EVALUATING THE EFFECT OF APPLYING THE FDA DEFINITION OF WHOLE GRAINS TO HEALTH CLAIMS FOR RISK REDUCTION OF CARDIOVASCULAR DISEASE AND DIABETES

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ABSTRACT

The U.S. Food and Drug Administration (FDA) defines whole grains as consisting of the intact, ground, cracked or flaked fruit of the grains whose principal components—the starchy endosperm, germ and bran—are present in the same relative proportions as they exist in the intact grain. The Life Sciences Research Office (LSRO) evaluated the effect of applying the FDA definition of whole grains on the strength of scientific evidence in support of claims for risk reduction of cardiovascular disease (CVD) and diabetes. We concluded that using the FDA definition for whole grains as a selection criterion is limiting because the majority of existing studies often use a broader meaning to define whole grains. When we considered only whole grain studies that met the FDA definition, we found insufficient scientific evidence to support a claim that whole grain intake reduces the risk of CVD. However, a whole grain and CVD health claim is supported when using a broader concept of whole grain to include studies that included intake of bran and germ as well as whole grains. The scientific evidence on the relationship of whole grain consumption and diabetes is suggestive but inconclusive whether or not the definition of whole grains was in accordance with that of the FDA. This type of analysis is complicated by variation among different types of whole grains due to their diversity in nutrients and bioactive components. This project was sponsored by Kellogg Company, USA.

LSRO STUDY OBJECTIVES

LSRO conducted an independent review of the scientific literature to evaluate the effect of applying the FDA definition of whole grains on the strength of scientific evidence in support of whole grains health claims for risk reduction of CVD and diabetes. This project was undertaken in consultation with an independent Expert Panel that was composed of scientific experts in the fields of epidemiology, nutrition, cereal chemistry, and food regulation.

LSRO STUDY APPROACH

LSRO conducted a literature search at MEDLINE for articles published through February, 2008. Keywords used were: (whole grain OR whole grains) AND (cardiovascular disease OR heart OR coronary heart disease OR stroke OR blood pressure OR myocardial infarction OR health OR diabetes). The inclusion criteria were derived from the specifications of the FDA guidelines for studies eligible to establish a health claim (U.S. Food and Drug Administration, 2007):

- Human intervention and observational studies;
- Studies that measured a validated endpoint or a surrogate endpoint for CVD and/or diabetes;
- Healthy US population and population representative of the U.S.

We first evaluated only studies that meet the FDA definition of whole grain (**FDA definition approach**). Later, we expanded our analysis to include additional studies that were conducted with whole grains but were not defined according to the FDA specifications or included bran or fiber (**Expanded approach**).

RESULTS

Five studies conformed to the FDA definition of whole grains. There was insufficient evidence to draw a firm conclusion about the effect of whole grain intake on the risk of CVD or diabetes when only these five studies were considered.

Reference	Study Design	Country	Gender	Age	Number of Subjects	Outcome
Andersson et al. 2007	Randomized Crossover	US	F/M	59 ± 5	22/8	Whole grain intake (112 g/day) for 6 weeks: CVD: no significant change in TC, LDL-C, or BP Diabetes: no significant change in fasting blood glucose, plasma insulin, and insulin resistance
Rave et al. 2007	Randomized Crossover	Germany	F/M	51 ± 13	18/13	Hypo-energetic diet with whole grain (200 g/day) compared with a hypo-energetic diet alone for 4 weeks CVD: no significant change in TC, LDL-C, or BP among the two treatments Diabetes: A hypo-energetic diet with whole grain improved fasting serum insulin (-1.8 ± 2.8 µU/mL) and HOMA-IR (-1 ± 0.2 µU/mL x mmol/L) both p < 0.05
Jensen et al. 2004	Prospective Cohort	US	M	40-74	42,850	CVD: RR=0.82 (95% CI: 0.70-0.96; *P* for trend = 0.01); whole grain intake 42.2 vs 3.5 g/d
Jensen et al. 2006	Cross-sectional	US	F/M	F: 25-42 M: 40-74	F: 470 M: 468	CVD: Reduction in total cholesterol (*P* for trend = 0.02); whole grain intake 43.8 vs 8.2 g/d
De Munter et al. 2007	Prospective Cohort	US	F	37-65	73,327	Diabetes: RR=0.63 (95% CI: 0.57-0.69; *P* for trend < 0.001); whole grain intake 31.2 vs 3.7 g/d
			F	26-46	88,410	Diabetes: RR=0.68 (95% CI: 0.57-0.81; *P* for trend < 0.001); whole grain intake 39.9 vs 6.2 g/d

References: Andersson et al. J Nutr 2007 (137):1401-1407; De Munter et al. Public Library of Science Medicine. 2007 (8):e261.; Jensen et al. Am J Clin Nutr 2004 (80):1492-1499; Jensen et al. Am J Clin Nutr 2006 (83):275-283; Rave et al. Br J Nutr 2007: 1-8. HOMA-IR: Homeostasis model assessment for insulin resistance; TC: total cholesterol; LDL-C: low density lipoprotein-cholesterol; BP: blood pressure.

When we expanded our analysis to include studies that were not restricted to the FDA definition of whole grains, the studies considered were as follows:

❖ **CVD**: 29 (15 intervention and 14 observational) studies. Intervention studies generally reported a beneficial effect and all 14 observational studies suggested a protective association between whole grain consumption and risk of CVD.

❖ **Diabetes**: 21 (10 intervention and 11 observational) studies. Results from intervention and observational studies were suggestive but inconclusive for the association between whole grain intake and risk of diabetes.

BACKGROUND

A whole cereal grain is the fruit (also known as the seed, caryopsis, or kernel) of plants belonging to the *Poaceae* (or *Gramineae*) family. Some examples of cereal grains are wheat, rice, barley, corn, rye, oats, millets, sorghum, teff, triticale, canary seed, Job's tears, fonio, and wild rice. Although all grains contain three anatomical parts (endosperm, bran, and germ) there is great variability among the whole grains in their content of macronutrients, micronutrients and bioactive components.

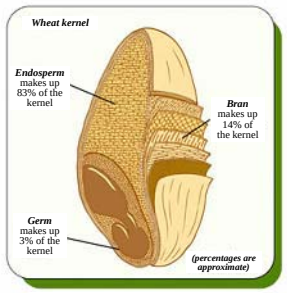

Figure 1. Wheat Kernel

Diversity of Whole Grain Composition

Nutrient[a]	Barley (hulled)	Oats	Rye	Wheat
Proximates				
Energy, Kcal	354	389	335	327
Protein, g	12.5	16.9	14.8	12.6
Total lipid, g	2.3	6.9	2.5	1.5
Carbohydrate[b], g	73.5	66.3	69.8	71.2
Fiber, total dietary, g	17.3	10.6	14.6	12.2
Minerals				
Calcium, mg	33	54	33	29
Iron, mg	3.6	4.7	2.7	3.2
Magnesium, mg	133	177	121	126
Phosphorus, mg	264	523	374	288
Potassium, mg	452	429	264	363
Sodium, mg	12	2	6	2
Zinc, mg	2.8	3.9	3.7	2.7
Copper, mg	0.5	0.6	0.5	0.4
Manganese, mg	1.9	4.9	2.7	4.0
Selenium, µg	37.7	-	35.3	70.7
Vitamins[c]				
Thiamin, mg	0.7	0.8	0.3	0.3
Riboflavin, mg	0.3	0.1	0.3	0.1
Niacin, mg	4.6	0.9	4.3	5.5
Pantothenic acid, mg	0.3	1.4	1.5	0.9
Vitamin B6, mg	0.3	0.1	0.3	0.3
Folate, µg	19	56	60	38
Choline, total, mg	-	-	30.4	31.2
Vitamin A, IU	22	0	11	9
Vitamin E [c], mg	0.6	-	1.3	1.0
Vitamin K, µg	2.2	-	5.9	1.9
Other				
Beta-carotene, µg	13	-	7	5
Lutein + Zeaxanthin, µg	160	-	210	220

Phytochemicals	Whole Cereal Grain				Bran			
	Barley	Oat	Rye	Wheat	Barley	Oat	Rye	Wheat
Lignan[2,3] (µg/100g)								
Total	58	13.7	112	35.5	63	179	299	110
Matairesinol	0	0.3	65	2.6	0	155	167	0
Secoisolariciresinol	58	13.4	47	32.9	63	24	132	110
Isoflavonoids[2] (µg/100g)								
Total	21.7	0	0	0	22.7	0	0	10.4
Daidzein	14	0	0	0	6.4	0	0	3.5
Genistein	7.7	0	0	0	16.3	0	0	6.9
Phenolic acids[4-6] (µg/g,dw)								
Total	478	9.4	1210	640	-	360	3360	5655
Ferulic	478	2.1	1035	640	-	360	2780	5410
Sinapic	-	-	120[b]	-	-	-	390	75
p-coumaric	-	7.3	55[b]	-	-	-	190[b]	170
Phenolic lipids[8-10] (µg/g)								
Alkylresorcinols	45	-	734	583	-	ND	2758	2211
Sterols[11] (mg/100g,wb)								
Total sterols	67.8	33.5	88.7	66.4	-	-	-	-
Campesterol	17	4	17	12	-	-	-	-
Campestanol	0.8	trace	8.3	6.5	-	-	-	-
Stigmasterol	3	1.6	3.4	1.9	-	-	-	-
Sitosterol	46	27	48	36	-	-	-	-
Sitostanol	1	0.9	12	10	-	-	-	-

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Whole Grain Health Claims

Health claims for food labels are authorized in the U.S. by two amendments to the Federal Food, Drug and Cosmetic Act: the Nutrition Labeling and Education Act of 1990 (NLEA) and the Food and Drug Administration Modernization Act (FDAMA) of 1997.

A FDAMA health claim addressing whole grains has been authorized by the FDA based on the following authoritative statement from the National Academy of Sciences (NAS) report :

"Diets high in plant foods—i.e., fruits, vegetables, legumes, and ***whole grain*** *cereals*—are associated with lower occurrence of CHD and cancers of the lung, colon, esophagus, and stomach."

At present, there are no health claims that relate grain products to diabetes.

CONCLUSIONS

❖ Using the FDA definition for whole grains as a selection criterion is limiting. This is because a consistent definition of whole grains has not been applied in existing research about risk of CVD and diabetes. As such, drawing specific conclusions on benefits of "whole grains" in general from the body of scientific evidence is confounded, typically with bran/dietary fiber.

❖ Whole grain consumption and CVD: there is no consistent scientific evidence to support a whole grain and CVD risk health claim if only whole grain studies that conform to the FDA whole grain definition are considered. However, a whole grain and CVD health claim is supported using a broader concept of whole grains, to include products with 25% bran content which was a common addition in the observational research.

❖ Whole grain consumption and Diabetes: the association is suggestive but inconclusive whether the analysis was restricted to studies that defined whole grain according to the FDA definition, or included studies using a wider classification of whole grains.

❖ Because whole grains differ in their type and amount of nutrients and bioactive components, the health benefits observed from consumption of one whole grain do not necessarily reflect the same type or magnitude of benefit from other whole grains.

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