marketing of Value-Add Rice Products in Japan: Germinated Brown Rice and Rice Bread.* Symposium, Rome: FAO International; 2004.
55. Kimura T, Hayashida H, Murata M, Takamatsu J. Effect of ferulic acid and angelica archangelica extract on behavioral and psychological symptoms of dementia in frontotemporal lobar degeneration and dementia with Lewy bodies. *Geriatr Geront Int.* 2011; 11: 309-314. Web site. <http://www.citeulike.org/user/applebyb/author/Kimura:T>. Accessed July 13, 2016
56. Sakomoto S, Hayashi T, Hayashi K, et al. Pre-germinated brown rice could enhance maternal mental health and immunity during lactation. *Eur J Nutr.* 2007; 46: 391-396. doi: [10.1007/s00394-007-0678-3](https://doi.org/10.1007/s00394-007-0678-3)
57. Matsushita K, Araki E, Kawase S, Sunohara Y, Iida S. Haiibuki, a rice variety with giant embryo, accumulates high amount of GABA. In: Tsukuba Agriculture Research Gallery, ed. *Rice Studies, Present and Future.* Tokyo, Japan: Sankyo Pub Co. Ltd.; 2012: 314.
58. Mori H. Cancer prevention by rice and rice bran. *Clin Funct Nutriol.* 2013; 5(3): 126-129.
59. Tomita H, Kuno T, Yamada Y, et al. Preventive effect of fermented brown rice and rice bran on N-methyl-N'-nitro-N-nitrosoguanidine-induced gastric carcinogenesis. *Oncol Report.* 2008; 19(1): 11-15. doi: [10.3892/or.19.1.11](https://doi.org/10.3892/or.19.1.11)
60. Katayama M, Yoshimi N, Yamada Y, et al. Preventive effect of fermented brown rice and rice bran against colon carcinogenesis in male F344 rats. *Oncol Report.* 2002; 9(4): 817-822. doi: [10.3892/or.9.4.817](https://doi.org/10.3892/or.9.4.817)
61. Prior RL, Hoang H, Gu L, et al. Assays for hydrophilic and lipophilic antioxidant capacity (oxygen radical absorbance capacity (ORAC(FL))) of plasma and other biological and food samples. *J Agric Food Chem.* 2003; 51: 3273-3279. doi: [10.1021/jf0262256](https://doi.org/10.1021/jf0262256)
62. Prior RL, Wu X, Schaich K. Standardized methods for the determination of antioxidant capacity and phenolics in foods and dietary supplements. *J Agric Food Chem.* 2005; 53: 4290-4302. doi: [10.1021/jf0502698](https://doi.org/10.1021/jf0502698)
63. Serafini M, Del Rio D. Understanding the association between dietary antioxidants, redox status and disease: Is the total antioxidant capacity the right tool? *Redox Rep.* 2004; 9: 145-152. doi: [10.1179/135100004225004814](https://doi.org/10.1179/135100004225004814)
64. Takebayashi J, Oki T, Chen J, et al. Estimated average daily intake of antioxidants from typical vegetables consumed in Japan: A preliminary study. *Biosci Biotechnol Biochem.* 2010; 74: 2137-2140. doi: [10.1271/bbb.100430](https://doi.org/10.1271/bbb.100430)
65. Tatsumi Y, Ishihara J, Morimoto M, Ohno Y, Watanabe S for the JPFC FFQ Validation Study Group. Seasonal differences in total antioxidant capacity intake from foods consumed by a Japanese population. *Eur J Clin Nutr.* 2014; 68(7): 799-803. doi: [10.1038/ejcn.2014.65](https://doi.org/10.1038/ejcn.2014.65)
66. Hirakawa A, Watanabe S, Izumi Y, Nishiumi S, Yamada M. Brown rice is the complete meal. *Anti Aging Med.* 2012; 8(4): 585-591.