ECRONICON OPEN ACCESS

EC NUTRITION
Mini Review

Medical Rice: Brown Rice for Health and Low Protein Rice for Preventing CKD

Norihiro Takei[1], Sayuri Kodama[2], Azusa Hirakawa[3], Shoichi Mizuno[4], Keiji Saika[5] and Shaw Watanabe[6]*

[1]*Forica Foods Co. Ltd, Japan*

[2]*Sagami Women's Junior College, Japan*

[3]*Otsuma Women's University, Cabinet Office of Japan, Japan*

[4]*National Cancer Medical Research Center, East, Japan*

[5]*Toyo Rice Co. Ltd, Japan*

[6]*Lifescience Promoting Association, Asia Pacific Clinical Nutrition Society, Japan*

***Corresponding Author**: Shaw Watanabe, Lifescience Promoting Association, Asia Pacific Clinical Nutrition Society, Japan.

Received: November 14, 2018; **Published:** January 28, 2019

Abstract

In many countries, rice contributes to overall better health by supplying dietary energy, proteins, fat and various micronutrients. Many different species of rice have been developed in Japan and other rice producing countries. Some varieties are expected to prevent many types of 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 dietary therapy. Japanese food has become a world heritage and has become popular all over the world, but knowledge about the benefits of rice eating is limited. In this paper, we would like to focus on the benefits of brown rice eating, and recently developed wax free brown rice (WFBR) and its protein reduced low protein brown rice (LPBR) for disease prevention.

Keywords: *Medical Rice; Brown Rice; Health; Wax Free Brown Rice (WFBR); Low Protein Brown Rice (LPBR); CKD*

Health effects of brown rice

Until the late 19th century, Japanese traditional meals were composed of unpolished brown rice, miso (fermented soy) soup and side dishes cooked with vegetables, soybean products, and various varieties of roots. 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 World War II, polished rice, meat, eggs, and dairy products became the major food items. Consequently, new dietary habits largely account for the high prevalence of metabolic syndrome and other lifestyle related chronic diseases.

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, such as obesity, diabetes, hypertension. Wellness and a higher quality of life are observed among brown rice eaters [1-4].

Brown rice shows many health benefits for the body, but some people disagree with it. It is said that brown rice has more risk of mycotoxin, arsenic and cadmium contamination than polished white rice. Those people also say; brown rice digestion is bad, the pesticide remains in brown rice, phytic acid in brown rice interferes mineral absorption, and abscisic acid damages mitochondria. We examined the validity of above bad reputation by critical review on scientific reports, statistical facts, and the current state of eating habits in relation to above points [5].

Mycotoxin contamination in rice is usually lower as in wheat or corn. Tanaka., *et al.* [6] extensively measured mycotoxins such as aflatoxin B_1, B_2, G_1, G_2 (AFS), citrinin, deoxynivalenol (DON), fumonisin B_1, B_2, B_3 (FMS), fusarenon-X (Fus.-X), nivalenol (NIV), ochratoxin A (OTA), sterigmatocystin (STE), and zearalenone, and none of 48 brown rice samples were contaminated with STE, AFS and FMS. They found that the mycotoxin contamination occurs very seldom in Japan, because post-harvest rice is preserved in warehouses where moisture and temperature are strictly controlled.

Brown rice often contains higher levels of arsenic compared to white rice. This is because arsenic is mainly concentrated in the husk of the rice, which is more common in wholegrain products [7-10]. Since arsenic is naturally present in the soil it is not possible to affect the level of arsenic by using organic culture.

A particular country or region has higher or lower levels of arsenic in its rice compared to another. Cadmium is similarly contaminated in wide area, and its tolerance in rice is well studied by Uraguchi., *et al* [10]. In Japan, both minerals are legislated by the Ministry of Agriculture, Forestry and Fishery, and the survey on the actual condition of domestic agriculture and livestock products clarified that rice has a higher arsenic concentration than other agricultural crops, most of arsenic in rice is inorganic arsenic, and the hijiki (sea weed) has been found to have a much higher inorganic arsenic concentration than other foods.

Since arsenic comes from irrigation water and cadmium comes from soil, it is difficult to take measures to alleviate both at the same time. However, the Ministry of Agriculture, Forestry and Fishery is searching for ways by organizing projects to reduce grain cadmium accumulation. So far, there is no obvious health problem by ingestion of arsenic or cadmium through brown rice at present.

The pesticide residue of brown rice is far more trace than the statutory residual pesticide standard. Organic culture diminish herbicide completely. Phytic acid in brown rice are already bonded with the mineral, so it does not interfere mineral absorption. Abscisic acid in brown rice is a plant hormone included in brown rice. The concentration is 1/20 or less than that of harmful limit in the literature. Therefore, the bad reputation of brown rice eating does not have any evidence [5].

In addition to the functional effects of ingredients in brown rice, the frequency of mastication influences the strength of oro-pharyngeal muscles and brain function [11,12]. In Japan, fast foods with soft texture have recently become popular among the younger generation, so the mastication frequency has been decreasing in proportion. Brown rice increases the chewing number of times than in meat or fish dishes. The National Health and Nutrition Survey, Labour and Welfare (2010) showed it was only 800 times per American meal compared to 30,000 times in a genmai meal. Longer eating time acts to prevent fast eating, which would lead to obesity, and relaxes stress by enjoying breakfast and/or dinner more with family and friends [13].

Brown rice for health: Organic brown rice
Rice for diabetes: Low glycemic index
Rice for kidney disease: Low protein rice
Rice for mental health: High GABA, gamma oryzanol, ferulic acids
Rice for cancer prevention: High antioxidant ability
Wax free brown rice (WFBR)
Low protein brown rice (LPBR)

Table 1: *Candidate of medical rice.*

Intestinal microbiota of brown rice eaters

The health benefits of brown rice are well-known, but consumers prefer polished white rice.

We are performing GENKI study (Genmai Epidemiology of Nutrition for Kenko (health) Innovation) to find integrated solution by collecting multidimensional evidences for healthy longevity [14-16]. Brown rice eaters show lower body mass index (BMI) in men and women at all ages. Average BMI in males was 22.0 ± 3.2 kg/m2 and 20.7 ± 2.8 kg/m2 in females. Dietary habits with brown rice, rich vegetables, avoiding meat should support the healthy life and quality of life (QOL). A good bowel movement and stool figure of brown rice eaters suggested a good intestinal environment which led to avoid obesity and keep in good health [16].

Brown rice eaters showed a high prevalence of *Fermicutes* and low prevalence of *Fusobacterium* in phylum. Frequency of microbiota at species level showed a high prevalence of *Faecalibacterium prausnitzii* (5.28%), and then *Blautia wexlerae* (3.67%), *Fusicatenibacter saccharivorans* (3.41%), *Megamonas funiformis* (3.35%), *Collinsella aerofaciens* (3.21%), and *Bacteroides vulgatus* (3.12%). They belong to *Fermicutes* phyla and butyrate producing bacteria. *Blautia* is considered to control intestinal immunity. *Bifidobacterium adolescentis* (2.35%) and *B. longum* (1.92%), *Bacteroides uniformis* (2.22%), *B. plebelius* (1.96%), and *B. dorei* (1.71%), and *Akkermansia muciniphila* (2.16%) were followed [16].

Brown rice eaters, compared with the white rice eaters, showed less *Actinobacteria* (12.1 vs. 8.5% p = 0.078) and Fusobacterium (1.6 vs. 0.018%, p = 0.011). These are pathogenic in intestinal condition.

From recent intestinal bacterial research short chain fatty acids, such as acetate, propriate and butyrate, are a focus of the study [17-19]. Butyrate is the preferred energy source for the colon epithelial cells, and contributes to the maintenance of the epithelial barrier functions of intestinal mucosa, and has immunomodulatory and anti-inflammatory properties. Dietary fibers in brown rice seems to be the most important factors, but other ingredients could give various influences for bacterial co-existing [19].

Wax free brown rice (WFBR)

Brown rice has not become popular, due to its hardness for mastication, not good palatability, and some people feel gastric distress. The wax layer of brown rice disturbs immersion of water when boiling, which results in hardness of boiled rice. So, Keiji Saika elaborated to invent a new rice processing machine to remove only the surface wax layer, and succeeded in making a wax free brown rice (WFBR) [20,21]. Further treatment to extract protein from WHBR was succeeded [22].

Removal of wax layer did not affect the nutritional values of brown rice. A slight reduction of energy source was caused by immersion of cooked water, which made soft palatability like white polished rice (Figure 1).

WFBR broadly reduced all 18 amino acids about 20%. γ-oryzanol and antioxidant (antioxidant unit (AOU)-Lipid and AOU-P olyphenol) activity of brown rice were remained (Table 2). GABA remained 85.7% of brown rice in WFBR. AOU in Japan corresponds to the oxygen radical absorbance capacity (ORAC), in which 6-hydroxy-2,5,7,8- tetramethylchroman- 2-carboxylic acid (Trolox) [23-25].

Item	Unit	Brown rice	WFBR 1)	LPBR 2)
Energy	kcal/1008	149.0 ± 1.4	125.0 ± 1.4**	157.5 ± 0.7*
Water	g/100g	63.9 ± 0.5	69.9 ± 0.4**	62.2 ± 0.5
Protein	g/100g	2.5 ± 0.1	2.1 ± 0.2	0.7 ± 0**
Lipid	g/100g	1.4 ± 0.1	1.2 ± 0.0	1.2 ± 0.4
Carbohydrate	g/100g	31.8 ± 0.4	26.5 ± 0.1**	35.4 ± 0.6*
Ash	g/100g	0.6 ± 0.1	0.4 ± 0.0	0.1 ± 0*
DF total	g/100g	1.8 ± 0.1	1.4 ± 0.1	1.3 ± 0.3
DF water	g/100g	0.2 ± 0.1	0.2 ± 0.1	0.1 ± 0.0
DF insoluble	g/100g	1.6 ± 0.1	1.2 ± 0.1*	1.4 ± 0.0
Vit. E α	mg/100g	0.40 ± 0.00	0.30 ± 0.14	0.0
Vit. B1	mg/100g	0.12 ± 0.03	0.11 ± 0.01	0.0
Vit. B2	mg/100g	0.03 ± 0.02	nd	nd
Niacin	mg/100g	2.10 ± 0.00	1.40 ± 0.00	0.0
Folic acid	ug/100g	11.00 ± 1.41	7.00 ± 0.00	2.0
Panthoteic a	mg/100g	0.41 ± 0.02	0.33 ± 0.01*	0*
GABA	mg/100g	3.50 ± 0.71	3.00 ± 0.00	2.0
y oryzanol	mg/100g	10.00 ± 0.00	5.55 ± 0.5**	nd
AOU	Unit	3.50 ± 0.00	3.50 ± 0.00	0.0
AOU-L	Unit	3.50	3.50	0.0
AOU-P	Unit	0.00	0.00	0.0
Na	mg/100g	2.50 ± 0.57	2.50 ± 0.14	1.85 ± 0.21
K	mg/100g	85.30 ± 2.26	63.75 ± 2.05*	0.25 ± 0.35***
Ca	mg/100g	6.00 ± 0.00	5.00 ± 0.00	8.0
Mg	mg/100g	47.55 ± 0.07	34.10 ± 0.57**	4***
Mo	ug/100g	nd	nd	6.0
P	mg/100g	115.00 ± 7.07	84.50 ± 0.71*	18*
Fe	mg/100g	0.40 ± 0.00	0.30 ± 0.00	0.3
Zn	mg/100g	0.76 ± 0.06	0.64 ± 0.06	0.3
Cu	mg/100g	0.10	nd	0.1
Mn	mg/100g	0.83 ± 0.01	0.60 ± 0.01**	0.1**
Se	0.1 ug/100	nd	nd	0.0
NaCI	g/100g	0.01 ± 0.00	0.01 ± 0.00	0.0

Table 2: *Nutrients, functional ingredients and amino acids in 3 differently processed rice (boiled).*
BR: Brown Rice; WFBR: Wax Free Brown Rice; LPBR: Low Protein Brown Rice; na: Not Applicable; nd: Not Detected.

Figure 1: *Raw Brown Rice (Upper Left), and Wax Free Brown Rice (Upper Right). Boiled rice; brown rice, wax free brown rice, and BG Rinse-Free Rice (Lower Half). Brown rice particles (Left) are smaller compared to the white rice (Right). Wax free brown rice (middle) shows the same size of white rice due to food Immersion of water at boiling.*

Low protein brown rice (LPBR)

The protein in rice is stored in two different types of compartments [26]. The major proteins are prolamin and glutelin. Prolamin is the alcohol soluble protein that remained after salt extraction of globulin. Glutelin is the dilute-acid or dilute-alkaline soluble protein after prolamin extraction. Most of the prolamin is present at the periphery in whole rice grains, so prolamin could be easily removed by enzymatic digestion on polished white rice, but it has been hard from brown rice directly.

Extraction of protein from WFBR was performed by the enzyme method [22]. Removal of rice protein yielded low protein brown rice (LPBR) which is beneficial for chronic kidney disease patients. The LPBR was made by proteolytic enzymes to digest and remove the protein in WFBR [21]. In our method, an enzyme mix consisting of *Aspergillus oryzae, Rhizopus niveus* and *Aspergillus niger* was used. The main component was protease in the aspartic protease family (EC 3.4.23). The raw LPBR was spread out evenly into a thickness of 30 to 50 mm, then steamed for 4 to 10 minutes using superheated steam of at least 105°C. Immediately after steaming, the steamed LPBR was separated loosely and dried by warm air so that the moisture level was uniform throughout, at 16% to 20%. It was the continuous production conveyor-system.

Extraction of rice protein from WFBR becomes possible to reduce undesirable nutrients. The remaining minerals were only 0.3% in potassium, 8.4% in magnesium, 9.6% in manganese, 15.7% in phosphate, and 39.5% in zinc (Table 2). Reduction of these minerals is a great benefit for CKD patients, because hyperkalemia and hyperphosphatemia are often difficult to reduce by eating meat. Dietary fibers remained as same as the brown rice, although water-soluble fiber seemed to be more easily solved out than insoluble dietary fiber during boiling.

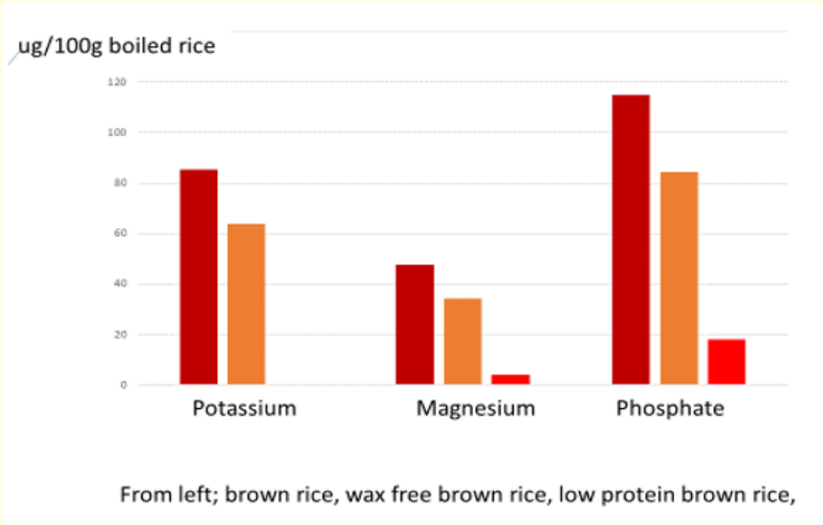
Nutrients WFBR and PFBR contents are compared with brown rice (Figure 2). As for the micronutrients, vitamin B1 was remained almost 90% in WFBR, but vitamin E, niacin, folic acid and pantothenic acid were lost for 30 to 40%. The palatability was comparable to polished white rice. LPBR decreased 70 - 80% of rice proteins, two third phosphate and almost all potassium that were toxic for chronic kidney disease (CKD) patients, so LPBR could be available for patients with renal insufficiency. Dietary fibers and functional ingredients of bran should yield a good effect for intestinal microbiota as prebiotics, as described earlier.

Newly made LPBR could be expected to have wide usage in clinical nutrition [27]. CKD patients have a necessity to reduce phosphorus and potassium intake in addition to decrease protein intake. At the same time, there is a need to ensure the patient takes in enough energy source. LPBR meets all of these requirements as a staple food for CKD patients. In addition to the dietary fibers, vitamins, γ-oryzanol, ferulic acid and antioxidant activity, low salt and gluten free LPBR meal is also beneficial to improve hypertension and gut distress.

Dietary therapy for chronic kidney disease

According to the survey conducted by the Japan Society of Dialysis Medicine, number of hemodialysis patients were 324,986, an increase of 4,538 from the previous year in 2015. Diabetic kidney disease (DKD) was the most common, with 120,278 patients, account-

ing for 38.4% of dialysis patients overall, but DKD in newly started dialysis in the past one year was 16,072, accounting for 43.5% of the new hemodialysis [28,29]. According to the aging society, number of old patients more than 80 years old for hemodialysis seemed to be increasing.



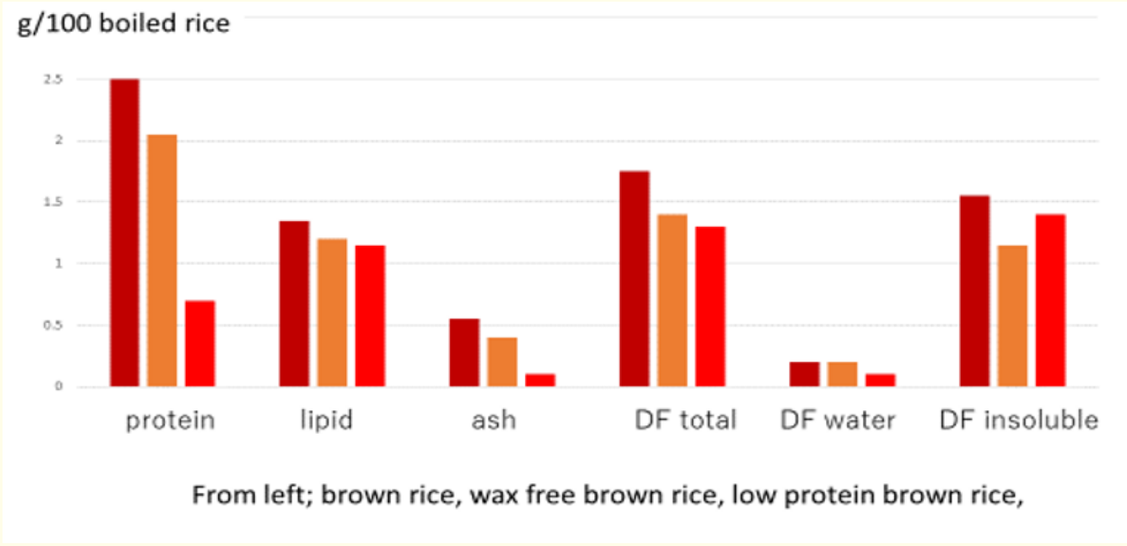


Figure 2: *Comparison of Protein, Lipid, Ash and Dietary Fibers (upper). Marked reduction of protein and ash is noticed, while the dietary fibers were stored. (lower) Potassium was lost more than 99% and phosphate 85% [21].*

Prevention of hemodialysis is very important, both for reducing medical costs and for improving patients' QOL. Prevention of hypertension and low protein diet are two major strategies against CKD progression [30]. We have reported on the Saku population-based cohort study, in which the decline of eGFR was 1 ml/min/1.73m^2/year by ordinary lifestyle of aging, while it was nearly 5 ml among people whose daily meat consumption was large [31].

One of the benefits of a low-protein diet is the preservation of the kidney function [27,30]. 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.

Protein overload promotes glomerular hyper-infiltration which causes prefibrotic effects [32].

High protein diets acutely elevate the glomerular filtration rate. Palatini [32] administered 1g of protein/kg body weight as a beef steak meal to nine, healthy male subjects and measured glomerular filtration rate (GFR; inulin clearance), renal plasma flow (p-amino hippurate clearance), plasma renin activity, aldosterone and plasma and urinary catecholamines to characterize the response. The subjects ingested

the meal on three separate days and were pretreated with either placebo, 50 mg indomethacin to inhibit renal prostaglandin synthesis, or 10 mg enalapril to inhibit angiotensin II synthesis. Following placebo treatment protein feeding significantly increased GFR, from a pre-meal level of 101 +/- 7 ml/min/1.73m^2 to a post-meal level of 130 +/- 6 ml/min/1.73m^2. A parallel rise in renal plasma flow and a fall in renal vascular resistance were noted. Enalapril pretreatment had no significant effect on protein-induced glomerular hyperfiltration. Protein feeding following placebo or indomethacin did not alter plasma renin activity while enalapril administration rose plasma renin activity.

Over the past 90 years, a protein-restricted diet has been successfully used to treat chronic renal failure. Mizuno analyzed the Ideura's data and confirmed the effects of a low-protein diet on patients with CKD [31]. At the threshold of renal failure of 6 mg serum creatinine/dl, low protein diet had started. With a content of 0.4 - 0.5g protein/kg bwt, the median survival was 4 years until ESKD. With a content of 0.6 and 0.7 g/kg, no beneficial effect was observed compared with a control group (> 0.8g protein/kg bwt). The optimal low-protein content was 0.3 g/kg bwt. Excessive renal mTOR activation increases protein synthesis and decreases autophagy. This process may lead to cellular apoptosis to lead end stage kidney disease (ESKD).

Recently, the therapy of CKD targeted at reducing hyperfiltration within the glomerular capillaries by using the angiotensin converting enzyme inhibitor or angiotensin receptor blocker to dilates the glomerular arteriole [33,34]. Other classes of diabetes medications, such as GLP-1 agonists, DPP-4 inhibitors and SGLT2 inhibitors, are also thought to slow the progression of diabetic nephropathy. However, the dietary therapy is more cost/effective.

Sun., *et al.* [35] performed a preliminary study in Huadong Hospital (Shanghai, China), examining the effects of a 12-week low-protein rice as dietary therapy (0.6 g/kg body weight) for CKD patients. Cooked rice was provided 3 packs/day containing 1.35g proteins and 900 kcal energy. 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). 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 significantly changed. After 12 weeks, urinary protein levels decreased from 0.4 g/d to 0.1 g/d. Urine albumin decreased from 130.8 mg/24h 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. Recently, we finished a randomized clinical trial in Bangkok by using protein reduced Indica rice, and had a report of similar effectiveness for CKD.

Medical rice for CKD should contain enough energy source and low proteins, as well as low potassium and phosphate. However, relatively little is known about the optimal way to coordinate, finance and regulate the care for people with CKD, especially patients living in inequality present low-and-middle income countries.

Critical dose of protein restriction is still in debate [36]. In the Cochran's review the definition of a low protein diet was defined between 0.6 g/kg to 0.5 g/kg body weight, and very low protein diet was below 0.4 g/kg body weight [37]. Normal diet with 0.8 g/kg body weight account as normal control.

Our clinical review on 241 CKD patients, with a serum creatinine level greater than 5 mg/dl, eGFR kept decline within 1.0 ml/min/yr by every 0.2 g/kg bwt reduction of daily protein intake. At serum creatinine level lower than 5 mg/dl, a daily protein intake of 0.5 g/kg bwt could decrease urinary protein approximately 1.1 g/day in a relatively short time span. The survival until ESKD was better by a daily protein intake of 0.3 - 0.5 g/kg bwt with enough energy source intake, while more than 0.6 g/kg bwt showed the same poor prognosis as control [33].

In case of the Modification of Diet in Renal Disease (MDRD study) [38], the low protein diet and control protein intake were 0.6 g/kg bwt/day vs. 1.3 g/kg bwt/day, and an LPD set of 0.6 g/kg bwt/day vs. very low protein diet set of 0.28 g/kg bwt/day. The last set was prescribed a daily amino acid-keto acid supplement (0.28 g/kg bwt) and multivitamin tablet. Energy intake was set at 30 kcal/kg bwt. Follow-up period of 2.2 yrs in average and an additional 9-month follow-up showed poor prognosis in the very low protein diet group. The actual protein intake was found to be above the set level, and the energy intake had been less than 70% (22 - 20 kcal/kg bwt), so that the malnutrition would be the cause of death. In our opinion, failure of the MDRD study to demonstrate efficacy of LPD, was mostly explained by insufficient energy intake.

Conclusion

New rice processing to peel off waxy layer of brown rice produces a wax free brown rice (WFBR) with palatability of white rice and nutrients rich bran layer. It made it possible to extract protein from WFBR and yield low protein brown rice (LPBR). CKD patients have a necessity to reduce phosphorus and potassium intake in addition to decrease protein intake. At the same time, remaining dietary fiber and functional nutrients act as prebiotics for intestinal microbiota. Increase of butyrate producing *Fermicutes* phyla and low prevalence of *Fusobacterium* would contribute to healthy environment including good bowel condition and immunity.

Rice is the main staple food for approximately 70 percent of the world's population, mainly living in ten areas of the Asia-Pacific region [39,40]. In many countries, rice contributes to overall better health by supplying dietary energy, proteins and fat. It accounts for more than 50% of the diet in Bangladesh, Myanmar, Lao PDR, Viet Nam and Indonesia. In this regard, the nutritional aspects of rice should be re-evaluated, and further development should produce wonderful medical rice [11,41-44].

Conflict of Interest

Dr. Takei is an employee of Forica Foods Co. Ltd, and Mr. Saika is CEO of Toyo Rice Co. Ltd.

Bibliography

1. Ishida E. "Genmai-Brown Rice for Better Health". Tokyo, Japan: Japan Pub Inc (1989).
2. Nishijima C., *et al*. "Macrobiotic lifestyle and health". *Clinical and Functional Nutriology* 6.3 (2014): 144-151.
3. Jushi M and Jack A. "The Macrobiotic Path to Total Health". New York, USA: Ballantine Books (2004).
4. Kushi LH., *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: A Cancer Journal for Clinicians* 56.5 (2006): 254-281.
5. Yamaguchi M. "The ingredients of brown rice and health: Truth of bad reputation". *Clinical and Functional Nutriology* 10.3 (2018): 139-142.
6. Tanaka K., *et al*. "Mycotoxins in rice". *International Journal of Food Microbiology* 119.1-2 (2007): 59-66.
7. FAO/WHO. "Cadmium IN Safety evaluation of certain contaminants in food, Prepared by the Seventy-third meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA)". World Health Organization, Geneva (2011).
8. FAO/WHO. "Arsenic IN Safety evaluation of certain contaminants in food, Prepared by the Seventy-second meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). World Health Organization, Geneva, 2011, and Food and Agriculture Organization of the United Nations, Rome, 2011. WHO Food Additives Series 63, FAO JECFA MONOGRAPHS 8 (2011).
9. Kikuchi T., *et al*. "The input-output balance of cadmium in a paddy field of Tokyo". *Chemosphere* 67.5 (2007): 920-927.
10. Uraguchi S and Fujiwara T. "Cadmium transport and tolerance in rice: perspectives for reducing grain cadmium accumulation". *Rice (N Y)* 5.1 (2012): 5.
11. Smit HJ., *et al*. "Does prolonged chewing reduce food intake? Fletcherism revisited". *Appetite* 57.1 (2011): 295-298.
12. Watanabe S., *et al*. "Food as medicine: The new concept of "medical rice"". *Advances in Food Technology and Nutritional Sciences-Open Journal-Open Journal* 2.2 (2016): 38-50.
13. Muran 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 Technology and Therapeutics* 16.5 (2014): 317-325.
14. Watanabe S., *et al*. "Effects of Brown Rice on Obesity: GENKI Study I (Cross Sectional Epidemiological Study)". *Journal of Obesity and Chronic Diseases* 2.1 (2018): 12-19.
15. Watanabe S., *et al*. "Dietary life habits of obese people and brown rice eaters among GENKI Study". *Clinical and Functional Nutriology* 10.2 (2018): 79-86.

16. Hirakawa A., *et al*. "The nested study on the intestinal microbiota in GENKI Study with special reference to the effect of brown rice eating". *Journal of Obesity*.

17. Duncan SH., *et al*. "Human colonic microbiota associated with diet, obesity and weight loss". *International Journal of Obesity* 32.11 (2008): 1720-1724.

18. Schwiertz A., *et al*. "Microbiota and SCFA in lean and overweight healthy subjects". *Obesity* 18.1 (2010): 190-195.

19. de Vos WM and de Vos EA. "Role of the intestinal microbiome in health and disease: from correlation to causation". *Nutrition Reviews* 70.1 (2012): S45-S56.

20. Saika K and Watanabe S. "Producing rinse-free rice by the bran-grind method: A way to stop environmental pollution from rice industry waste water". *Advances in Food Technology and Nutritional Sciences-Open Journal* 3.1 (2017): 45-50.

21. Watanabe S., *et al*. "Medical rice: A new wax-free brown rice and its protein reduced rice". *Advances in Food Technology and Nutritional Sciences-Open Journal* 4.1 (2018): 10-16.

22. Takei N., *et al*. "Low-protein rice (LPR) product: Processing method and product safety". *Advances in Food Technology and Nutritional Sciences-Open Journal* 3.1 (2017): 33-41.

23. Takebayashi J., *et al*. "Estimated average daily intake of antioxidants from typical vegetables consumed in Japan: A preliminary study". *Bioscience, Biotechnology, and Biochemistry* 74.10 (2010): 2137-2140.

24. Tatsumi Y., *et al*. "Seasonal differences in total antioxidant capacity intake from foods consumed by a Japanese population". *European Journal of Clinical Nutrition* 68.7 (2014): 799-803.

25. Cao G., *et al*. "Oxygen-radical absorbance capacity assay for antioxidants". *Free Radical Biology and Medicine* 14.3 (1993): 303-311.

26. Masumura T and 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.

27. Watanabe S. "Low-protein diet for the prevention of renal failure". *Proceedings of the Japan Academy. Series B, Physical and Biological Sciences* 93.1 (2017B): 1-9.

28. The Japanese Society for Dialysis Therapy.

29. Kopple JE., *et al*. "Effect of dietary protein restriction on nutritional status in the modification of diet in renal disease study". *Kidney International* 52.3 (1997): 778-791.

30. Kopple JD and Massry SG. "Nutritional Management of Renal Disease". Baltimore, Maryland, USA: Williams and Wilkins (1997).

31. Mizuno S. "A secondary analysis of Ideura data of low protein diet practice for progressive chronic kidney disease patients". *Clinical and Functional Nutriology* 1.5 (2009): 242-245.

32. Palatini P. "Glomerular hyperfiltration: a marker of early renal damage in pre-diabetes and pre-hypertension". *Nephrology Dialysis Transplantation* 27.5 (2012): 1708-1714.

33. Taal MW and Brenner BM. "Renoprotective benefits of RAS inhibition: from ACEI to angiotensin II antagonists". *Kidney International* 5.57 (2000): 1803-1817.

34. Mallamaci F., *et al*. "ACE inhibition is renoprotective among obese patients with proteinuria". *American Society of Nephrology* 22.6 (2011): 1122-1128.

35. Sun J-Q and 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 Standardization of Rice Function (2014): 49-50.

36. Zoccali C., *et al*. "Phosphate may promote CKD progression, attenuate renoprotective effect of ACE inhibition". *Journals of the American Society of Nephrology* 22.10 (2011): 1923-1930.

37. Cochrane Database of Systematic Reviews.

38. Watanabe S. "Evaluation of modification of diet in renal disease (MDRD) Study". *Clinical and Functional Nutriology* 1.5 (2009): 238-241.

39. World Health Organization (WHO). Diet, food supply and obesity in the Pacific. Manila, Philippines: WHO West Pacific Regional Office (2003).

40. Papademetrou MK. "Rice production in the Asia Pacific Region: Issues and perspectives". Food and Agriculture Organization of the United Nations.

41. Hirakawa A., *et al*. "Brown rice is the complete meal". *Journal of Anti-Aging Medicine* 8.4 (2012): 585-591.

42. Shimabukuro M., *et al*. "Effects of brown rice diet on visceral obesity and endothelial function: The BRAVO study". *British Journal of Nutrition* 111.2 (2013): 310-320.

43. Nakamura S., *et al*. "Palatable and bio-functional wheat/rice bread from pre-germinated brown rice of super hard cultivar, EM10". *Bioscience, Biotechnology, and Biochemistry* 74.6 (2010): 1164-1117.

44. Tungtrakul P. "Innovative rice products in Thailand". Proceedings of the East Asia Conference on Standardization of Rice Function. Kyoto, Japan (2013) 61-62.

Volume 14 Issue 2 February 2019