European Journal of Clinical Nutrition (2011) 65, 864–871

0954-3007/11

www.nature.com/ejcn

ORIGINAL ARTICLE

Beta-glucan- or rice bran-enriched foods: a comparative crossover clinical trial on lipidic pattern in mildly hypercholesterolemic men

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Background/ Objectives: There has been growing interest in using dietary intervention to improve the lipid profile. This work aims at analyzing the effects and the comparison of the enrichment of a diet with beta-glucans or rice bran in mildly hypercholesterolemic men.

Subjects/Methods: The subjects initially consumed a 3-week Step 1 American Heart Association diet with rice bran-enriched foods. After this adaptation period, volunteers were randomly assigned to follow a crossover, controlled trial that consisted of two treatment with beta-glucan- or rice bran-enriched foods, each of 4 weeks, with a 3-week wash-out, like the adaptation period, between periods. Fasted blood samples were collected on days 0, 21, 49, 70 and 98 in both study arms for measuring low-density lipoprotein (LDL)-cholesterol (primary outcome), total cholesterol, high-density lipoprotein (HDL)-cholesterol, triglycerides, apolipoprotein (apo) A-I, apo B and glucose levels.

Results: Twenty-four men (mean age: 50.3 ± 5.3, mean body mass index: 24.9 ± 1.9) completed the 14-week trial. Subjects in the 3-week adaptation period experienced significant reductions in the mean change of LDL cholesterol, total cholesterol, total cholesterol/HDL cholesterol, LDL cholesterol/HDL cholesterol, apo A-I, apo A-I/apo B and glucose. During the intervention diet periods, a difference was found between treatment groups for the mean change in LDL (0.21 (95% confidence interval (CI): 0.02–0.40), $P=0.033$) and total cholesterol (0.34 (95% CI: 0.20–0.47), $P<0.001$). Other parameters evaluated were not significantly affected by the diet consumed.

Conclusions: The results of the present crossover clinical trial showed that beta-glucan-enriched foods are more effective in lowering serum LDL levels, compared with rice bran-enriched foods.

European Journal of Clinical Nutrition (2011) **65,** 864–871; doi:10.1038/ejcn.2011.48; published online 20 April 2011

Keywords: serum cholesterol; dietary fiber; beta-glucan; barley; rice bran

Introduction

Lowering serum cholesterol reduces the risk of coronary heart disease (National Cholesterol Educational Program, Adult Treatment Panel III, 2002). The protective effects of dietary fiber against cardiovascular disease (CVD), mediated through a reduction in serum lipids, were first reported >40 years ago by Keys *et al.* (1960); later research led to the dietary fiber hypothesis proposed by Burkitt *et al.* (1974) and Trowell (1975) that states that a high intake of starchy carbohydrates and fiber is protective against CVD. Many trials showed a hypocholesterolemic effect of an increased intake of fiber from cereals, such as barley, rice and oats; the active component in barley has been identified as beta-glucans, which reduces serum total cholesterol by 5–10% (according to Anderson, 1987; McIntosh *et al.*, 1991; Shimizu *et al.*, 2008; Talati *et al.*, 2009) and by 20% (according to Behall *et al.*, 2004), although not all studies

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Received 28 September 2010; revised 17 February 2011; accepted 9 March 2011; published online 20 April 2011

(Keogh *et al*., 2003) showed barley beta-glucans to be hypocholesterolemic.

Although all the possible mechanisms explaining the cholesterol-lowering effect of beta-glucans are not well known, the most likely explanation is that water-soluble fibers lower the re-absorption of bile acids (Kirby *et al*., 1981; Lia *et al*., 1995). As a result, the hepatic conversion of cholesterol into bile acids increases and the hepatic pools of free cholesterol decrease. Consequently, hepatic low-density lipoprotein (LDL)-cholesterol receptors become upregulated to re-establish hepatic cholesterol stores, thus promoting a decrease of serum LDL cholesterol (Reihner *et al*., 1990). Moreover, a recent study showed that the reduced intestinal fatty acid uptake observed with beta-glucans is associated with the inhibition of genes regulating intestinal uptake and with synthesis of lipids (Drozdowski *et al*., 2010).

As regards rice, active components with cholesterol-lowering effect have been identified in bran and are, over insoluble fiber, novel compounds such as desmethyl tocotrienol and didesmethyl tocotrienol (Qureshi *et al*., 2000), gamma-oryzanol (Sugano *et al*., 1999) and polyphenolic ferulic acid (Wilson *et al*., 2007).

In recent years, the US Food and Drug Administration has endorsed the relationship between an increase in soluble fiber and a decrease in serum total cholesterol by ratifying health claims for barley (FDA, 2005). Overall, the question as to whether various types of fibers exert different effects, and if so to what extent, is not yet conclusive (Brown *et al*., 1999); moreover, results from different clinical trials vary depending on whether dietary fiber is given to volunteers as a natural ingredient in food sources or as an isolated food supplement.

Given this background, this study aimed (I) at testing the effects of beta-glucan-enriched food on lipid pattern in mildly hypercholesterolemic men and (II) at comparing, in a crossover clinical trial, the effects of a soluble fiber (beta-glucans from barley) and an insoluble fiber (bran from rice) on lipid levels in this population.

Subjects and methods

Subjects

Subjects were recruited from Pavia by advertising in national newspapers and were screened through a procedure involving a clinical evaluation, an interview and an estimation of plasma total and LDL cholesterol levels.

Twenty-four men aged 18–60 years, body mass index 19–30 kg/m^2, with mild hypercholesterolemia (5.4–7.0 mmol/l) and no history of CVD, volunteered for the trial. The men were not taking any medication that was likely to affect lipid metabolism and they were free of overt liver, renal, metabolic disease such as diabetes and thyroid disease. Screening excluded men who smoked or drank more than two standard alcoholic beverages per day (20 g per day of alcohol). The experimental protocol was approved by the Ethics Committee of the University of Pavia and volunteers gave their written informed consent.

Before beginning the study, energy and nutrient intakes of the volunteers were assessed using the food record method for 3 days. Once the data were collected, the food intake registered was converted into energy and nutrients using the Rational Diet (Milan, Italy).

Diets were fed in a crossover manner. The intervention consisted of an adaptation period (3 weeks) and two diet periods (beta-glucan- and rice bran-enriched foods, 4 weeks each), with a wash-out period (3 weeks) in between (Figure 1).

At adaptation and during the wash-out period, subjects consumed a Step 1 American Heart Association diet (American Heart Association, 1988) consisting of a 7-day rotating menu enriched with rice bran fiber (on average 30 g per day). Each week, volunteers were supplied with foods and instructed to use them within a personalized normocaloric and balanced diet prepared by a dietitian on the basis of a specific single subject's requirement of energy and nutrients. As regards beta-glucan-enriched foods, every day each subject consumed 100 g of pasta with beta-glucans, together with tomato sauce with beta-glucans (100 g), 200 g of vegetable

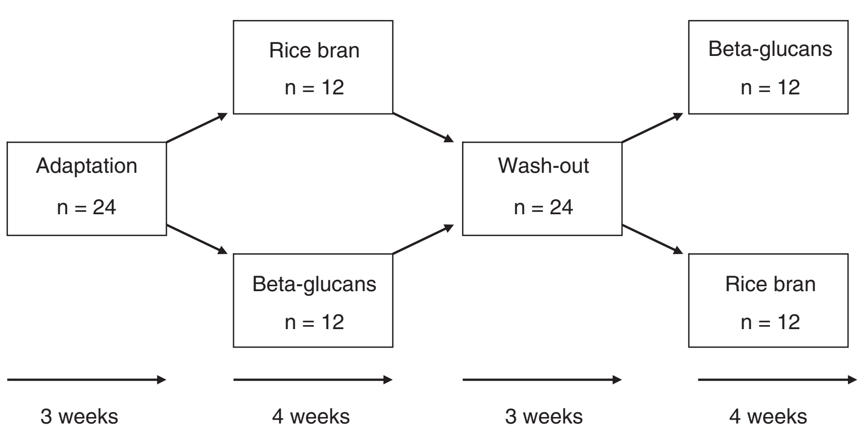

Figure 1 Summary of the treatment periods and the study design.

Table 1 Nutritional composition of 100 g of foods enriched with beta-glucans or rice bran

	Rice pasta enriched with beta-glucans	*Whole pasta*	*Bread rice enriched with beta-glucans*	*Bread rice enriched with rice bran*	*Rice cakes with beta-glucans*	*Rice cakes with rice bran*	*Tomato sauce with beta-glucans*	*Tomato sauce with rice bran*	*Vegetable soup with beta-glucans*	*Vegetable soup with rice bran*
Energy (kJ)	1459	1429	1142	1159	1515	1652	292	330	150	197
Protein (g)	7.0	12.5	9.8	9.3	9.6	8.8	2.3	2.3	2.8	2.3
Fat (g)	1.9	2.0	4.8	5.3	1.6	3.9	4.1	5.0	0.7	1.6
Saturated fatty acids (g)	0.8	0.5	1.15	1.27	0.7	1.04	0.98	1.15	0.23	0.73
Carbohydrate (g)	74.7	67.2	45.4	45.1	76.0	77.7	4.2	3.9	3.3	4.6
Complex (g)	70.4	63.7	40.0	42.88	75.7	76.68	0.62	1.06	1.64	3.64
Simple (g)	4.3	3.5	5.4	2.22	0.3	1.02	3.58	2.84	1.66	0.96
Dietary fiber (g)	3.5	7.3	3.3	4.8	4.0	4.6	3.7	4.9	2.6	2.5
Insoluble (g)	2.1	7.1	2.0	3.3	3.0	4.1	2.1	3.9	1.5	2.1
Soluble (g)	1.4	0.2	1.3	1.5	1.0	0.5	1.6	1.0	1.1	0.4
Beta-glucans (g)	1.7	—	1.2	—	1.4	—	1.5	—	0.9	—

soup with beta-glucans, 95 g of bread with beta-glucans (four slices) and 55 g of rice cakes with beta-glucans (seven rice cakes). As regards rice bran-enriched foods, every day each subject consumed 100 g of whole pasta together with tomato sauce with rice bran (100 g), 200 g of vegetable soup with rice bran, 95 g of bread with rice bran (four slices) and 55 g of rice cakes with rice bran (seven rice cakes).

Intervention foods

Palatable, beta-glucan- or rice bran-enriched foods were developed and manufactured by Riso Scotti (Pavia, Italy).

The rice pasta with beta-glucans was produced using 91% rice flour, 2% rice germ and 7% Barley Balance (PolyCell Technologies, Crookston, MI, USA), which is a type of beta-glucan-enriched barley flour. Barley Balance is a dry, processed, high-molecular-weight beta-glucan concentrate that contains about 30% beta-glucans (method: AOAC 995.16, 18th edn, 2005). Control rice pasta was produced using 100% whole durum wheat instead of rice flour, rice germ and Barley Balance.

The rice cakes with beta-glucans were produced using rice and water, except for replacing 7% of rice with Barley Balance (6%) and rice germ (1%). Control rice cakes were prepared replacing 100% Barley Balance with Orybran (Riso Scotti), a type of rice bran.

The bread with beta-glucans was produced on a laboratory scale. To obtain 1 kg of wheat flour type '0', 0.55 kg of rice flour, 0.05 kg of rice germ, 0.15 kg of Barley Balance, 1.5 kg of water, 0.1 kg of rice oil, 0.08 kg of 0.06 dextrose, 0.035 g of salt and 0.055 yeast were used. The control bread was produced in the same manner, except for replacing 100% Barley Balance with Orybran.

The sauces with beta-glucans, packed in single pouches, were produced by mixing, for each pouch, 71 g of water, 31 g of tomatoes, 6 g of rice oil, 6 g of Barley Balance, 6 g of mixed vegetables and 0.5 g of salt. The control sauces were produced replacing 100% Barley Balance with Orybran.

The cream soups with beta-glucans, packed in a single pouch, were produced by mixing, for each pouch, 98 g of water, 95 g of mixed vegetables, 6 g of Barley Balance and 0.5 g of salt. The control cream soups were produced replacing 100% Barley Balance with Orybran.

The chemical composition of enriched foods is presented in Table 1.

Nutritional status

Every week, body weight was assessed and body mass index was calculated. Skinfold thicknesses, assessed following a standardized technique (Frisancho, 1984), and sagittal abdominal and waist girth were measured on days 0, 21, 49, 70 and 98.

Health-related quality of life

The studied subjects were tested using the Short-Form 36-Item Health Survey (SF-36) (Ware *et al*., 1993) in order to evaluate their quality of life.

The Wexner score for constipation was assessed (Agachan *et al*., 1996).

Analyses

Fasted blood samples were collected between 0745 and 1000 hours on days 0, 21, 49, 70 and 98 in both study arms for measuring direct LDL-cholesterol, total cholesterol, high-density lipoprotein (HDL)-cholesterol, triglycerides, apolipoprotein (apo) A-I, apo B and glucose levels. These parameters were measured enzymatically using an autoanalyzer (Hitachi, Tokyo, Japan).

Compliance and palatability
Sensory acceptance of the enriched foods and treatment-related side effects were assessed at each study visit.

Statistical analysis
Sample size. The difference in levels in LDL-cholesterol after 4 weeks of treatment (primary end point) was used to compute the sample size of the study. Computations were based on data from McIntosh *et al*. (1991). A sample size of 24 will have 80% power to detect a difference of 0.33 mmol/l in means (corresponding to final LDL-cholesterol levels of 4.87 mmol/l in control and 4.54 mmol/l in treated patients), assuming a common standard deviation (s.d.) of differences of 0.54, using a paired Student's *t*-test with a 0.050 two-sided significance level. After accounting for a 10% dropout rate, we planned to enroll 26 patients per group. Query advisor 4 (Statistical Solutions, Cork, Ireland) was used.

Randomization and masking. A randomly permuted block randomization list for the two possible sequences was generated. Masking was guaranteed by identical packages for both treatments, labeled with A or B according to the randomization arm.

Analysis of the primary and secondary end points. Descriptive statistics were computed for each treatment and end point (mean and s.d. for continuous variables and counts and % for categorical variables). Mean changes from screening to baseline and from baseline to the final values of the considered outcome variables were computed for each arm, together with their 95% confidence intervals (95% CI), and assessed with the paired Student's *t*-test. For both primary and secondary end points, the final levels of LDL-cholesterol (and other biological parameters) were compared between treatments with a multilevel mixed-effects linear regression (with a random effect for patients and unstructured covariance), including also baseline values and period as covariates. The treatment effect was presented as the mean difference between final values (95% CI), adjusted for baseline values and period effect.

A two-sided *P*-value <0.05 was considered statistically significant. Stata 11 (StataCorp., College Station, TX, USA) was used for computation. *Post hoc* comparisons within treatments were tested at the 0.025 level (Bonferroni correction).

Results

Dietary intake and body weight
The nutritional composition of the diets consumed daily by the volunteers at screening and during the different periods of the trial is shown in Table 2. Body mass index remained stable (at screening: 24.92 ± 1.93; at the end of the study: 24.82 ± 2.01).

Cardiovascular risk variables
All the 24 men (mean age: 50.33 ± 5.34) completed the 14-week trial and their characteristics at the commencement and at the end of the 3-week adaptation period of the study are shown in Table 3.

Subjects in the 3-week adaptation period experienced significant reductions in the mean level of lipid and glucose parameters (Table 3): the average percentage reduction in LDL, total cholesterol, apo A-I and glucose was 13, 8, 14 and 3%, respectively.

The effects of intervention diets on cardiometabolic risk variables are summarized in Table 4. During the intervention diet periods, a difference of 0.21 mmol/l was found between the treatment groups for the mean change of the primary end point, which is the LDL-cholesterol ($P<0.033$); the decrease was greater in the beta-glucans group than in the rice bran arm ($P=0.012$ and 0.66, respectively): the average percentage reduction in LDL-cholesterol was 8.6% in the beta-glucans arm and only 1.1% in the rice bran arm.

Further, a difference was found between the treatment groups for the mean change of total cholesterol ($P<0.001$); the decrease in total cholesterol was significant only in the beta-glucans group and not in the rice bran arm ($P=0.001$ and 0.25, respectively): the average percentage reduction in total cholesterol was 5.0% in the beta-glucans arm and the average percentage increase in total cholesterol in the rice bran arm was 1.3%.

Serum lipid profile and glucose were not significantly affected by the diet consumed in both groups; hence, no significant intergroup difference was observed for these parameters.

Health-related quality of life
As regards the SF-36 score, the results showed that treatment with beta-glucans did not have a different effect from treatment with rice bran (Table 4).

The mean changes in the scores of the Wexner scale were not significantly different in both groups, although the final score was lower in the latter (Table 4).

Compliance and palatability
Treatment was well tolerated by all subjects, with excellent compliance. The fact that there were no study dropouts further indicates the tolerability of the study treatments. No adverse events were reported.

Discussion

The effect of dietary fiber on cholesterol metabolism has been studied extensively (Keys *et al*., 1960; Burkitt *et al*., 1974; Trowell, 1975), even if results between studies on the effects of different kinds of fibers on LDL-cholesterol concentrations are variable (Anderson, 1987; McIntosh *et al*., 1991; Talati *et al*., 2009). This variability may be due to several

Table 2 Nutritional intakes of volunteers' previous enrolment in the crossover clinical trial and nutritional composition of total diet and of foods enriched with beta-glucans or rice bran and of other nutrients consumed daily by the volunteers during the different periods of the crossover clinical trial

	Pretreatment period[a]	*Periods 1 and 3 total diet*[a]	*Beta-glucans period*[a]		*Rice bran period*[a]	
			Total diet	*Foods enriched with beta-glucans*	*Total diet*	*Foods enriched with rice bran*
Energy (kJ)	11058.73 (780.87)	11181.87 (754.56)	10972.3 (391.63)	3972.88	11166.69 (688.47)	4167.58
Protein (g)	96.67 (18.17)	79.41 (6.72)	85.81 (6.89)	29.49	88.95 (6.55)	33.07
(% energy)	14.72 (3.11)	11.89 (0.74)	12.95 (0.79)	—	13.38 (0.71)	—
Fat (g)	81.77 (16.49)	73.91 (5.08)	78.29 (3.39)	12.81	80.60 (3.53)	17.37
(% energy)	27.81 (5.17)	24.92 (1.27)	26.65 (1.73)	—	27.32 (1.35)	—
Saturated fatty acids (%)	9.58 (2.92)	6.09 (1.05)	6.22 (1.56)	—	6.55 (1.65)	—
Carbohydrate (g)	404.16 (62.88)	447.32 (35.27)	406.24 (31.38)	170.74	397.96 (34.04)	166.21
(%)	57.28 (7.61)	62.74 (1.31)	57.44 (1.53)	—	56.03 (1.59)	—
Complex (g)	326.04 (57.28)	357.62 (35.98)	302.44 (33.20)	154.29	305.73 (41.93)	155.29
(%)	46.18 (6.97)	50.11 (2.08)	42.72 (2.76)	—	42.16 (2.59)	—
Simple (g)	78.01 (20.27)	89.70 (9.44)	103.79 (8.48)	16.44	98.16 (8.60)	10.92
(%)	11.10 (2.93)	12.63 (1.55)	14.72 (1.35)	—	13.87 (1.35)	—
Dietary fiber (g)	19.73 (3.03)	26.74 (3.16)	39.33 (3.33)	17.74	45.70 (3.49)	24.29
Soluble (g)	7.01 (1.10)	9.12 (0.91)	13.74 (0.93)	6.98	10.36 (0.95)	3.69
Insoluble (g)	12.69 (2.21)	17.62 (2.44)	24.89 (2.15)	10.76	34.63 (2.24)	20.60
Beta-glucans (g)		—	5.99	5.99	—	—
Cholesterol (mg)	287 (89)	275 (93)	279 (99)		281 (93)	

[a]Mean (s.d.); Nutritional evaluation from Carnovale E, Marletta L: 'Tabelle di composizione degli alimenti', Istituto Nazionale della Nutrizione, Roma, 1997 and from the results of the laboratory assessment, according to the following methods: Proteins: Protein determination through acid-catalyzed mineralization, with alkaline ammoniacal nitrogen. The ammonia produced is determined through titrimetric measuring. The value of ammonia obtained is multiplied for the factor 6.25 (ISO 937-1978 (E), AOAC Official Method 'Nitrogen in Beer' 950.53, AOAC Official Method 'Nitrogen in Liquid eggs' 932.08, AOAC Official Method 'Nitrogen in milk' 991.20, AOAC Official Method 'Nitrogen in wines' 920.70). Fats: Determination by gravimetric, with acid hydrolysis of the sample and subsequent extraction with petroleum ether in Soxhlet (ISTISAN 1996/34, pp 41–43). Fatty acids: The methyl esters obtained by transmethylation of fatty material are separated in capillary gas chromatography column (Method NGD C2—1989; Method NGC C41/42—1976, Regulation (CEE) No. 2568/91; Method COI/T.20/Doc. No. 24—2001, Regulation (CE) No. 796/2002). Carbohydrates: Value obtained by difference to 100, with known values of water, ash, fat, protein and dietary fibers content in the food. Simple sugars: The sugars are extracted with hot water, clarified with the Carez reagent and silanized. The revelation of the trimethylsilyl ethers is carried out in gas chromatography (GC-FID) on a capillary column. Dietary fibers: Gravimetric determination—with enzymatic precipitation of soluble fiber with hot ethanol (AOAC 985.29 and 17th 2003).

Table 3 Cardiovascular risk variables at screening and after adaptation period

Parameter	*At screening*[a]	*After adaptation period*[a]	*Mean change (95% CI)*	P*-value*
LDL-cholesterol (mmol/l)	4.17 (0.56)	3.64 (0.86)	−0.53 (−0.79 to −0.26)	<0.001
Total cholesterol (mmol/l)	6.44 (0.55)	5.90 (0.68)	−0.54 (−0.75 to −0.33)	<0.001
HDL-cholesterol (mmol/l)	1.52 (0.42)	1.61 (0.49)	0.09 (−0.07 to 0.24)	0.28
Total cholesterol/HDL-cholesterol	4.58 (1.45)	4.03 (1.32)	−0.55 (−0.88 to −0.22)	0.002
LDL-cholesterol/HDL-cholesterol	3.00 (1.06)	2.55 (1.09)	−0.45 (−0.75 to −0.15)	0.005
Apolipoprotein A1 (g/l)	1.31 (0.31)	1.15 (0.23)	−0.16 (−0.23 to −0.09)	<0.001
Apolipoprotein B (g/l)	1.27 (0.20)	1.31 (0.23)	0.04 (−0.04 to 0.12)	0.33
Apolipoprotein A1/apolipoprotein B	1.06 (0.33)	0.91 (0.27)	−0.15 (−0.21 to −0.09)	<0.001
Triglycerides (mmol/l)	1.63 (0.99)	1.42 (0.82)	−0.21 (−0.50 to 0.09)	0.16
Glucose (mmol/l)	5.21 (0.36)	5.04 (0.38)	−0.17 (−0.30 to −0.05)	0.009

Abbreviations: CI, confidence interval; LDL, low-density lipoprotein; HDL, high-density lipoprotein.
[a]Mean (s.d.).

factors, such as fiber intake, baseline serum cholesterol concentrations, mode of administration, food matrix, and solubility or molecular weight of the fiber. This study was dedicated to comparatively studying, by a crossover clinical trial, the effects of two different kinds of dietary fibers on lipidemic pattern in mildly hypercholesterolemic subjects. To our knowledge, this is the first time that water-soluble fiber beta-glucans and non-soluble fiber rice bran have been

Table 4 Comparison of treatments on cardiovascular risk variables, the mental component summary and physical component summary of SF-36 score and Wexner score for constipation at baseline and at the end of intervention

Parameter	*Treatment*	*Baseline* [a]	*Final, after 4 weeks of intervention periods* [a]	*Mean change (95% CI)*	*P-value for change*	*Treatment effect* [b]	*Treatment comparison P-value*
LDL-cholesterol (mmol/l)	**Beta-glucans**	**3.84 (0.64)**	**3.51 (0.66)**	**−0.33 (−0.58 to −0.08)**	**0.012**	**−0.21 (−0.40 to −0.02)**	**0.033**
	Rice bran	**3.68 (0.87)**	**3.63 (0.63)**	**−0.04 (−0.29 to 0.19)**	**0.66**		
Total cholesterol (mmol/l)	Beta-glucans	6.14 (0.53)	5.83 (0.46)	−0.30 (−0.47 to −0.14)	0.001	−0.34 (−0.47 to −0.20)	<0.001
	Rice bran	5.99 (0.72)	6.07 (0.57)	0.08 (−0.06 to 0.23)	0.25		
HDL-cholesterol (mmol/l)	Beta-glucans	1.65 (0.41)	1.70 (0.49)	0.05 (−0.13 to 0.23)	0.59	0.01 (−0.10 to 0.11)	0.91
	Rice bran	1.65 (0.46)	1.68 (0.49)	0.03 (−0.09 to 0.16)	0.58		
Total cholesterol/HDL-cholesterol	Beta-glucans	3.94 (1.01)	3.76 (1.26)	−0.18 (−0.57 to 0.21)	0.35	−0.18 (−0.38 to 0.01)	0.07
	Rice bran	3.96 (1.32)	3.96 (1.46)	0.00 (−0.37 to 0.37)	1.00		
LDL-cholesterol/HDL-cholesterol	Beta-glucans	2.51 (0.84)	2.33 (1.05)	−0.18 (−0.54 to 0.17)	0.30	−0.11 (−0.26 to 0.04)	0.17
	Rice bran	2.44 (1.03)	2.38 (1.07)	−0.07 (−0.36 to 0.23)	0.64		
Apolipoprotein A1 (g/l)	Beta-glucans	1.15 (0.22)	1.13 (0.21)	−0.02 (−0.08 to 0.05)	0.61	−0.06 (−0.13 to 0.01)	0.10
	Rice bran	1.12 (0.21)	1.15 (0.24)	0.04 (−0.04 to 0.11)	0.31		
Apolipoprotein B (g/l)	Beta-glucans	1.23 (0.17)	1.10 (0.12)	−0.14 (−0.09 to −0.18)	<0.001	−0.04 (−0.09 to 0.01)	0.12
	Rice bran	1.18 (0.21)	1.11 (0.11)	−0.07 (−0.01 to −0.14)	0.03		
Apolipoprotein A1/apolipoprotein B	Beta-glucans	0.95 (0.23)	1.06 (0.29)	0.11 (0.18 to 0.04)	0.004	0.02 (−0.06 to 0.10)	0.58
	Rice bran	0.98 (0.28)	1.06 (0.30)	0.08 (0.13 to 0.03)	0.005		
Triglycerides (mmol/l)	Beta-glucans	1.41 (0.72)	1.36 (0.61)	−0.05 (−0.27 to 0.18)	0.67	−0.19 (−0.48 to 0.10)	0.20
	Rice bran	1.38 (0.84)	1.55 (0.85)	0.17 (−0.16 to 0.50)	0.29		
Glucose (mmol/l)	Beta-glucans	4.97 (0.48)	4.82 (0.56)	−0.15 (−0.33 to 0.03)	0.10	−0.08 (−0.29 to 0.13)	0.44
	Rice bran	4.88 (0.36)	4.81 (0.46)	−0.08 (−0.27 to 0.11)	0.42		
SF-36 physical component summary	Beta-glucans	52.35 (8.13)	53.32 (7.11)	0.97 (−1.06 to 3.00)	0.33	0.89 (−0.17 to 1.96)	0.10
	Rice bran	52.35 (8.13)	54.25 (7.20)	1.90 (−0.17 to −3.62)	0.032		
SF-36 mental component summary	Beta-glucans	53.87(10.88)	56.47 (8.83)	2.60 (−0.27 to −4.94)	0.03	−0.31 (−1.39 to 0.77)	0.57
	Rice bran	53.87(10.88)	56.17 (8.88)	2.30 (−0.33 to −4.93)	0.08		
Wexner score for constipation	Beta-glucans	2.46 (2.93)	2.29 (2.90)	−0.17 (−0.55 to 0.22)	0.38	0.55 (−0.08 to 1.17)	0.09
	Rice bran	2.65 (2.35)	1.91 (2.48)	−0.74 (−0.20 to −1.28)	0.01		

Abbreviations: LDL, low-density lipoprotein; HDL, high-density lipoprotein; SF-36, Short-Form 36-Item Health Survey.
[a]Mean (s.d.).
[b]Mean difference between final values (95% CI) adjusted for baseline values of each period and for period effect.
Bold entries emphasize that this result concerns the primary end point.

compared with regard to their efficacy on lipid pattern in a crossover study. The studied fiber sources, namely, beta-glucans from barley and bran from rice, were selected from among cereals because of their particular hypocholesterolemic properties, the mechanisms of action of which on lipidic pattern are very different. Beta-glucans are water-soluble dietary fibers, having gel-forming properties that cause effects on lipid pattern (Marlett *et al*., 1994; Drozdowski *et al*., 2010), whereas rice bran is a water-insoluble fiber with active components having a cholesterol-lowering effect (Qureshi *et al*., 2000; Wilson *et al*., 2007).

The first result of this trial is that the subjects after the 3-week adaptation period with rice bran-enriched foods experienced significant reductions in blood LDL-cholesterol, total cholesterol, apo A-I, total/HDL-cholesterol and glucose, in agreement with previous large studies (Keys *et al*., 1960; Burkitt *et al*., 1974; Trowell, 1975; Cheng *et al*., 2010). The mean fiber intake of the volunteers before the start of the study (12 ± 2 g per day) was lower than the recommended daily intake (30 g per day), in agreement with previous studies on the adherence of the general Italian population to the recommendations for correct nutritional behavior (Avellone *et al*., 1997; Rivellese *et al*., 2008). The increase in the intake of fiber, including water-insoluble fiber, such as rice bran, caused a significant cholesterol-lowering effect. These results show that therapeutic dietetic changes remain an essential modality in clinical management of hypercholesterolemia (Grundy *et al*., 2004).

Moreover, the comparison of the treatment effects clearly indicated that beta-glucans fiber exhibited the most marked influence on cholesterolemia: in the study, participants receiving beta-glucan-enriched foods had statistically significant reductions in LDL-cholesterol (−0.33 mmol/l) and total cholesterol (−0.31 mmol/l), compared with participants receiving rice bran-enriched foods. In reality, the therapy of mild hypercholesterolemia is lacking. The use of statins, the 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors that are the mainstay in the pharmacological management of dyslipidemia, has been reserved in patients with at least one other risk of CVD. Moreover, the unwanted side effects of statins are numerous, frequent and dangerous (Kostapanos *et al*., 2010). On the contrary, the consumption of foods enriched in beta-glucans has no known side effects, and, moreover, permits a higher intake per serving with a minimum decrease in palatability (Jenkins *et al*., 2002). The food products used in this study were developed taking into consideration the problem of compliance. Rice bread and pasta, sauces and soups enriched with beta-glucans are ready to use and are hence easy to eat. Moreover, these foods are well known to contain adequate amounts of beta-glucans and rice bran because the analysis for the amount of fibers has been carried out in finite products. Finally, another possible advantage of beta-glucan-enriched foods compared with drug therapy is lower costs.

A limitation of the study is that it was conducted exclusively in a group of men. The choice of including only men in the study accrued from two considerations: (1) hypercholesterolemia is a disease more commonly found in male subjects than in female subjects; and (2) many confounding factors related to hormonal status (cycle time, pre-, peri- or post-menopausal phase) may be present in women. Further studies are needed to collect evidence in women.

As regards health-related quality of life, there were no significant differences for the SF-36 scores; the results of this study showed that general health parameters in each group did not differ from each other at baseline and did not change appreciably during the course of the study. A significant change in the SF-36 was not expected; it was included in this study to rule out any adverse effects on general health functioning in either group.

In conclusion, health practitioners should feel comfortable recommending barley beta-glucan-enriched foods to their patients with mild hypercholesterolemia to help reduce total and LDL-cholesterol concentrations. It is well established that an elevated LDL-cholesterol concentration is a risk factor for CVD (National Cholesterol Educational Program, Adult Treatment Panel III, 2002). Studies have shown that, for each milligram per deciliter (0.0026 mmol/l) reduction in a patient's LDL-cholesterol level, their relative risk of having a coronary heart disease event is decreased by 1%; therefore, this reduction in LDL cholesterol observed with food enriched with beta-glucans is likely to be clinically significant as well (Grundy *et al*., 2004). Moreover, such changes in cardiovascular risk factors, when applied to the whole population, have significant potential for reducing CVD (Kottke *et al*., 1985).

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

We are grateful to the volunteers for their participation and commitment to the study, to Francesca Mendozza (Riso Scotti) for her coordination in the intervention foods preparation and to Marco Caspani (DKSH Italia s.r.l.) and Tom Jorgens (PolyCell Technologies) for their linguistic and conceptual revision.

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