PETITION FOR THE INCLUSION OF

BARLEY BETAFIBER

ON THE NATIONAL LIST OF ALLOWED SUBSTANCES IN ORGANIC FOODS 205.606

Cargill Regulatory & Scientific Affairs, MS #163 *15407 McGinty Road West, Wayzata MN 55391*

CBI Copy

Petition to Add to the National List 205.606: "Barley Betafiber"

JUN 0 1 2011

Appendix 1: Petition – CBI Deleted Version

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September 10, 2009 updated 5/25/2011 LwK

Dr. Barbara Robinson, Acting Program Manager
c/o Richard Matthews
USDA/AMS/TM/NOP
Room 4004-S
Ag Stop 0268
1400 Independence Ave., SW
Washington, DC 20250-0268

JUN 0 1 2011

Dear Dr. Robinson:

Re: Petition Requesting Addition of Barley Betafiber to National List 205.606

Enclosed is a petition requesting the inclusion of the non-organically produced agricultural substance "Barley betafiber" onto the National List section 205.606.

Barley betafiber (barley β-glucan) is a natural component of barley and has relatively recently been identified as providing health benefits to consumers. The FDA has approved a health claim for barley betafiber related to soluble fiber and reduced risk of heart disease. In addition, laboratory and clinical studies have shown the benefits of using β-glucans in the control of blood sugar. As a fiber source, it may also play a positive role as a tool for weight management by helping to promote satiety. Cargill, Incorporated respectfully submits this petition because we believe that consumers of organic foods would benefit from an enhanced level of barley betafiber in these foods and that this benefit is not easily derived from ingredients currently available for use in organic foods.

Eventually we expect that barley betafiber will be available in an organic form. In order to be certified, however, specific cultivars of barley must be grown as organic, a sufficient supply of organic ethanol must be located and the processing facility must be audited by the certifier to confirm it is suitable for manufacture of the organic barley betafiber. This is likely a several year conversion. Cargill has already begun investigating the possibility of organic cultivation of these strains of barley. In the meantime, Cargill is requesting addition of this agricultural ingredient to 205.606 in order to make it available to the organic market. Interest from the organic sector and sales of the ingredient will support efforts to convert barley betafiber to an organic source and organic processing.

Please contact me if you have any questions or if I can provide any additional information.

We appreciate your consideration of our request.

Sincerely,

Lore W Kolberg

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PETITION FOR THE INCLUSION OF

BARLEY BETAFIBER

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PETITION WITH CBI DELETED

Cargill Regulatory & Scientific Affairs MS 163

15407 McGinty Road West Wayzata, MN 55391

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Petition to Add to the National List 205.606: "Barley Betafiber"

Item A

1. Category

Non-organically produced agricultural products allowed in or on processed products labeled as "organic". §205.606.

2. Justification for this category

The petitioned substance is a natural component of an agricultural commodity -- barley. There are bonds broken in the process of isolating this component but this is achieved through the use of food grade enzymes, therefore, this substance is not synthetic. Barley betafiber is isolated through a process which has similarities to those used for inulin from chicory and soy lecithin, both listed on 205.606.

Item B

1. The common name of the substance.

Barley betafiber is a natural dietary fiber source. It is β-glucan soluble fiber in barley and represents approximately 30% of the total barley fiber. The trade name used by Cargill, Incorporated for this product is Barliv™ barley betafiber. Ingredient statements for this component would be barley betafiber, barley soluble fiber, barley beta-glucan or barley fiber.

NOTE: While barley betafiber can be labeled barley beta-glucan, barley soluble fiber and barley fiber, other ingredients labeled using these names may not be labeled as barley betafiber. To be classified as barley betafiber, the substance must comply with 21CFR 101.81 (c)(2)(ii)(A)(6).

2. The manufacturer.

Barliv™ barley betafiber is manufactured by Cargill, Incorporated. The plant location is:

Cargill France SAS
Rue de Seves
50500 Baupte
France

At this time, there are no other manufacturers of barley betafiber. There are other products derived from barley that use the generic names of whole grain barley fiber, barley β-glucan and β-glucan. Examples are Sustagrain® from Conagra, Glucagel™ from GraceLinc and Viscofiber® from Natraceutical Group. These products do not meet the definition of barley betafiber, have not been authorized by FDA as an eligible source of soluble fiber for the health claim and are distinctly different in composition. These other barley fiber concentrates are not included as part of this petition. While these other products may be suitable for use in organic products, Cargill does not know exactly how they are manufactured and cannot represent them with this petition.

3. The intended or current use of the substance.

The FDA approves the use of specific health claims on packages if they feel the claim has "significant scientific agreement". These are the current claims that are allowed with fiber related items bolded (21 CFR 101 Subpart E):

101.72 Health claims: calcium and osteoporosis.
101.73 Health claims: dietary lipids and cancer.
101.74 Health claims: sodium and hypertension.
101.75 Health claims: dietary saturated fat and cholesterol and risk of coronary heart disease.
101.76 Health claims: fiber-containing grain products, fruits, and vegetables and cancer.
101.77 Health claims: fruits, vegetables, and grain products that contain fiber, particularly soluble fiber, and risk of coronary heart disease.
101.78 Health claims: fruits and vegetables and cancer.
101.79 Health claims: Folate and neural tube defects.
101.80 Health claims: dietary noncariogenic carbohydrate sweeteners and dental caries.
101.81 Health claims: **Soluble fiber from certain foods and risk of coronary heart disease (CHD).**

Eligible sources of soluble fiber are:

1. Oat bran
2. Rolled oats
3. Whole oat flour
4. Oatrim
5. Whole grain barley and dry milled barley
6. **Barley betafiber**

101.82 Health claims: Soy protein and risk of coronary heart disease (CHD).
101.83 Health claims: plant sterol/stanol esters and risk of coronary heart disease (CHD).

http://www.fda.gov/Food/LabelingNutrition/LabelClaims/HealthClaimsMeetingSignificantScientificAgreementSSA/default.htm

Barley betafiber is intended for use as a source of dietary fiber; it is generally recognized as safe (GRAS) for use in all foods with the exception of infant formula and meat and poultry muscle tissue. It is a shelf-stable powder that is easily added to dry mixes or liquid products. Typical use levels will not change the flavor or the texture of the finished food. No special food processing equipment is required to utilize this ingredient. While barley betafiber will generally be a small part of a food formula (less than 1%), the health benefit provided to the consumer is significant. These properties make barley betafiber an ideal ingredient to increase heart healthy fiber in a wide range of foods. It has been incorporated into prototypes for beverages, snacks, cereals, juices, clear beverages, etc.

The FDA has examined research on Barliv™ barley betafiber and cholesterol reduction. The FDA states (Federal Register Feb. 25, 2008): "Based on the totality of publicly available scientific evidence, FDA now has concluded that in addition to certain whole oat and whole grain barley products, barley betafiber is also an appropriate source of β-glucan soluble fiber." The FDA now allows foods with Barliv™ barley betafiber to carry a health claim "*Diets low in saturated fat and cholesterol that include 3 grams per day of β-glucan soluble fiber from barley betafiber may reduce the risk of heart disease*". Three grams is only 12% of the daily value for fiber so it is clear that a

small consumption can have a positive health impact. See Appendix 5 for FDA Interim and Final Rules.

Bolthouse Farms has a product on the market, Heart Healthy Pear Merlot juice blend that is made with Barliv™ barley betafiber. The Barliv™ barley betafiber provides the health benefit and still allows the product to have desirable organoleptic properties.

4. The handling activities for which the substance will be used and its mode of action.

Barley betafiber will be used as a supplement to a wide range of foods as a source of soluble fiber to help reduce the risk of heart disease and to support healthy lipid metabolism. It may also be added to foods for other health benefits that are supported by clinical trials but not yet allowed by the FDA as a specific claim including reducing glycemic index of foods, helping to maintain normal blood sugar levels, and (potentially) promoting satiety.

Barley betafiber is consumed and not digested. It impacts health through its presence in the intestinal tract. Several mechanisms have been suggested as to how β-glucan lowers cholesterol including binding to the bile acids in the intestine, fermentation by colonic bacteria to produce fatty acids that inhibit cholesterol synthesis, and delaying gastric emptying which slows absorption of dietary fat and sugars. One or more of these likely results in the beneficial effects demonstrated by barley betafiber.

5. The source of the substance and a detailed description of its manufacturing or processing procedures.

Barley betafiber is defined as the ethanol precipitated soluble fraction of cellulose- and alpha-amylase-hydrolyzed whole grain barley flour 21CFR101.81(c)(2)(ii)(6) (Appendix 5). It is produced by extracting the natural soluble fiber from barley through solubilization, enzyme treatment to break down starches to make them easier to remove from the soluble fiber, filtration and subsequent separation of the barley soluble fiber through precipitation in ethanol. See Appendix 2A for the detailed manufacturing procedure used by Cargill for barley betafiber.

A few processing aids are used in the manufacture of barley betafiber which are removed during the manufacturing process. All processing aids are food grade and GRAS for food manufacture. All non-agricultural processing aids are included in the National List 205.605a or 205-605b.

The bonds broken in the process of isolating this component are broken by enzymes only, therefore, this substance is not synthetic. The process has similarities to extracting inulin from chicory or extracting beta-carotene from carrots. For these reasons, we believe barley betafiber should be added to 205.606: Nonorganically produced agricultural products allowed as ingredients in or on processed products labeled as "organic."

Ethanol (non-synthetic alcohol derived from natural fermentation of agricultural ingredients) is used in the isolation process to enhance the extraction of the soluble barley fiber. Tests are completed by Cargill on every lot of barley betafiber to confirm the residual ethanol level is <0.5%.

The manufacture of barley betafiber can be achieved using practices and processing aids approved in the NOP so it is inevitable that we will see organic barley betafiber available in the future similar to the current availability of organic inulin and organic lecithin. To encourage manufacture of an organic source, a reasonable first step is to make the ingredient, barley

betafiber, available for use to the organic sector through addition to 205.606. Once there is demand, organic versions will inevitably follow. Because this natural substance provides substantial benefit to consumer health, addition of it to the National List will support the further development of healthy organic foods.

6. A summary of any available previous reviews of the petitioned substance by State or private certification programs or other organizations.

To the best of our knowledge, barley betafiber has not been reviewed by State or private certification programs in the past. It has been reviewed by FDA (see point 7).

7. Information regarding EPA, FDA, and State regulatory authority registrations.

Barley betafiber is a food, not a food additive. The GRAS determination by independent experts is included in Appendix 3: Report of the Expert Panel on the Generally Recognized as Safe (GRAS) Status of Barley Betafiber.

Barley betafiber is approved by regulatory agencies for food use in a number of countries including Australia, New Zealand, Italy, France and Belgium. Other approvals are pending with no expectation of any issues. Further information is available on request.

8. The Chemical Abstract Service (CAS) numbers of the substance and labels of products that contain the petitioned substance.

CAS # 9041-22-9

This CAS number applies to β-D-glucan of any origin (e.g., barley, oats, mushrooms, etc.)

CAS # 55965-23-6

This CAS number applies to mixed-linkage (1→3), (1→4) β-D-glucans.

Beta-glucan from barley is not a distinct/pure chemical substance. It is a polysaccharide of unbranched, linear, mixed-linkage β-glucans. CAS # 9041-22-9 applies to β-D-glucans of any origin. CAS # 55965-23-6 applies to the majority of β-glucans in barley betafiber.

The isolation process for barley betafiber results in β-glucans of average lower molecular weight than the average of those in native barley. These lower molecular weight β-glucans are present in native barley yet are enhanced in the manufacture of barley betafiber.

The Barliv™ barley betafiber Technical Data Sheet is shown in Appendix 4.

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CBI End

The label for Bolthouse Farms' Heart Healthy Pear Merlot juice blend is shown in Appendix 9.

9. The substance's physical properties and chemical mode of action including:

(a) chemical interactions with other substances, especially substances used in organic production;

Barley betafiber is soluble in water. It has lower viscosity than native barley β-glucan because of the enhancement of lower molecular weight barley β-glucan in the isolation process. This makes barley betafiber more suitable for food applications that would benefit from the addition of fiber yet where no increase in viscosity is desired/required.

Barley betafiber has excellent chemical and thermal stability. It is stable in ambient storage for up to 3 years. In aqueous solutions, it is stable in the pH range of 3 to 10. Under temperature conditions applied during the typical processing and storage of food, barley betafiber is stable.

Barley betafiber is a relatively inert component of food that has no known reports of interacting with substances to form other compounds.

(b) toxicity and environmental persistence;

Barley betafiber is non-toxic. In studies with rats and mice, the highest level tested (10% of the diet) gave no observed adverse effect (NOAEL) in 28 day feeding trials. (Delaney *et al.*, 2003)

Barley betafiber exists in nature as a natural component of barley. There are no issues of environmental persistence. It is environmentally harmless.

(c) environmental impacts from its use or manufacture;

The production process involves water and enzyme extraction of barley to isolate the barley soluble fiber. See "Barley Betafiber Production Process" in Appendix 2A. The residues from the manufacture of barley betafiber are all naturally occurring components (enzyme digested starch, solubilized protein and insoluble fiber) which have no toxicity or environmental persistence.

The ethanol used in the manufacture of this item is repeatedly reused and not released into the environment in any significant quantities. This is both cost effective and optimal for the environment.

(d) effects on human health;

The positive effect of barley and barley β-glucan/soluble fiber in human health has been reported in numerous studies over the past 20 years. Initial studies involved the positive impact of barley and oat β-glucan on lipid metabolism. More recent studies have involved the ability of barley and oat β-glucan to reduce glycemic and insulinemic responses in foods and help enhance satiety.

In passing through the digestive tract, β-glucan is not absorbed to any significant degree because of its large molecular size. Therefore, the benefits of barley betafiber occur through associations with other components and microorganisms in the digestive tract. See Appendix 3 for the Report of the Expert Panel on the Generally Recognized as Safe (GRAS) Status of Barley Betafiber.

Appendix 8 includes several articles on clinical trials using barley betafiber.

(e) effects on soil organisms, crops, or livestock.

Barley betafiber is used in handling, not crop production. It has no effect on soil organisms, crops or livestock.

10. Safety information about the substance.

Barley is a traditional food with a long history of safe use. The primary component of barley betafiber is β-glucan which is widely present in numerous grains and other plants. Adverse effects of consequence due to the consumption of β-glucans from such foods have not been reported. Particularly relevant in this regard is the safe use of oat-derived β-glucan isolates for more than 10 years (for example, Oatrim™ from Conagra, with a β-glucan content of up to 15%).

In some regions of the world, barley is a food staple and used in a variety of traditional foods. For example in Maghreb countries (e.g., Morocco, Algeria, Tunisia), barley consumption provides approximately 6 grams per person per day of pure β-glucan. This is eight times the level required to make a health claim in the US. No adverse effects have been reported due to the high level of β-glucan consumption via barley in these countries.

While barley β-glucan isolates have only recently been introduced to the market, oat β-glucans have been available and consumed in large quantities for over 10 years. Millions of pounds of β-glucan concentrates are consumed per year (Oatrim™ from Conagra, OatVantage™ from GTC Nutrition, etc.) in the US. This β-glucan is widely recognized and considered safe.

The Material Safety Data Sheet for Barliv™ barley betafiber is attached as Appendix 6.

Appendix 3 contains a scientific review of the safety of barley betafiber. Appendix 7 contains information on lead and mycotoxins. Regarding heavy metals, Cargill currently tests for lead as a marker for heavy metal content (per specs). Previous testing for other heavy metals consistently was negative so the decision was made to regularly test for lead only.

There is no substance report on barley betafiber from the National Institute of Environmental Health Studies (National Toxicology Program); barley betafiber is a natural component of food not expected to have any environmental impact.

11. Comprehensive research reviews and research bibliographies, including reviews and bibliographies which present contrasting positions.

While we were able to find information on fiber contents from organic food sources, we were not able to find an article that identified organic sources for high levels of β-glucan that are suitable for the FDA claim.

The articles in Appendix 8 are a limited number of those available on the results of clinical trials using barley betafiber and the reports of beneficial health impacts from consumption of barley betafiber.

Organic barley betafiber is not currently available. Organic barley is available but not in the cultivars of barley that are highest in fiber and currently used for isolation of the betafiber. Cargill is currently determining if growers of this barley can convert to organic production, however required volumes need to increase to justify this conversion. This is expected to occur in future if barley betafiber is listed on 205.606. Organic ethanol is currently available however it is believed the

quantities are low. Investigation will be needed and suppliers contracted to develop sufficient quantities at the time when organic barley of the variety required is available. At this time, Cargill does not anticipate any problem certifying the manufacture of this item in its production facility given the availability of organic ethanol and their specific cultivar of organic barley.

12A ``Petition Justification Statement'' which provides justification for inclusion of a non-organically produced agricultural substance onto the National List.

Need for Dietary Fiber: Health of the Organic Consumer

Intake of dietary fiber in general is associated with lower risk of heart disease, diabetes and obesity. Soluble dietary fiber provides health benefits of lowering LDL cholesterol and triglycerides in the blood. It also may help the consumer maintain healthy blood sugar levels and assist with digestion and appetite control. While most consumers are aware there are benefits to eating fruits, vegetables, whole grains and other products that contain fiber, consumers generally do not eat the daily recommended amount of fiber. According to USDA and NHANES, Americans eat an average of about 15 grams of fiber a day, only 60% of the recommended daily intake. See Nutrient Intakes from Foods in Appendix 10. Americans need to increase the amount of fiber in their diets to achieve the health benefits associated with this dietary component. Barley betafiber supplementation is one way to do this.

Organic consumers justifiably believe that consuming organic foods is both beneficial to the earth as well as beneficial to their health. Product selection for organic consumers can include more nutritious products because these consumers are more likely to select whole foods (fruits, vegetables, whole grains, etc.). However, the need for convenient foods that are either ready to consume or easy to prepare means that organic consumers will continue to select some processed foods for their diets.

Processed foods can contain fewer nutrients such as fiber because they are formulated to provide optimum flavor and texture as well as product stability on the shelf. Examples of processed products with less fiber are:

- orange juice relative to whole fruit consumption: juice provides a convenient way to consume oranges; fruit juice contains less fiber than the whole fruit.
- wheat flour with bran and germ removed relative to whole wheat flour: use of wheat flour without bran and germ reduces the flavor contribution from wheat (desired in some products) and extends the shelf-life.

There are numerous organic foods that are sources of fiber however many of them have low fiber contents and so must be eaten at high levels to impact the total fiber content of the food. Examples of these include broccoli, whole wheat flour, barley, oats, black beans, etc. There are a few organic ingredients such as organic oat bran that have enhanced levels of fiber and so can be used in lesser quantities. These products are still much lower in fiber than barley betafiber and cannot be used in a wide range of food without impacting the flavor and texture. Organic psyllium fiber can be used at even lower levels however, because it swells in water and becomes very thick, it contributes a distinct mouthfeel and thickness that is not suitable for many/most foods.

The table below shows the amounts of organic rye, oats, barley and oat bran required for addition to a prepared food to achieve 0.75 grams of soluble β-glucan fiber and the amount of organic psyllium fiber to achieve 1.7 grams. The amounts are extremely high and prohibit their use in most products as they would significantly change the character of the finished product. NOTE: In

the beverage example, the other sources would be added in the form most suitable for the beverage application, i.e., as a fine flour rather than as whole pieces.

Source of Soluble Fiber	Trade Name	Quantity (approx) of Soluble Fiber or β-glucan (per 100 g)	Amount to Supplement 1 Serving	Impact on Finished Beverage (example)
Barley Betafiber	Barliv™	75	1.0 grams	Minimal
Sources of β-Glucan and Soluble Fiber Currently Available for Use in Organic Foods				
Organic Rye	Generic	2	38 grams	Unpalatable
Organic Oats	Generic	5	15 grams	Unpalatable
Organic Barley	Generic	5	11 grams	Unpalatable
Organic Oat Bran	Generic	7	11 grams	Unpalatable
Organic Psyllium Husk	Generic	70	2.4 grams	Thick, gelatinous, not a beverage
Other Sources of Soluble Fiber/β-Glucan Currently Not Available as Organic				
Barley Bran	Generic*	7	11 grams	Unpalatable
Oatrim	Generic*	8	9.4 grams	Unpalatable

* Not available as organic (OTA Organic Pages On-Line) so could only be used in MWO products as an agricultural ingredient (as long as non-GMO, no irradiation and no sewage sludge requirements are met).

Note that barley betafiber can be added at very low levels to achieve a significant β-glucan / soluble fiber content. This makes barley betafiber suitable for a wide range of applications. A beverage example has been included to demonstrate that barley betafiber can be used where other sources cannot because they negatively impact texture and/or result in excessive water binding.

Therefore, we have concluded that there is no organic equivalent to barley betafiber that provides this high level of heart healthy fiber that is easy to incorporate in a wide range of foods that will be well accepted by consumers.

Need for Barley Betafiber by the Organic Market

Heart disease has been the leading cause of death in the United States for at least 50 years. Diabetes is on the rise. Preventing these conditions has become a priority for many US consumers, particularly health oriented individuals. Barley betafiber is a natural ingredient now available to the conventional market. It is important for organic foods to continue to be identified as the most nutritious food source rather than a food sector that is limited in its use of natural fiber sources. Use of barley betafiber by the organic foods sector would allow the creation of more foods to combat these diseases and provide a wider variety of products to consumers interested in maintaining and/or improving their health.

Item 12G Organic Non-Availability of Barley Betafiber

Barley betafiber is preferably derived from specific strains of barley that are high in beta-glucan. Information on these strains is provided in Appendix 2B. Organic barley betafiber production would rely on the availability of appropriate organic strains of barley. High beta glucan food barley varieties are typically grown on a contract basis and organic seed for those cultivars is not presently available. In order to create foundation organic seed stocks, a 3 year transition period would be required for selected varieties. From organic foundation seed stocks to commercial organic barley would take an additional 3 years. Cargill has already begun investigating the possibility of organic cultivation of these specific strains of barley. In the meantime, Cargill is requesting addition of this agricultural ingredient to 205.606 in order to make it available to the organic market. Interest from the organic sector and sales of the ingredient will support efforts to convert barley betafiber to an organic source and organic processing.

13. Confidential Business Information

This document contains Confidential Business Information. CBI has been indicated in the right margin with a bracket and "CBI". Appendix 1 is the version with CBI deleted (information removed but spacing maintained so page numbers are identical to the CBI Copy). "CBI Deleted" is indicated in the right margin where information has been removed. The CBI identified in this petition relates to the manufacturing process, quality control test results and commercial information.

Appendices

Appendix 1: Petition – CBI Deleted Version

Appendix 2A: Manufacturing Process for Barley Betafiber

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CBI End

Appendix 2B: Information to Support Eventual Organic Manufacture

- Information Supporting Select Strains of Barley Needed

Appendix 3: GRAS Information

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CBI End

- FDA GRAS Notice No. GRN 000207, December 19, 2006

Appendix 4: Technical Information for Barliv™ Barley Betafiber

- Barliv™ Barley Betafiber Technical Data Sheet

Appendix 5: FDA Rules on Soluble Fiber from Certain Foods and Risk of Coronary Heart Disease

- FDA Interim Rule February 25, 2008
- FDA Final Rule August 15, 2008
- CFR 101.81 Health Claims: Soluble fiber from certain foods and risk of coronary heart disease

Appendix 6: Material Safety Data Sheet (MSDS) for Barliv™ Barley Betafiber

Appendix 7: Toxicology and Safety Reviews

CBI Start

CBI Deleted

CBI End

Appendix 8: Clinical Trials Using Barley Betafiber and Beta-Glucan

Selected articles (additional available on request):

- Keenan, J.M.; Goulson, M.; Shamliyan, T.; Knutson, N.; Kolberg, L.; Curry, L. 2007. The effects of concentrated barley β-glucan on blood lipids in a population of hypercholesterolemic men and women. Br J Nutr 97:1162-8.
- Talati, R,; Baker, W.; Pabilonia, M.; White, M. 2009. The effects of barley-derived soluble fiber on serum lipids. Annals of Family Medicine 7(2): 157-163.
- Behall, K.; Scholfield, D.; Hallfrisch, J. 2006. Barley β-glucan reduces plasma glucose and insulin responses compared with resistant starch in men. Nutrition Research 26: 644 – 650.
- Behall, K.; Scholfield, D.; Hallfrisch, J.; Liljeberg-Elmstahl, H. 2006. Consumption of both resistant starch and β-glucan improves postprandial plasma glucose and insulin in women. Diabetes Care 29(5): 976 – 981.

Appendix 9: Example of Label for Product Using Barley Betafiber

- Bolthouse Farms -- Heart Healthy Pear Merlot juice blend

Appendix 10: Additional Reference Articles and Information

- Conway, J.; Behall, K. 2005. Health Effects of Barley Consumption.
- USDA NHANES Nutrient Intakes from Food, 2005 – 2006.
- USDA Nutrient Intakes, 1994 - 96

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Barley β-Glucan and Barley Strain Variations

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2. Henry, R.J. 1987. Pentosan and (1→3), (1→4)- β-glucan concentrations in endosperm and wholegrain of wheat, barley, oats and rye. J Cereal Sci 6:253-258.
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6. Xue, Q.; Newman, R.K.; Newman, C.W.; McGuire, C.F. 1991. Waxy gene effects on β-glucan, dietary fiber content and viscosity of barleys. Cereal Res Comm 19(4):399-404.

Health Related – Lipid Metabolism and Coronary Heart Disease

1. 21 CFR § 101.81 Health claims: Soluble fiber from certain foods and risk of coronary heart disease (CHD).
2. Anderson, J.W.; Hanna, T.J. 1999. Impact of nondigestible carbohydrates on serum lipoproteins and risk for cardiovascular disease. J Nutr 129:1457-1466.
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5. Behall, K. M., Scholfield, D. & Hallfrisch, J. 2004b. Diets containing barley reduce lipids significantly in moderately hypercholesterolemic men and women. Am J Clin Nutr 80:1185-93.
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Petition to Add to the National List 205.606: "Barley Betafiber"

Appendix 1: Petition – CBI Deleted Version

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Petition to Add to the National List 205.606: "Barley Betafiber"

Appendix 2A: Manufacturing Process for Barley Betafiber

CBI Start

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CBI End

Petition to Add to the National List 205.606: "Barley Betafiber"

Appendix 2B: Information to Support Eventual Organic Manufacture

- Information Supporting Select Strains of Barley Needed

INFORMATION SUPPORTING THE CLAIM THAT THERE ARE STRAINS OF BARLEY WITH HIGH BETA-GLUCAN LEVELS

US Patent 6083547 - Method for obtaining a high beta-glucan barley fraction

FIELD OF INVENTION

The present invention relates to a method for separating a high beta-glucan barley fraction from the remainder of the barley grain, specifically the remainder of barley flour formed from barley grain. More specifically, the present invention relates to a method for treating barley flour so that the high beta-glucan barley fraction is produced, with the barley fraction having an increased beta-glucan content, a viscosity higher than the barley flour, and an improved mouthfeel.

BACKGROUND OF THE INVENTION

Beta-glucan, a cell wall polysaccharide, is present in grains, such as oats and barley, with the beta-glucan desired for human consumption because it has been found that beta-glucan can reduce serum cholesterol and lower the glycemic response in humans. The beta-glucan is found primarily in the endosperm cell wall portion of a barley grain. The beneficial effects of barley, and in particular beta-glucan, are discussed in articles by Macintosh et al. and Newman et al. (1,2). Because of the above discussed benefits it is desired to consume products containing an amount of beta-glucan, and more preferably an increased amount of beta-glucan.

It has further been found that barley often contains a relatively high amount of beta-glucan as compared to other grains so that barley is preferred for obtaining an adequate amount of beta-glucan. Generally, beta-glucan is found in barley in an amount ranging between about 5% and about 18% by weight of the barley. More typically, barley contains between about 5% and about 7% by weight beta-glucan, however, enhanced barley strains have been developed, Prowashonupana for example, which have between about 15% and about 18% by weight beta-glucan.

http://www.patentstorm.us/patents/6083547/description.html

Petition to Add to the National List 205.606: "Barley Betafiber"

Appendix 3: GRAS Information

CBI Start

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CBI End

- FDA GRAS Notice No. GRN 000207, December 19, 2006

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740

DEC 1 9 2006

Lore W. Kolberg
Mgr. Regulatory & Scientific Affairs
Cargill Inc.
15407 McGinty Road West
Wayzata, MN 55391

Re: GRAS Notice No. GRN 000207

Dear Ms. Kolberg:

The Food and Drug Administration (FDA) is responding to the notice, dated June 21, 2006, that you submitted in accordance with the agency's proposed regulation, proposed 21 CFR 170.36 (62 FR 18938; April 17, 1997; Substances Generally Recognized as Safe (GRAS); the GRAS proposal). FDA received the notice on June 23, 2006, filed it on June 23, 2006, and designated it as GRAS Notice No. GRN 000207.

The subject of the notice is barley fiber. The notice informs FDA of the view of Cargill Inc. (Cargill) that barley fiber is GRAS, through scientific procedures, for use as an ingredient in food in general, except for infant formula and meat and poultry products.

As part of its notice, Cargill includes the report of a panel of individuals (Cargill's GRAS panel) who evaluated the data and information that are the basis for Cargill's GRAS determination. Cargill considers the members of its GRAS panel to be qualified by scientific training and experience to evaluate the safety of substances added to food. Cargill's GRAS panel discusses barley fiber's identity, specifications, method of manufacture, proposed estimated dietary intake, and published and unpublished studies on barley fiber. Based on this review, Cargill's GRAS panel concludes that barley fiber is GRAS, by scientific procedures, when used as an ingredient in foods in general, except for infant formula and meat and poultry products, at levels consistent with current Good Manufacturing Practices (cGMP).

Cargill describes the identity and method of manufacture of barley fiber, and provides information on its composition. Barley fiber is obtained from food grade barley by water extraction at an elevated temperature. Starch is removed during the extraction process by treatment with alpha-amylases that are safe and suitable for food use. The barley fiber is recovered by centrifugation after treatment with denatured food grade ethanol. The obtained fiber product has a weight average molecular weight of 50 to 400 kDa. Barley fiber is composed of about 91% carbohydrate, 3% protein, 3% inorganic salts, and less than 1% lipids. Cargill provides specifications for barley fiber including a specification for ≥70% beta-glucan.

In estimating the consumer intake of barley fiber, Cargill assumes that use levels of barley fiber are self-limiting for technologieal reasons. Excessive levels of barley fiber impact taste. In most food applications, the concentration of barley fiber approaches a technically feasible maximum

level of approximately 4.3 grams (g) of barley fiber per serving. Cargill estimates that the average intake of barley fiber by consumers of the proposed uses would be 10.5-28.2 g per day. Cargill estimates that barley fiber would be added at levels up to 4.3 g per serving, resulting in approximately 3 g of beta-glucan per serving.

Cargill concluded that there was no reason to conduct any classical absorption, disposition, metabolism and excretion studies since beta-glucan, the main component of barley fiber, is not digested by human digestive enzymes and its molecular size precludes absorption of significant amounts while passing through the small intestine. Nevertheless, in the notice Cargill described the results of a rat study, a mouse study, and a bone marrow micronucleus study to further reinforce the safety of barley fiber and its constituent, beta-glucan. These animal studies did not identify any adverse reactions or toxicity as revealed by histopathologic examinations, among various endpoints studied. The bone marrow micronucleus study demonstrated that barley fiber and its beta-glucan are not genotoxic.

Cargill describes several published studies on barley derived beta-glucan and on barley fiber. Some of these studies show that beta-glucan, ingested with barley-based foods, is solubilized and extracted from the food matrix during the initial stages of digestion and then it is entirely utilized by the intestinal flora.

Standards of Identity

In the notice, Cargill states its intention to use barley fiber in several food categories, including foods for which standards of identity exist, located in Title 21 of the Code of Federal Regulations. We note that an ingredient that is lawfully added to food products may be used in a standardized food only if it is permitted by the applicable standard of identity.

Conclusions

Based on the information provided by Cargill as well as other information available to FDA, the agency has no questions at this time regarding Cargill's conclusion that barley fiber is GRAS under the intended conditions of use. The agency has not, however, made its own determination regarding the GRAS status of the subject use of barley fiber. As always, it is the continuing responsibility of Cargill to ensure that food ingredients that the firm markets are safe, and are otherwise in compliance with all applicable legal and regulatory requirements.

In accordance with proposed 21 CFR 170.36(f), a copy of the text of this letter responding to GRN 000207, as well as a copy of the information in this notice that conforms to the information in the proposed GRAS exemption claim (proposed 21 CFR 170.36(c)(1)), is available for public review and copying on the homepage of the Office of Food Additive Safety (on the Internet at http://www.cfsan.fda.gov/~lrd/foodadd.html).

Sincerely,

Laura M. Tarantino, Ph.D.
Director
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

Petition to Add to the National List 205.606: "Barley Betafiber"

Appendix 4: Technical Information for Barlív™ Barley Betafiber

- Barlív™ Barley Betafiber Technical Data Sheet

technical data

Barliv™ barley betafiber

Product Code
BBF-100

Product Description
Barliv™ barley betafiber is a natural, concentrated beta–glucan soluble fiber derived from whole grain barley. Barliv™ has been clinically shown to reduce total and LDL cholesterol when consumed as part of a low saturated fat, low cholesterol diet. Barley betafiber (Barliv™) is authorized as a source of soluble fiber for the FDA health claim:
"Diets low in saturated fat and cholesterol that include 3 grams of beta-glucan soluble fiber per day from barley betafiber may reduce the risk of heart disease."

Application / Functionality
Barliv™ is a patent-pending product characterized by high purity (≥70% beta glucan) and reduced molecular weight (lower viscosity). These characteristics enable customers to use Barliv™ barley betafiber in a wide variety of food-products and beverages with broad consumer appeal, including juices, clear and carbonated beverages, snacks and cereals, as well as specialty bakery products.

Specifications (Analytical methods available on request)

Chemical and Physical	
Beta-glucan content (% on dry basis)	≥ 70
Moisture (%)	≤ 12
Molecular weight (kDalton)	120 - 400
Residual ethanol (%)	≤ 0.5
Residual isopropanol (ppm)	≤ 10
Lead (ppm)	≤ 0.2
Microbiological	
Total Aerobic Plate Count (cfu/g)	≤ 10,000
Salmonella	neg/375g
Deoxynivalenol (ppm)	< 0.25

Typical Characteristics

Particle Size (∝m)	< 250
Appearance	white to light tan powder
Taste	bland

Allergen Status
In accordance with the 2004 Food Allergen Labeling and Consumer Protection Act (FALCPA), no allergen declarations are required for this product.

Contains no preservatives.

Storage / Shelf-life
18 months in dry conditions, in original sealed container.
Packaging: 25 kg in a poly-lined box

Applicable certifications
KOSHER
HALAL

Barliv™ barley betafiber is sourced from barley of conventional origin and processed such that the labeling provisions of 1829/2003/EC and 1830/2003/EC do not apply.

Regulatory Status
Generally Recognized as Safe (GRAS)
(Additional information available upon request).

Labeling: May be labeled on ingredient list as one of the following: Barley betafiber, barley soluble fiber, barley beta-glucan, barley fiber

Produced by
Cargill France SAS
Rue de Seves
50500 Baupte, France

Petition to Add to the National List 205.606: "Barley Betafiber"

Appendix 5: FDA Rules on Soluble Fiber from Certain Foods and Risk or Coronary Heart Disease

- FDA Interim Rule February 25, 2008
- FDA Final Rule August 15, 2008
- CFR 101.81 Health Claims: Soluble fiber from certain foods and risk of coronary heart disease

Federal Register Interim Final Rule 73 FR 9938 February 25, 2008: Food Labeling: Health Claims; Soluble Fiber From Certain Foods and Risk of Coronary Heart Disease

[Federal Register: February 25, 2008 (Volume 73, Number 37)]
[Rules and Regulations]
[Page 9938-9947]
From the Federal Register Online via GPO Access [wais.access.gpo.gov]
[DOCID:fr25fe08-3]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 101

[Docket No. FDA-2008-P-0090] (formerly Docket No. 2006P-0393)

Food Labeling: Health Claims; Soluble Fiber From Certain Foods and Risk of Coronary Heart Disease

AGENCY: Food and Drug Administration, HHS.

ACTION: Interim final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the health claim regulation entitled ``Soluble fiber from certain foods and risk of coronary heart disease (CHD)'' to add barley betafiber as an additional eligible source of beta-glucan soluble fiber. Barley betafiber is the ethanol precipitated soluble fraction of cellulase and alpha-amylase hydrolyzed whole grain barley flour. FDA is taking this action in response to a health claim petition submitted by Cargill, Inc. FDA previously concluded that there was significant scientific agreement that a claim characterizing the relationship between beta-glucan soluble fiber of certain whole oat and whole grain barley products and CHD risk is supported by the totality of publicly available scientific evidence. Based on the totality of publicly available scientific evidence, FDA now has concluded that in addition to certain whole oat and whole grain barley products, barley betafiber is also an appropriate source of beta-glucan soluble fiber. Therefore, FDA is amending the health claim regulation entitled ``Soluble fiber from certain foods and risk of CHD'' to include barley betafiber as another eligible source of beta-glucan soluble fiber.

DATES: This interim final rule is effective February 25, 2008. Submit written or electronic comments by May 12, 2008.

ADDRESSES: You may submit comments, identified by Docket No. FDA-2008-P-0090 (formerly Docket No. 2006P-0393), by any of the following methods:

Electronic Submissions

Submit electronic comments in the following way:

<bullet> Federal eRulemaking Portal: http://www.regulations.gov. Follow the instructions for submitting comments.

Written Submissions

Submit written submissions in the following ways:

<bullet> FAX: 301-827-6870.

<bullet> Mail/Hand delivery/Courier [For paper, disk, or CD-ROM submissions]: Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

To ensure more timely processing of comments, FDA is no longer accepting comments submitted to the agency by e-mail. FDA encourages you to continue to submit electronic comments by using the Federal eRulemaking Portal, as described previously, in the ADDRESSES portion of this document under Electronic Submissions.

Instructions: All submissions received must include the agency name and Docket No(s). and Regulatory Information Number (RIN) (if a RIN number has been assigned) for this rulemaking. All comments received may be posted without change to http://www.regulations.gov, including any personal information provided. For additional information on submitting comments, see the ``Comments'' heading of the SUPPLEMENTARY INFORMATION section of this document.

Docket: For access to the docket to read background documents or comments received, go to http://www.regulations.gov and insert the docket number(s), found in brackets in the heading of this document, into the ``Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Jillonne Kevala, Center for Food Safety and Applied Nutrition (HFS-830), Food and Drug Administration,

5100 Paint Branch Pkwy., College Park, MD 20740-3835, 301-436-1450 .

SUPPLEMENTARY INFORMATION:

I. Background

A. The Nutrition Labeling and Education Act of 1990

The Nutrition Labeling and Education Act of 1990 (the 1990 amendments) (Public Law 101-535) amended the Federal Food, Drug, and Cosmetic Act (the act) in a number of important ways. One aspect of the 1990 amendments was that they clarified FDA's authority to regulate health claims on food labels and in food labeling.

FDA (we) issued several new regulations in 1993 that implemented the health claim provisions of the 1990 amendments. Among these were 21 CFR 101.14, Health claims: general requirements (58 FR 2478, January 6, 1993) and Sec. 101.70 (21 CFR 101.70), Petitions for health claims (58 FR 2478), which set out the general requirements for the authorization and use of health claims and established a process for petitioning the agency to authorize health claims about substance-disease relationships

and set out the types of information that any such petition must include. These regulations became effective on May 8, 1993.

When implementing the 1990 amendments, FDA also conducted a review of evidence for a relationship between dietary fiber and cardiovascular disease (CVD). Based on this review, the agency concluded that the available scientific evidence did not justify authorization of a health claim relating dietary fiber to reduced risk of CVD (58 FR 2552, January 6, 1993) (1993 dietary fiber and CVD health claim final rule). However, FDA did conclude there was significant scientific agreement that the totality of publicly available scientific evidence supported an association between types of foods that are low in saturated fat and cholesterol and that naturally are good sources of soluble dietary fiber (i.e., fruits, vegetables, and grain products) and reduced risk of CHD\1\. Therefore, FDA authorized a health claim about the relationship between diets low in saturated fat and cholesterol and high in vegetables, fruit, and grain products that contain soluble fiber and a reduced risk of CHD (21 CFR 101.77; 58 FR 2552 at 2572). In the 1993 dietary fiber and CVD health claim final rule, FDA commented that if a manufacturer could document with appropriate evidence that consumption of the type of soluble fiber in a particular food has the effect of lowering blood low density lipoprotein (LDL) cholesterol, and has no adverse effects on other heart disease risk factors (e.g., high density lipoprotein cholesterol), it should petition for authorization of a health claim specific for that particular dietary fiber-containing food (58 FR 2552 at 2567).

\1\ Cardiovascular disease means diseases of the heart and circulatory system. Coronary heart disease, one form of cardiovascular disease, refers to diseases of the heart muscle and supporting blood vessels.

B. Soluble Fiber from Certain Foods and Risk of CHD Health Claim (21 CFR 101.81)

In 1995, FDA received a petition for a health claim on the relationship between oat bran and rolled oats and reduced risk of CHD. FDA concluded there was significant scientific agreement that the totality of publicly available scientific evidence supported the relationship between consumption of whole oat products and reduced risk of CHD. FDA further concluded that the type of soluble fiber found in whole oats, i.e., beta-glucan soluble fiber, is the component primarily responsible for the hypocholesterolemic effects associated with consumption of whole oat foods as part of a diet that is low in saturated fat and cholesterol (62 FR 3584 at 3597 and 3598, January 23, 1997). As such, the final rule authorized a health claim relating the consumption of beta-glucan soluble fiber in whole oat foods, as part of a diet low in saturated fat and cholesterol, and reduced risk of CHD (the 1997 oat beta-glucan health claim final rule). The source of beta-glucan soluble fiber in foods bearing this health claim had to be one of three eligible whole oat products; i.e., oat bran, rolled oats, or whole oat flour (see Sec. 101.81(c)(2)(ii)(A)). In the 1997 oat beta-glucan health claim final rule, FDA anticipated the likelihood that other sources and types of soluble fibers could also affect blood lipid

levels, and thus, may reduce heart disease risk (62 FR 3584 at 3587). At that time, FDA considered structuring the final rule as an umbrella regulation authorizing the use of a claim for ``soluble fiber from certain foods`` and risk of CHD. Such action would have allowed flexibility in expanding the claim to other specific food sources of soluble fiber when consumption of those foods has been demonstrated to help reduce the risk of heart disease. However, the agency concluded that it was premature to do so because FDA had not reviewed the totality of evidence on other, non-whole oat sources of soluble fiber (62 FR 3584 at 3588).

The agency amended Sec. 101.81 (21 CFR 101.81), in response to a health claim petition to add a health claim relating soluble fiber from psyllium seed husk and CHD risk (63 FR 8103, February 18, 1998). At this time, FDA also modified the heading in Sec. 101.81 from ``* * * Soluble fiber from whole oats and risk of coronary heart disease" to ``* * * Soluble fiber from certain foods and risk of coronary heart disease (CHD)" (63 FR 8103). FDA has also amended Sec. 101.81, in response to health claim petitions, to include oatrim, whole grain barley, and certain dry milled barley grain products as eligible sources of beta-glucan soluble fiber. In 2002, FDA amended Sec. 101.81 to add oatrim, which is the soluble fraction of alpha-amylase hydrolyzed oat bran or whole oat flour, as an eligible source of beta-glucan soluble fiber (67 FR 61733, October 2, 2002), and finally, FDA amended Sec. 101.81 to add whole grain barley and certain dry milled barley grain products as eligible sources of beta-glucan soluble fiber in 2005 (70 FR 76150, December 23, 2005).

II. Petition and Grounds

A. The Petition

Cargill, Inc. (petitioner), submitted a health claim petition to FDA on June 20, 2006, under section 403(r)(4) of the act (21 U.S.C. 343(r)(4)). The petition requested that the agency expand the ``Soluble fiber from certain foods and risk of coronary heart disease health claim" (Sec. 101.81) to include ``barley betafiber" (described in section II.B of this document) as an eligible food ingredient source of beta-glucan soluble fiber in addition to the oat and whole grain and dry milled barley ingredients now listed (Ref. 1). On September 28, 2006, the agency notified the petitioner that it had completed its initial review of the petition and that the petition was being filed for further action in accordance with section 403(r)(4) of the act. If the agency does not act, by either denying the petition or issuing a proposed regulation to authorize the health claim, within 90 days of the date of filing for further action, the petition is deemed to be denied unless an extension is mutually agreed upon by the agency and the petitioner (section 403(r)(4)(A)(i) of the act and Sec. 101.70(j)(3)(iii)). The petitioner and FDA subsequently mutually agreed to extend the deadline for the agency's decision on the petition to March 6, 2008. The petitioner also requested that FDA issue an interim final rule by which labeling of foods that contain ``barley betafiber" in appropriate amounts could bear the health claim prior to publication of a final rule.

B. Nature of the Substance

The substance that is the subject of the oat/barley portion of current Sec. 101.81 is beta-glucan soluble fiber from the specific oat and barley food products listed in Sec. 101.81(c)(2)(ii)(A). Current Sec. 101.81(c)(2)(ii)(A) has been amended twice previously to list additional oat or barley food products as eligible sources (67 FR 61773 and 70 FR 76150). Similar to these previous actions, FDA is now, in response to Cargill's health claim petition, amending Sec. 101.81(c)(2)(ii)(A) to list barley betafiber as an eligible source of barley beta-glucan soluble fiber.

The petition states that barley betafiber is a concentrated barley beta-glucan soluble fiber product derived from whole barley flour. The petitioner's description of the barley betafiber manufacturing process reflects information contained in the petitioner's patent entitled ``Improved Dietary Fiber Containing Materials Comprising Low Molecular Weight Glucan" (World Intellectual Property Organization, International Publication Number WO 2004/086878 A2) (Ref. 2) and a report of an expert panel on the generally recognized as safe (GRAS) status of barley betafiber commissioned by the petitioner (Ref. 3). The patent and the GRAS status report provide information on multiple variations of procedures for manufacturing concentrated barley beta-glucan soluble fiber products; these procedures differ from the manufacturing procedures for producing the unique barley betafiber substance that is the subject of the petition. Further, the clinical trial reported in the petition tested two different barley beta-glucan soluble fiber concentrates--a high molecular weight concentrate and a low molecular weight concentrate. The petitioner specified that the barley betafiber product, which is the subject of the petition, is only the low molecular weight concentrate studied in the clinical trial (Ref. 4). FDA was not satisfied that the information in the petition was sufficiently specific in describing the manufacturing process for the unique barley betafiber product for which there is scientific evidence to permit a showing that the product is comparable in cholesterol-lowering ability to the other oat and barley food products listed in current Sec. 101.81(c)(2)(ii)(A). Discussion between the agency and the petitioner resulted in the description of the barley betafiber manufacturing process presented in the following paragraph and in final Sec. 101.81(c)(2)(ii)(A)(6) (Refs. 2 through 5).

Barley betafiber is produced from an aqueous slurry of whole grain barley flour, starting with addition of an exogenous grain liquefying enzyme preparation with cellulase and alpha-amylase activity, derived from Bacillus amyloliquefaciens. The cellulase activity of the enzyme preparation acts on the beta-glucan soluble fiber in barley flour, since beta-glucan is a type of cellulose, and the alpha-amylase activity of the enzyme preparation acts on the starch in the barley flour. The temperature of the slurry is kept at or above the gelatinization temperature of the barley starch but below cellulase enzyme inactivation temperature; i.e., about 65[deg] C, for about 30 to 60 minutes, to facilitate a partial hydrolysis of both the beta-glucan soluble fiber and starch. The pH of the slurry is kept in the range of about 5 to 7. When the cellulase enzymatic hydrolysis of barley flour has modified the beta-glucan soluble fiber to the desired extent, the cellulase activity of the enzyme preparation is heat inactivated. After

the cellulase activity of the enzyme preparation has been deactivated, an exogenous thermo-stable amylolytic enzyme is added to the barley flour slurry for continued hydrolysis of starch molecules at the higher temperature. The slurry is held at the higher temperature until substantially all the starch has been hydrolyzed. A clear aqueous extract, which contains barley betafiber and the sugars and dextrins resulting from substantial hydrolysis of starch is then separated from insoluble material by centrifugation. Barley betafiber is precipitated from the aqueous extract supernatant with ethanol to separate it from other soluble components (i.e., substantially hydrolyzed starch, protein, lipids and other minor components) that remain suspended in the aqueous extract supernatant. The resultant barley betafiber precipitate is then dried and milled. The molecular weight range of barley betafiber produced by this procedure is 120 to 400 kilodaltons (Refs. 2, 3, and 5). The molecular weight range of barley betafiber is substantially reduced from that of native barley beta-glucan soluble fiber. The molecular weight range of native barley beta-glucan soluble fiber has been reported to range from about 500 to 3,330 kilodaltons depending upon the cultivars and applied extraction procedures, although lower molecular weight values of 80 to 300 kilodaltons have also been reported (Ref. 1). In final Sec. 101.81(c)(2)(ii)(A)(6), FDA defines barley betafiber by its manufacturing process, as follows ``Barley betafiber. Barley betafiber is the ethanol precipitated soluble fraction of cellulase and alpha-amylase hydrolyzed whole grain barley. Barley betafiber is produced by hydrolysis of whole grain barley flour, as defined in paragraph (c)(2)(ii)(A)(5) of this section, with a cellulase and alpha-amylase enzyme preparation, to produce a clear aqueous extract that contains mainly partially hydrolyzed beta-glucan and substantially hydrolyzed starch. The soluble, partially hydrolyzed beta-glucan is separated from the insoluble material by centrifugation, and after removal of the insoluble material, the partially hydrolyzed beta-glucan soluble fiber is separated from the other soluble compounds by precipitation with ethanol. The product is then dried, milled and sifted. Barley betafiber shall have a beta-glucan soluble fiber content of at least 70 percent on a dry weight basis."

C. Review of Preliminary Requirements for a Health Claim

1. The Substance Is Associated With a Disease for Which the U.S. Population Is at Risk

CHD continues to be a disease that has a large impact on mortality and morbidity in the general adult U.S. population. As explained in the existing beta-glucan soluble fiber health claim (Sec. 101.81(b)), FDA recognizes the CHD risk reduction benefit of certain foods that are sources of soluble dietary fiber resulting from effects on lowering blood total and LDL cholesterol. Although age-adjusted CHD mortality rates in the United States had been steadily decreasing since approximately 1960, recent evidence has suggested that the decline in CHD mortality has slowed (Ref. 6). Heart disease has been recognized as the leading cause of death in the United States for at least the last 50 years (Ref. 6). Based on these facts, FDA concludes that, as required in Sec. 101.14(b)(1), CHD is a disease for which the U.S. population is at risk.

2. The Substance Is a Food

The substance of the health claim is beta-glucan soluble fiber from listed oat and barley sources. The petitioner requests an amendment to add barley betafiber to the list of eligible sources of beta-glucan soluble fiber. Barley betafiber is derived from whole barley flour. Barley flour is a commonly consumed human food and beta-glucan soluble fiber is a nutrient component of this food. Thus, the beta-glucan soluble fiber from barley betafiber, a processed whole barley flour product, is a ``substance" as defined in Sec. 101.14(a)(2). Health claim general requirements provide that where a substance is to be consumed at ``other than decreased dietary levels," the substance must contribute taste, aroma, nutritive value, or any other technical effect as listed in 21 CFR 170.3(o), and must retain that attribute when consumed at levels necessary to justify the claim (Sec. 101.14(b)(3)(i)). The level necessary to justify the claim is 0.75 g beta-glucan soluble fiber per serving. The term ``nutritive value" is defined in Sec. 101.14(a)(3) as ``a value in sustaining human existence by such processes as promoting growth, replacing lost essential nutrients, or providing energy." The petitioner provided several examples of food categories (bars, beverages, bread, breakfast cereals, cookies, crackers, instant rice, pasta, muffins, salad dressings, snack chips, soups, tortillas and taco shells, vegetarian patties/crumbles, and reduced fat yogurt) in which barley betafiber could be used as an ingredient at a maximum level of 3 grams (g) beta-glucan soluble fiber per serving. Beta-glucan soluble fiber at 0.75 to 3 g per serving contributes nutritive value because it provides a source of calories and soluble fiber. In addition to its role as a source of beta-glucan soluble fiber, barley betafiber also has technical effects, including food applications as a thickener (e.g., soups), texturizer (e.g., snack foods), humectant (e.g., retain moisture of tortillas), or fat replacer (e.g., dressings for salads). Therefore, FDA concludes that the preliminary requirement of Sec. 101.14(b)(3)(i) is satisfied.

3. The Substance Is Safe and Lawful

Section 101.14(b)(3)(ii) requires that the substance be a food or a food ingredient or a component of a food ingredient whose use at the levels necessary to justify a claim has been demonstrated by the proponent of the claim, to FDA's satisfaction, to be safe and lawful under the applicable food safety provisions of the act. The petitioner asserts that the use of barley betafiber as a food ingredient is GRAS. The petitioner included in its health claim petition documentation of its 2003 GRAS self-determination for barley betafiber, which contains 70 percent or more pure barley beta-glucan soluble fiber as evidence that barley betafiber meets the safe and lawful requirement (Ref. 3). FDA also received a notice informing FDA that the petitioner determined, through scientific procedures, that the use of barley betafiber is GRAS. FDA issued a letter (Ref. 7) in response to this notice stating that the agency had no questions at the time regarding petitioner's conclusions that barley betafiber is GRAS under the intended conditions of use.

The 2003 Cargill GRAS self-determination stipulates that barley betafiber is obtained from food-grade whole grain barley flour by water

extraction at elevated temperature, while starch is removed during the extraction process by treatment with enzymes that are GRAS for use in food manufacturing processes, specifically alpha-amylases from Bacillus licheniformis and B. amyloliquefaciens. The extracted barley betafiber is recovered by precipitation with denatured ethanol suitable for food production, and contains 70 percent or more beta-glucan, 2 to 12 percent protein, and less than 3 percent of each sugars, lipids, and inorganic salts. The basis of the safety determination relies on the fact that barley betafiber contains only native components of barley and is formed by the action of applied food-grade enzymes, residues, or processing aids.

In addition, barley is a traditional food with a long history of safe use, since at least 8,000 B.C. based on archeological discoveries (Ref. 3). In the Maghreb countries of Morocco, Algeria, Libya, and Tunisia, barley is used in a variety of traditional foods (bread, soup, porridge), resulting in an average intake of up to 172 g per person per day (Morocco). With this intake of barley, about 6 g per person per day of pure beta-glucan soluble fiber is consumed. The preparation of these traditional foods involves baking or boiling for longer periods of time, which ensures extraction of beta-glucan from its natural context (cell walls, complexes with proteoglycans). The physiological properties of beta-glucan as a dietary fiber may, therefore, be found in these traditional foods as is intended to be achieved with the addition to processed foods of barley beta-glucan concentrate.

The intended uses of barley betafiber listed as a food ingredient stated in the 2003 Cargill GRAS self-determination include the following food categories: Bars, beverages, bread (whole grain and specialty), breakfast cereals (ready to eat and cooked), cookies (lite), crackers (reduced fat), instant rice, macaroni products, muffins (reduced fat), salad dressings (lite), snack chips (reduced fat), soups, tortillas and taco shells, vegetarian patties/crumbles, and reduced fat yogurt. The maximum incorporation rate for each of these food applications is 3 g beta-glucan soluble fiber from barley betafiber per serving.

FDA concludes that the petitioners have satisfied the preliminary requirement of Sec. 101.14(b)(3)(ii) to demonstrate, to FDA's satisfaction, that the use of beta-glucan soluble fiber from barley betafiber at levels necessary to justify the health claim is safe and lawful under the applicable food safety provisions of the act. The agency has not made its own determination regarding the GRAS status of barley betafiber or beta-glucan soluble fiber from barley betafiber. Furthermore, the agency notes that a regulation to authorize a health claim for a substance should not be interpreted as affirmation that the substance is GRAS.

III. Review of Scientific Evidence of the Substance-Disease Relationship

A. Basis for Evaluating the Relationship Between Beta-Glucan Soluble Fiber from Barley Betafiber and CHD

The types of data that FDA has recognized in previous CHD health claim evaluations as useful for assessing CHD risk reduction are:

Coronary events (myocardial infarction, ischemia), cardiovascular death, atherosclerosis, high blood pressure, serum total cholesterol, and serum LDL cholesterol. FDA considers high blood pressure, serum total cholesterol, and serum LDL cholesterol levels to be the only currently validated surrogate measures for CHD risk (Ref. 8). Elevated levels of serum total and LDL cholesterol, a prerequisite for atherosclerotic disease, is a major modifiable risk factor in the development of CHD (Ref. 8). For these reasons, the agency based its original evaluation of the relationship between oat beta-glucan soluble fiber and CHD risk (62 FR 3584) and subsequent evaluations to add oatrim (67 FR 61773) and barley as eligible sources of beta-glucan soluble fiber (70 FR 76150) in the health claim, primarily on evidence for serum total and LDL cholesterol-lowering effects of beta-glucan soluble fiber containing food ingredients. As such, our evaluation of the evidence supporting the petitioned request to extend the eligible barley sources to include barley betafiber (as described in section II.B of this preamble), focused on evidence from human randomized controlled trials of the effects of consuming beta-glucan soluble fiber from barley betafiber on blood lipids. This focus is consistent with existing Sec. 101.81 in which FDA concluded that there is significant scientific agreement that the relationship between CHD risk and consumption of beta-glucan soluble fiber from certain oat and barley food ingredients is mediated primarily by the effect of the beta-glucan soluble fiber on serum lipids.

FDA's determination of significant scientific agreement that the totality of publicly available scientific evidence supports the relationship between beta-glucan soluble fiber from certain oat and barley foods and CHD risk is documented in rulemaking for Sec. 101.81. When issuing the 1997 oat beta-glucan health claim final rule, the agency concluded that the beta-glucan soluble fiber component of oat products plays a significant role in the relationship between whole grain oats and the risk of CHD based, in part, on evidence that there is a dose response between the level of beta-glucan soluble fiber from whole oats and the level of reduction in serum LDL cholesterol, and evidence that intakes at or above 3 g per day were more effective in lowering serum lipids than lower intake levels (62 FR 3584 at 3585). In the 2002 and 2005 amendments to the health claim to add oatrim and whole grain and dry milled barley products, respectively, as eligible sources of beta-glucan soluble fiber, the agency considered evidence that beta-glucan soluble fiber from those sources had comparable cholesterol-lowering effects to that from the sources previously listed in Sec. 101.81(c)(2)(ii)(A) as further support for FDA's previous determination that there is significant scientific agreement that a relationship exists between consumption of certain beta-glucan soluble fiber sources and reduced risk of CHD (67 FR 61773 at 61779 and 70 FR 76150 at 76155). Similarly, FDA considers that scientific evidence to establish that the cholesterol-lowering effects of beta-glucan soluble fiber from barley betafiber are comparable to the effects of beta-glucan soluble fiber from the oat/barley products in current Sec. 101.81(c)(2)(ii)(A) builds on the substantial base of scientific evidence that already establishes significant scientific agreement for the association between consumption of the oat/barley products now listed and reduced risk of CHD. FDA's review of the evidence to support the petitioned amendment of the health claim regulation entitled ``Soluble fiber from certain foods and risk of CHD'' was conducted

consistent with FDA published guidance on significant scientific agreement in the review of health claims (Ref. 9) and focused on evidence from intervention studies.

B. Assessment of Intervention Studies

This petition identified one relevant human randomized controlled trial of how consumption of beta-glucan soluble fiber from barley betafiber affects heart disease risk and serum lipid levels. A summary of this trial was included in the petition and subsequently published in a peer reviewed scientific journal (Ref. 4). FDA also evaluated reported results from randomized controlled trials of other types of beta-glucan concentrates, extracts, and gums (Refs. 10 through 19).

The study reported in Keenan et al. 2007 (Ref. 4) investigated the effects of consuming concentrated barley beta-glucan soluble fiber-enriched foods (fruit drink and corn flakes) on blood lipids in hypercholesterolemic men and women. The study was conducted as a randomized, double-blind, placebo-controlled, parallel arm study of five groups with 30 to 32 subjects per group. The study included a total of 155 hypercholesterolemic adult subjects, between 25 and 73 years of age, with baseline serum LDL cholesterol levels between 140 and 190 milligrams per deciliter (mg/dL). The subjects were instructed to follow a diet low in saturated and trans fatty acids (less than 10 percent kilocalories (kcals) per day) and to consume three servings of the concentrated barley beta-glucan soluble fiber-enriched test foods per day, one serving with each of three major meals. The concentrated barley beta-glucan soluble fiber-enriched test foods were formulated to provide either 3 or 5 g of beta-glucan soluble fiber per day; a placebo version of the test foods without added barley beta-glucan extracts was also used. Two concentrated barley beta-glucan soluble fiber products were used; one is the barley betafiber produced from the manufacturing process described in section II.B of this preamble, and was described in the study report as a low molecular weight (LMW) extract; the other concentrated barley beta-glucan soluble fiber product of the study was described as a high molecular weight (HMW) beta-glucan extract. The HMW barley beta-glucan extract was processed in a fashion similar to that for barley betafiber but omitted the cellulase enzymatic hydrolysis step, thus producing a concentrated source of barley beta-glucan soluble fiber with a molecular weight similar to that of the endogenous beta-glucan soluble fiber in barley grain from which it was derived.

Following a 4-week run-in period to adjust to the low saturated/ trans fat diet, the subjects were randomly assigned to one of five treatment groups: placebo control, 3 g per day barley betafiber, 5 g per day barley betafiber, 3 g per day HMW beta-glucan extract, and 5 g per day HMW beta-glucan extract. Subjects consumed the test foods daily for 6 weeks. Consumption of 3 or 5 g beta-glucan per day from barley betafiber significantly lowered serum total cholesterol levels (6.0 percent and 9.9 percent, respectively) relative to the placebo control group. Consumption of 3 or 5 g beta-glucan per day from the HMW barley beta-glucan extract also significantly lowered serum total cholesterol (7.0 percent and 11.2 percent, respectively) relative to the placebo control group. Serum LDL cholesterol levels were significantly decreased in all active treatment groups. At the end of the 5-week intervention period, the mean serum LDL cholesterol level of the 3 g

per day beta-glucan from barley betafiber group was 10 mg/dL lower than the mean serum LDL cholesterol level of the placebo control group, representing a 7.5 percent reduction in LDL cholesterol relative to the placebo control group. The reduction in mean serum LDL cholesterol for the 5 g per day beta-glucan from barley betafiber group relative to the placebo control group was 16 mg/dL or 12 percent. The reduction in mean serum LDL cholesterol for the 3 g per day HMW beta-glucan group was 12 mg/dL or 8 percent relative to the placebo control group. For the 5 g per day HMW beta-glucan group, the reduction in mean LDL cholesterol was 19 mg/dL or 13 percent relative to the placebo control group. There were no statistically significant differences between barley betafiber and the HMW barley beta-glucan extract groups, or between 3 g per day or 5 g per day beta-glucan groups, in the magnitude of the cholesterol lowering effects.

The magnitude of cholesterol-lowering reported by Keenan et al. (Ref. 4) for 3 and 5 g per day beta-glucan from barley betafiber is consistent with the magnitude of cholesterol-lowering observed with similar barley beta-glucan soluble fiber intake levels consumed as dry milled barley foods (70 FR 76150 at 76153). The randomized controlled trials with dry milled barley foods that FDA considered when previously amending the health claim to add dry milled barley had reported mean serum LDL cholesterol reductions of between 10 and 19 mg/dL from barley beta-glucan intake levels of 3 to 8 g per day. Based on evidence from the randomized controlled trials of dry milled barley ingredients which FDA relied upon when adding barley products to the health claim, the data for barley betafiber from Keenan et al. are consistent with the expected magnitude of cholesterol-lowering from consumption of the barley products listed in current Sec. 101.81(c)(2)(ii)(A)(5).

Clinical trial evidence of oat/barley beta-glucan extracts other than barley betafiber indicate that not all oat/barley beta-glucan extracts affect serum total and LDL cholesterol levels as consistently as does consumption of the intact oat and barley grain from which they have been extracted (Refs. 10 through 19). This indicates that some extraction processes negatively affect whatever characteristics of beta-glucan soluble fiber in whole grain oats and barley that are responsible for the cholesterol-lowering effect. Accordingly, data from trials of beta-glucan extracts and concentrates other than barley betafiber support FDA's previous position (62 FR 3584 at 3587) that oat and barley products will be added to the health claim as eligible sources of beta-glucan soluble fiber only on a case-by-case basis when FDA is presented with adequate supporting evidence.

Evidence from the randomized controlled trial reported by Keenan et al. (Ref. 4) indicates that beta-glucan soluble fiber from barley betafiber, prepared as described in section II of this preamble, is comparable to beta-glucan soluble fiber from the oat and barley sources now included in current Sec. 101.81 in regard to cholesterol-lowering properties. Evidence from randomized controlled trials of other oat or barley beta-glucan extracts indicate that some forms of processing of oat and barley grain to extract or concentrate beta-glucan can negatively affect whatever properties of oat and barley beta-glucan are responsible for the cholesterol-lowering effect. Therefore, results from Keenan et al. can not be extrapolated to beta-glucan extracts other than the specific products tested in the trial. Results from the

Keenan et al. trial also demonstrate that the serum cholesterol-lowering effects were comparable for beta-glucan soluble fiber from barley betafiber (i.e., the LMW product in the Keenan et al. trial) and for the barley beta-glucan extract that was not subjected to beta-glucan hydrolysis (the HMW product in the Keenan et al. trial) (Ref. 4). This evidence demonstrates that the cholesterol-lowering ability of beta-glucan soluble fiber in barley betafiber is not affected by the process used in the manufacture of barley betafiber to reduce the molecular weight of the barley betafiber product.

IV. Decision to Amend the Health Claim

Available evidence demonstrates that foods enriched with beta-glucan soluble fiber from barley betafiber at levels sufficient to provide at least 3 g beta-glucan soluble fiber per day are effective in lowering serum LDL-cholesterol levels, which may reduce the risk of CHD. As noted previously, when issuing the 1997 oat beta-glucan health claim final rule the agency concluded that the beta-glucan soluble fiber component of oat products plays a significant role in the relationship between whole grain oats and the risk of CHD based, in part, on evidence that there is a dose response between the level of beta-glucan soluble fiber from whole oats and the level of reduction in serum LDL cholesterol, and evidence that intakes at or above 3 g per day were more effective in lowering serum lipids than lower intake levels (62 FR 3584 at 3585). The clinical trial results reported by Keenan et al. (Ref. 4) demonstrating the cholesterol-lowering effect of consuming beta-glucan soluble fiber from barley betafiber are consistent in magnitude with what would be expected based on the oat beta-glucan soluble fiber/cholesterol-lowering dose-response evidence, which was cited in the 1997 oat beta-glucan health claim final rule, and cholesterol-lowering effect of consuming beta-glucan soluble fiber from dry milled barley grain ingredients (70 FR 76150 at 76155). Thus, FDA concludes that the cholesterol-lowering effect of beta-glucan soluble fiber from barley betafiber is comparable to that of beta-glucan soluble fiber from whole grain oat and dry milled barley sources currently listed in Sec. 101.81(c)(2)(ii)(A). FDA also concludes that the scientific evidence supports a minimum daily effective intake of beta-glucan soluble fiber from barley betafiber the same as that which was previously found for whole oat and dry milled barley sources of beta-glucan soluble fiber, i.e., 3 g per day. Therefore, FDA is amending Sec. 101.81, by adding Sec. 101.81(c)(2)(ii)(A)(6) to list barley betafiber as an eligible source of beta-glucan soluble fiber. Consistent with current Sec. 101.81(c)(2)(i)(G)(1), the source of the 3 g or more per day of beta-glucan soluble fiber may be from whole oats or barley, including the barley betafiber source, or a combination of oats and barley eligible sources. In addition, consistent with the description of other oat and barley products listed in current Sec. 101.81, amended Sec. 101.81 will specify barley betafiber by the method of production as described in section II.B of this preamble. The agency is satisfied that the description of the method for producing barley betafiber appropriately characterizes the barley product being added to the regulation. Further, barley beta-glucan can be measured by the same quantitative analytical method as is currently specified in Sec. 101.81(c)(2)(ii)(A) for the determination of oat beta-glucan and barley beta-glucan from whole grain barley and dry milled barley products. Based on the totality of the publicly available scientific

evidence, FDA concludes there is significant scientific agreement, among experts qualified by scientific training and experience, for a claim about the relationship between certain beta-glucan soluble fiber sources and reduced risk of CHD. Thus, FDA is amending Sec. 101.81(c)(2)(ii)(A) to include barley betafiber derived from whole barley flour, prepared as described in section II.B of this document, as an additional source of beta-glucan soluble fiber.

The requirement in Sec. 101.81(c)(2)(iii)(A) states that a food bearing the claim on its label include one of the ingredients listed within Sec. 101.81(c)(2)(ii)(A) and that the ingredient provide at least 0.75 gram of beta-glucan soluble fiber per reference amount customarily consumed (RACC) of the food product. This level is based on the minimum daily effective intake of beta-glucan soluble fiber from barley betafiber and is the same as that which was previously found for whole oat and dry milled barley sources of beta-glucan soluble fiber, i.e., 3 g per day. FDA arrived at a value of 0.75 gram beta-glucan soluble fiber per RACC based on a standard assumption that the daily dietary intake is divided over four eating occasions per day (three meals and a snack) (62 FR 3584 at 3592). Thus, adding barley betafiber as an additional eligible source of beta-glucan soluble fiber will further increase the type and number of qualifying food products and make it easier for consumers to select barley and oat products at four eating occasions per day. Thus, FDA is retaining under the ``Nature of the food eligible to bear the claim'' section of the codified text of this interim final rule, the criterion that foods eligible to bear the claim contain at least 0.75 gram of soluble fiber (Sec. 101.81(c)(2)(iii)(A)(2)).

There is strong consistent scientific evidence that diets high in saturated fat and cholesterol are associated with elevated serum total and LDL cholesterol, and that elevated serum cholesterol levels are a major modifiable risk factor for CHD. Expert groups recommend lowering dietary saturated fat and cholesterol as a primary lifestyle change for reducing heart disease risk (Ref. 8). Comments to the 1997 oat beta-glucan health claim final rule expressed concern that a CHD risk claim that does not include a reference to a low saturated fat, low cholesterol diet may mislead consumers into thinking that the single food, e.g., oat products, would appear to be a ``magic bullet'' (62 FR 3584 at 3594). Further, based on the scientific evidence, the role of soluble fiber from whole oats in the diet is generally recognized as being of smaller magnitude in reducing CHD risk compared to consumption of a low saturated fat, low cholesterol diet. When issuing the 1997 oat beta-glucan health claim final rule, FDA concluded that although selection of foods with soluble fiber from whole oats is a useful adjunct to selection of diets low in saturated fat and cholesterol, in reducing CHD risk, it would not be in the best interest of public health nor consistent with the scientific evidence to imply that selecting diets with soluble fiber from whole oats is a substitute for consuming diets low in saturated fat and cholesterol (id.). Therefore, FDA required in the 1997 oat beta-glucan health claim final rule that the health claim statement include the phrase ``diets that are low in saturated fat and cholesterol and that include soluble fiber from * * *'' (Sec. 101.81(c)(2)(i)(A)). FDA reiterated this position and extended it to soluble fiber from listed barley products when the agency amended Sec. 101.81 to add whole grain barley and certain dry

milled barley products as eligible sources of beta-glucan soluble fiber in 2005 (70 FR 76150 at 76156).

Beta-glucan soluble fiber from barley betafiber functions comparably to beta-glucan soluble fiber from the listed oat and barley sources in current Sec. 101.81(c)(2)(ii)(A) in its effect on reducing LDL and total cholesterol. Barley betafiber, as a source of beta-glucan soluble fiber, is a useful adjunct to selection of diets low in saturated fat and cholesterol to reduce CHD risk. Thus, the agency is requiring that the beta-glucan soluble fiber from barley betafiber health claim be subject to the requirements in Sec. 101.81(c)(2)(i)(A). Including a reference to a low saturated fat, low cholesterol diet in the health claim will enable the public to understand the relative significance of the information in the context of a total daily diet (21 U.S.C. 343(r)(3)(A)(iii)).

V. Description of Amendments to the Soluble Fiber from Certain Foods and Risk of Coronary Heart Disease Health Claim Regulation

A. Nature of the Substance; Eligible Sources of Soluble Fiber

Section 101.81(c)(2)(ii) (nature of the substance) lists the types and sources of soluble fiber that have been demonstrated to FDA's satisfaction to have a relationship to a reduced risk of CHD. Section 101.81(c)(2)(ii)(A) lists beta-glucan soluble fiber from whole oat and barley sources, along with specifying an AOAC INTERNATIONAL method of analysis for beta-glucan soluble fibe, which will be used by FDA for verifying compliance. Section 101.81(c)(2)(ii)(A)(1) through (c)(2)(ii)(A)(5) identifies the whole oat and barley products that are eligible sources of beta-glucan, i.e., oat bran, rolled oats, whole oat flour, oatrim, whole grain barley, and dry milled barley.

FDA is amending Sec. 101.81(c)(2)(ii)(A) by adding Sec. 101.81(c)(2)(ii)(A)(6), which would specify barley betafiber as being the ethanol isolated, soluble fraction of cellulase and alpha-amylase hydrolyzed whole grain barley flour, with a beta-glucan content of at least 70 percent on a dry weight basis (dwb). Thus, Sec. 101.81(c)(2)(ii)(A)(6) will read as follows ``Barley betafiber. Barley betafiber is the ethanol precipitated soluble fraction of cellulase and alpha-amylase hydrolyzed whole grain barley. Barley betafiber is produced by hydrolysis of whole grain barley flour, as defined in paragraph (c)(2)(ii)(A)(5) of this section, with a cellulase and alpha-amylase enzyme preparation, to produce a clear aqueous extract that contains mainly partially hydrolyzed beta-glucan and substantially hydrolyzed starch. The soluble, partially hydrolyzed beta-glucan is separated from the insoluble material by centrifugation, and after removal of the insoluble material, the partially hydrolyzed beta-glucan soluble fiber is separated from the other soluble compounds by precipitation with ethanol. The product is then dried, milled and sifted. Barley betafiber shall have a beta-glucan soluble fiber content of at least 70 percent on a dry weight basis."

B. Nature of the Food Eligible to Bear the Claim

Section 101.81(c)(2)(iii)(A)(2) (nature of the food) currently states ``The food containing the oatrim from paragraph (c)(2)(ii)(A)(4)

of this section shall contain at least 0.75 g of beta-glucan soluble fiber per reference amount customarily consumed of the food product;"

Because FDA is amending Sec. 101.81 to add barley betafiber, FDA is amending Sec. 101.81(c)(2)(iii)(A)(2) as follows ``The food containing the oatrim from paragraph (c)(2)(ii)(A)(4) of this section or the barley betafiber from paragraph (c)(2)(ii)(A)(6) of this section shall contain at least 0.75 g of beta-glucan soluble fiber per reference amount customarily consumed of the food product;"

C. Other Requirements

All other requirements in Sec. 101.81(c)(1) through (c)(2)(i) and the optional information in Sec. 101.81(d) will apply to the use of the health claim authorized in Sec. 101.81 for barley betafiber-containing products.

D. Model Health Claims

This interim final rule to amend existing Sec. 101.81(c)(2) does not affect the model health claims specified in paragraph (e) of Sec. 101.81. Thus, the model health claims in Sec. 101.81(e) apply to a claim about beta-glucan soluble fiber from barley betafiber and a reduced risk of CHD.

VI. Analysis of Impacts

FDA has examined the impacts of this interim final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104-4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this interim final rule is not a significant regulatory action as defined by the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because this interim final rule concerns voluntary claims, the agency certifies that the interim final rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ``any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is $127 million, using the most current (2006) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this interim final rule to result in any 1-year expenditure that would meet or exceed this amount.

FDA has identified the following three options regarding this petition: (1) Deny the petition; (2) authorize the petition (add only barley betafiber to the ``Soluble fiber from certain foods and risk of coronary heart disease health claim`` in Sec. 101.81 (the soluble fiber and CHD health claim)); or (3) add barley betafiber to the soluble fiber-CHD health claim and also expand the scope of the claim to include all sources of soluble fiber. FDA concludes that authorizing the petition by adding barley betafiber to the soluble fiber and CHD health claim is the best option of those identified.

Option One: Deny the Petition

FDA can only define costs and benefits relative to a baseline. FDA usually selects the option of taking no action as the baseline because it helps readers identify the costs and benefits of actions that change the status quo. In this case, denying the petition would correspond to taking no action because it would imply no change in the soluble fiber and CHD health claim and thus the continuation of the status quo. By definition, the baseline itself has no costs or benefits. This does not mean that we ignore the costs and benefits of the baseline. Instead, it means that FDA expresses the costs and benefits of the baseline in how it calculates the costs and benefits of the other regulatory options.

Option Two: Authorize the Petition (Add Only Barley Betafiber to the Soluble Fiber and CHD Health Claim)

This option would allow producers who use barley betafiber to use the soluble fiber and CHD health claim on their product labels under certain conditions. Producers would only choose to change product labels or reformulate products if they believe that the benefits that they will derive from doing so are at least as great as the costs of making those changes. FDA has reviewed the data supplied in the petition and concludes that the claim is truthful and not misleading. If this interim final rule is finalized without change, FDA can be sure that to whatever extent producers use the claim, consumers will be in a better position, assuming that more information that is truthful and not misleading is always better for consumers. Based on this, FDA can conclude that adding barley betafiber to the soluble fiber and CHD health claim is better for social welfare than denying the petition.

Option Three: Add Barley Betafiber to the Soluble Fiber and CHD Health Claim and Also Expand the Scope of the Claim to Include All Sources of Soluble Fiber

This option would allow producers who use barley betafiber and all other sources of soluble fiber to use the soluble fiber and CHD health claim on their product labels under certain conditions rather than just listing specific sources of soluble fiber. Similar to option two, producers would only choose to change product labels or reformulate products if they believed that the benefits that they will derive from doing so are at least as great as the costs of making those changes. In addition, this option would reduce the future burden on manufacturers of petitioning FDA to use the soluble fiber and CHD health claim for additional sources of soluble fiber, and it would also reduce the agency's burden of evaluating each petition for each individual source of soluble fiber. However, by expanding the use of the claim to all

sources of soluble fiber without reviewing the scientific data on each source, FDA would not be able to verify that the claim was being used under circumstances where it is truthful and not misleading to consumers. If the expanded claim was used on a product that did not reduce the risk of CHD, then the expanded claim could actually result in an increase in CHD. This would happen if consumers were misled into thinking that they were reducing their risk of CHD by consuming a product that actually did not reduce the risk of CHD. As a result, they might not take other beneficial steps that would decrease their risk of CHD.

FDA cannot conclude that the cost savings of option three outweigh the increased risk of a false or misleading claim being made under the expanded claim. Therefore FDA cannot conclude that option three is better for social welfare than option two. Moreover, the agency believes that expanding the soluble fiber and CHD health claim to all sources of soluble fiber without reviewing the scientific data supporting such a claim of CHD risk reduction for each individual source of fiber would be a failure to carry out our statutory responsibility under section 403(r)(3)(B) of the act to issue health claim regulations only when the agency determines that there is significant scientific agreement that the claim is supported by the totality of publicly available scientific evidence.

VII. Environmental Impact

The agency has determined under 21 CFR 25.32(p) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Paperwork Reduction Act of 1995

FDA concludes that the labeling provisions of this interim final rule are not subject to review by the Office of Management and Budget because they do not constitute a ``collection of information'' under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). Rather, the food labeling health claim on the association between consumption of barley betafiber beta-glucan soluble fiber and CHD risk is a ``public disclosure of information originally supplied by the Federal Government to the recipient for the purpose of disclosure to the public'' (see 5 CFR 1320.3(c)(2)).

IX. Federalism

FDA has analyzed this interim final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule has a preemptive effect on State law. Section 4(a) of the Executive order requires agencies to ``construe * * * a Federal statute to preempt State law only where the statute contains an express preemption provision or there is some other clear evidence that the Congress intended preemption of State law, or where the exercise of State authority conflicts with the exercise of Federal authority under the Federal statute.'' Section 403A of the act (21 U.S.C. 343-1) is an express preemption provision. Section 403A(a)(5) of the act provides that ``* * * no State or political subdivision of a State may directly

or indirectly establish under any authority or continue in effect as to any food in interstate commerce--* * * any requirement respecting any claim of the type described in section 403(r)(1) of the act made in the label or labeling of food that is not identical to the requirement of section 403(r). * * *"

Currently, this provision operates to preempt States from imposing health claim labeling requirements concerning beta-glucan soluble fiber from barley betafiber and reduced risk of CHD because no such requirement had been imposed by FDA under section 403(r) of the act. This interim final rule, if finalized without change, would amend existing food labeling regulations to add barley betafiber as an eligible source of beta-glucan soluble fiber to the authorized health claim for soluble fiber from certain foods and risk of CHD. Although this rule would have a preemptive effect in that it would preclude States from issuing any health claim labeling requirements for beta-glucan soluble fiber from barley betafiber and a reduced risk of CHD that are not identical to those that would be required by this interim final rule, this preemptive effect is consistent with what Congress set forth in section 403A of the act. Section 403A(a)(5) of the act displaces both State legislative requirements and State common law duties. (Medtronic v. Lohr, 518 U.S. 470, 503 (1996) (Breyer, J., concurring in part and concurring in judgment); id. at 510 (O'Connor, J., joined by Rehnquist, C.J., Scalia, J., and Thomas, J., concurring in part and dissenting in part); Cipollone v. Liggett Group, Inc., 505 U.S. 504, 521 (1992) (plurality opinion); id. at 548-49 (Scalia, J., joined by Thomas, J., concurring in judgment in part and dissenting in part).

FDA believes that the preemptive effect of this interim final rule, if finalized without change, is consistent with Executive Order 13132. Section 4(e) of the Executive order provides that ``when an agency proposes to act through adjudication or rulemaking to preempt State law, the agency shall provide all affected State and local officials notice and an opportunity for appropriate participation in the proceedings." FDA provided the States with an opportunity for appropriate participation in this rulemaking on December 12, 2007, when FDA's Division of Federal and State Relations provided notice via fax and email transmission to State health commissioners, State agriculture commissioners, food program directors, and drug program directors as well as FDA field personnel of FDA's intent to amend the health claim regulation authorizing health claims for soluble fiber from certain foods and risk of CHD (Sec. 101.81). It advised the States of FDA's possible action and encouraged the States and local governments to review the petition and to provide any comments to the docket (Docket No. 2006P-0393), until January 12, 2008. FDA received no comments in response to the notice. FDA is also providing an opportunity for State and local officials to comment on this interim final rule.

In conclusion, the agency has determined that the preemptive effects of this interim final rule are consistent with Executive Order 13132.

X. Issuance of an Interim Final Rule and Immediate Effective Date

FDA is issuing this rule as an interim final rule, effective immediately, with an opportunity for public comment. Section 403(r)(7)

of the act authorizes us to make proposed regulations issued under section 403(r) of the act effective upon publication pending consideration of public comment and publication of a final regulation, if the agency determines that such action is necessary for public health reasons. This authority enables us to act promptly on petitions that provide for information that is necessary to: (1) Enable consumers to develop and maintain healthy dietary practices, (2) enable consumers to be informed promptly and effectively of important new knowledge regarding nutritional and health benefits of food, or (3) ensure that scientifically sound nutritional and health information is provided to consumers as soon as possible. Proposed regulations made effective upon publication under this authority are deemed to be final agency action for purposes of judicial review. The legislative history indicates that such regulations should be issued as interim final rules (H. Conf. Rept. No. 105-399, at 98 (1997)).

We are satisfied that all three of the criteria in section 403(r)(7)(A) of the act have been met for the amendment to the soluble fiber from certain foods and risk of CHD health claim to list barley betafiber as eligible source of beta-glucan soluble fiber. This health claim amendment will help enable consumers to develop and maintain healthy dietary practices. The health claim will also provide consumers with important knowledge regarding the effects of beta-glucan soluble fiber in reducing the risk of, and will provide consumers with scientifically sound information on the benefits of foods containing beta-glucan soluble fiber from barley betafiber. Therefore, we are using the authority given to us in section 403(r)(7)(A) of the act to issue an interim final rule authorizing a health claim for soluble fiber from barley betafiber and CHD, effective immediately.

FDA invites public comment on this interim final rule. The agency will consider modifications to this interim final rule based on comments made during the comment period. Interested persons may submit to the Division of Dockets Management, in any of the ways noted in the ADDRESSES section at the beginning of this document, comments regarding this interim final rule by (see DATES). Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

This regulation is effective upon publication in the Federal Register. The agency will address comments and confirm or amend the interim final rule in a final rule.

XI. Comments

Interested persons may submit to the Division of Dockets Management (see ADDRESSES) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Please note that on January 15, 2008, the FDA Web site transitioned

to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system. Electronic submissions will be accepted by FDA through FDMS only.

XII. References

The following references have been placed on display in the Division of Dockets Management (see ADDRESSES) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. (FDA has verified the Web site address, but FDA is not responsible for any subsequent changes to the Web site after this document publishes in the Federal Register.)

1. Cargill, Inc., ``Petition for Health Claim--Barley Betafiber and Coronary Heart Disease," (Docket 2006P-0393 CP1), June 20, 2006.
2. Cargill, Inc., "Petition for Health Claim--Barley Betafiber and Coronary Heart Disease," Appendix 4, (Docket 2006P-0393), June 20, 2006.
3. Cargill, Inc., ``Petition for Health Claim--Barley Betafiber and Coronary Heart Disease," Appendix 1, (Docket 2006P-0393), June 20, 2006.
4. Keenan, J.M., Goulson, M., Shamliyan, T., et al., "The Effects of Concentrated Barley Beta-Glucan on Blood Lipids in a Population of Hypercholesterolaemic Men and Women," British Journal of Nutrition, 97:1162-1168, 2007.
5. E-mail from Lore Kolberg, Cargill, Inc., to Jillonne Kevala, FDA, August 28, 2006.
6. Cooper, R., Cutler, J., Desvigne-Nickens, P., et al., ``Trends and Disparities in Coronary Heart Disease, Stroke, and Other Cardiovascular Diseases in the United States: Findings of the National Conference onCardiovascular Disease Prevention," Circulation, 102:3137-3147, 2000.
7. Agency Response Letter to Generally Recognized as Safe Notice No. GRN 000207, FDA, Center for Food Safety and Applied Nutrition, Office of Food Additive Safety, December 19, 2006.
8. National Heart, Lung, and Blood Institute; National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Pressure in Adults (Adult Treatment Panel III), Third Report of the NCEP Adult Treatment Panel III, Executive Summary, Bethesda (MD): National Institutes of Health, National Heart, Lung and Blood Institute, (www.nhlbi.nih.gov/guidelines/cholesterol/atp_iii.htm), May 2001.
9. Guidance for Industry: Significant Scientific Agreement in the Review of Health Claims for Conventional Foods and Dietary Supplements; Rockville, MD: U.S. Food and Drug Administration; December 1999, Available from: http://www.cfsan.fda.gov/~dms/ssaguide.html.
10. Bi[ouml]rklund, M., vanRees, A., Mensink, R.P., et al., ``Changes in Serum Lipids and Postprandial Glucose and Insulin Concentrations After Consumption of Beverages with [beta]-Glucans from Oats or Barley: A Randomized Dose-Controlled Trial," European Journal of Clinical Nutrition, 59:1272-1281, 2005.
11. Keogh, G.F., Cooper, G.J.S., Mulvey, T.B., et al., ``Randomized Controlled Crossover Study of the Effect of a Highly [beta]-Glucan-Enriched Barley on Cardiovascular Disease Risk Factors

in Mildly Hypercholesterolemic Men," American Journal of Clinical Nutrition, 78:711-718, 2003.

12. Kerckhoffs, D.A.J.M., Hornstra, G., and R.P. Mensink, ``Cholesterol-Lowering Effect of [beta]-Glucan from Oat Bran in Mildly Hypercholesterolemic Subjects May Decrease When [beta]-Glucan is Incorporated Into Bread and Cookies," American Journal of Clinical Nutrition, 78:221-227, 2003.

13. Lovegrove, J.A., Clohessy, A., Milon, H., et al, ``Modest Doses of [beta]-Glucan Do Not Reduce Concentrations of Potentially Atherogenic Lipoproteins," American Journal of Clinical Nutrition, 72:49-55, 2000.

14. Naumann, E., vanRees, A.B., [Ouml]nning, G., et al., ``[beta]-Glucan Incorporated Into a Fruit Drink Effectively Lowers Serum LDL-Cholesterol Concentrations," American Journal of Clinical Nutrition, 83:601-605, 2006.

15. Pick, M.E., Hawrysh, Z.J., Gee, M.I., et al., ``Oat Bran Concentrate Bread Products Improve Long-Term Control of Diabetes: A Pilot Study," Journal of the American Dietetic Association, 96:1254-1261, 1996.

16. Beer, M.U., Arrigoni, E., and R. Amado, ``Effects of Oat Gum on Blood Cholesterol Levels in Healthy Young Men," European Journal of Clinical Nutrition, 49:517-522, 1995.

17. Braaten, J.T., Wood, P.J., Scott, F.W., et al., ``Oat [beta]-Glucan Reduces Blood Cholesterol Concentration in Hypercholesterolemic Subjects," European Journal of Clinical Nutrition, 48:465-474, 1994.

18. Pomeroy, S., Tupper, R., Cehun-Anders, and P. Nestel, ``Oat [beta]-Glucan Lowers Total and LDL-Cholesterol," Australian Journal of Nutrition and Dietetics, 58:51-55, 2001.

19. T[ouml]rr[ouml]nen, R., Kansanen, L., Uusitupa, M., et al., ``Effects of an Oat Bran Concentrate on Serum Lipids in Free-Living Men with Mild to Moderate Hypercholesterolemia," European Journal of Clinical Nutrition, 46:621-627, 1992.

List of Subjects in 21 CFR Part 101

Food labeling, Nutrition, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 101 is amended as follows:

PART 101--FOOD LABELING

1. The authority citation for 21 CFR part 101 continues to read as follows:

Authority: 15 U.S.C. 1453, 1454, 1455; 21 U.S.C. 321, 331, 342, 343, 348, 371; 42 U.S.C. 243, 264, 271.

2. Section 101.81 is amended by adding paragraph (c)(2)(ii)(A)(6) and by revising paragraph (c)(2)(iii)(A)(2) to read as follows:

Sec. 101.81 Health claims: Soluble fiber from certain foods and risk of coronary heart disease (CHD).

* * * * *

(c) * * *

(2) * * *

(ii) * * *

(A) * * *

(6) Barley betafiber. Barley betafiber is the ethanol precipitated soluble fraction of cellulase and alpha-amylase hydrolyzed whole grain barley. Barley betafiber is produced by hydrolysis of whole grain barley flour, as defined in paragraph (c)(2)(ii)(A)(5) of this section, with a cellulase and alpha-amylase enzyme preparation, to produce a clear aqueous extract that contains mainly partially hydrolyzed beta-glucan and substantially hydrolyzed starch. The soluble, partially hydrolyzed beta-glucan is separated from the insoluble material by centrifugation, and after removal of the insoluble material, the partially hydrolyzed beta-glucan soluble fiber is separated from the other soluble compounds by precipitation with ethanol. The product is then dried, milled and sifted. Barley betafiber shall have a beta-glucan soluble fiber content of at least 70 percent on a dry weight basis.

* * * * *

(iii) * * *

(A) * * *

(2) The food containing the oatrim from paragraph (c)(2)(ii)(A)(4) of this section or the barley betafiber from paragraph (c)(2)(ii)(A)(6) of this section shall contain at least 0.75 g of beta-glucan soluble fiber per reference amount customarily consumed of the food product; or

* * * * *

Dated: February 15, 2008.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. E8-3418 Filed 2-22-08; 8:45 am]

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Federal Register Final Rule 73 FR 47828 August 15, 2008: Food Labeling: Health Claims; Soluble Fiber From Certain Foods and Risk of Coronary Heart Disease

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 101

[Docket No. FDA-2008-P-0090] (formerly Docket No. 2006P-0393)

Food Labeling: Health Claims; Soluble Fiber From Certain Foods and Risk of Coronary Heart Disease

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is adopting as a final rule, without change, the provisions of the interim final rule (IFR) that amended the regulation authorizing a health claim on soluble fiber from certain foods and risk of coronary heart disease (CHD), to add barley betafiber as an additional eligible source of beta-glucan soluble fiber. FDA is taking this action to complete the rulemaking initiated with the IFR.

DATES: This final rule is effective August 15, 2008.

FOR FURTHER INFORMATION CONTACT: Jillonne Kevala, Center for Food Safety and Applied Nutrition (HFS-830), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740-3835, 301-436-1450.

SUPPLEMENTARY INFORMATION:

I. Background

In the Federal Register of February 25, 2008 (73 FR 9938), FDA

published an IFR to amend the regulation in part 101 (21 CFR part 101) that authorizes a health claim on the relationship between soluble fiber from certain foods and CHD (Sec. 101.81), to include barley betafiber as an additional eligible source of beta-glucan soluble fiber. Under section 403(r)(3)(B)(i) and (r)(7) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 343(r)(3)(B)(i) and 343(r)(7)), FDA issued the IFR in response to a petition filed under section 403(r)(4) of the act. On June 20, 2006, Cargill Inc. (the petitioner), submitted a health claim petition to FDA requesting that the agency expand the ``Soluble fiber from certain foods and coronary heart disease" health claim (Sec. 101.81) to include barley betafiber as an eligible food ingredient source of beta-glucan soluble fiber. The petitioner requested that FDA grant an IFR by which foods containing barley betafiber could bear the health claim prior to publication of the final rule.

Section 403(r)(3)(B)(i) of the act states that the Secretary of Health and Human Services (and, by delegation, FDA) shall issue a regulation authorizing a health claim if he or she ``determines, based on the totality of publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), that there is significant scientific agreement, among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by such evidence." (See also Sec. 101.14(c).) Section 403(r)(4) of the act sets out the procedures that FDA is to follow upon receiving a health claim petition. Section 403(r)(7) of the act permits FDA to make a proposed regulation issued under section 403(r) effective upon publication pending consideration of public comment and publication of a final regulation if the agency determines that such action is necessary for public health reasons. FDA filed the petition for comprehensive review in accordance with section 403(r)(4) of the act on September 28, 2006.

As part of its review of the scientific literature on barley betafiber and CHD, FDA considered the scientific evidence presented in the petition as well as information previously considered by the agency on CHD risk reduction and the effects of beta-glucan soluble fiber containing food ingredients on lowering serum total and low density lipoprotein (LDL) cholesterol. The agency summarized this evidence in the IFR (73 FR 9938 at 9941 to 9943). Based on the available evidence, FDA concluded that barley betafiber, like the other whole oat and barley products listed in Sec. 101.81(c)(2)(ii)(A), lowers serum total and LDL cholesterol. Consequently, FDA amended Sec. 101.81(c)(2)(ii)(A) to broaden the health claim to include barley betafiber as an additional eligible source of beta-glucan soluble fiber.

II. Summary of Comments and the Agency's Response

FDA solicited comments on the IFR. The comment period closed on May 12, 2008. The agency received five letters of response, three from consumers, one from academia, and one from the Commonwealth of Kentucky. One consumer comment and the comment from academia supported the IFR. The Commonwealth of Kentucky advised the agency that FDA's ruling on the health claim would not adversely affect the State's actions or conflict with any State laws. The remaining consumer

comments addressed issues that are outside the scope of this rulemaking and will not be addressed here.

Given the absence of contrary evidence on the agency's decisions announced in the IFR, FDA is adopting as a final rule, without change, the IFR that amended Sec. 101.81 to include barley betafiber as an additional eligible source of beta-glucan soluble fiber.

III. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104-4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is not a significant regulatory action under the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because this final rule allows new voluntary behavior and imposes no additional restrictions on current practices, the agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement which includes an assessment of anticipated costs and benefits before proposing ``any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $127,000,000, using the most current (2006) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any one-year expenditure that would meet or exceed this amount.

FDA received no comments relevant to economic impact. The costs and benefits of available regulatory alternatives analyzed in the IFR (73 FR 9938 at 9944 and 9945) are adopted, without change, in this final rule. By now affirming that IFR, FDA has not imposed any new requirements. Therefore, there are no additional costs and benefits associated with this final rule.

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IV. Environmental Impact

The agency has determined under 21 CFR 25.32(p) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

V. Paperwork Reduction Act

FDA concludes that the labeling provisions of this final rule are

not subject to review by the Office of Management and Budget because they do not constitute a ``collection of information'' under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). Rather, the food labeling health claim on the association between consumption of barley betafiber and reduced risk of coronary heart disease is a ``public disclosure of information originally supplied by the Federal Government to the recipient for the purpose of disclosure to the public'' (5 CFR 1320.3(c)(2)).

VI. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule will have a preemptive effect on State law. Section 4(a) of the Executive order requires agencies to ``construe * * * a Federal statute to preempt State law only where the statute contains an express preemption provision or there is some other clear evidence that the Congress intended preemption of State law, or where the exercise of State authority conflicts with the exercise of Federal authority under the Federal statute.'' Section 403A of the act (21 U.S.C. 343-1) is an express preemption provision. Section 403A(a)(5) of the act provides that ``* * * no State or political subdivision of a State may directly or indirectly establish under any authority or continue in effect as to any food in interstate commerce--* * * any requirement respecting any claim of the type described in section 403(r)(1) made in the label or labeling of food that is not identical to the requirement of section 403(r). * * *''

On February 25, 2008, FDA published an IFR which imposed requirements under section 403(r) of the act. This final rule affirms the February 25, 2008, amendment to the existing food labeling regulations to add barley betafiber to the authorized health claim for soluble fiber from certain foods and CHD. Although this rule has a preemptive effect in that it precludes States from issuing any health claim labeling requirements for barley betafiber and reduced risk of CHD that are not identical to those required by this final rule, this preemptive effect is consistent with what Congress set forth in section 403A of the act. Section 403A(a)(5) of the act displaces both State legislative requirements and State common law duties (Riegel v. Medtronic, 128 S. Ct. 999 (2008)).

FDA believes that the preemptive effect of this final rule is consistent with Executive Order 13132. Section 4(e) of the Executive order provides that ``when an agency proposes to act through adjudication or rulemaking to preempt State law, the agency shall provide all affected State and local officials notice and an opportunity for appropriate participation in the proceedings.'' On December 12, 2007, FDA's Division of Federal and State Relations provided notice via fax and e-mail transmission to State health commissioners, State agriculture commissioners, food program directors, and drug program directors, as well as FDA field personnel, of FDA's intent to amend the health claim regulation authorizing health claims for soluble fiber from certain foods and CHD (Sec. 101.81).

In addition, the agency sought input from all stakeholders through publication of the IFR in the Federal Register on February 25, 2008. FDA received one comment from the Commonwealth of Kentucky, which noted that FDA's ruling on the health claim would not adversely affect the

State's actions or conflict with any State laws.

In conclusion, the agency believes that it has complied with all of the applicable requirements of Executive Order 13132 and has determined that the preemptive effects of this rule are consistent with the Executive order.

List of Subjects in 21 CFR Part 101

Food labeling, Nutrition, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 101 is amended as follows:

Accordingly, the interim final rule amending Sec. 101.81 that was published in the Federal Register of February 25, 2008 (73 FR 9938), is adopted as a final rule, without change.

Dated: August 7, 2008.
Jeffrey Shuren,
Associate Commissioner for Policy and Planning.
[FR Doc. E8-18863 Filed 8-14-08; 8:45 am]

BILLING CODE 4160-01-S

Title 21: Food and Drugs

PART 101—FOOD LABELING

Subpart E—Specific Requirements for Health Claims

§ 101.81 Health claims: Soluble fiber from certain foods and risk of coronary heart disease (CHD).

(a) *Relationship between diets that are low in saturated fat and cholesterol and that include soluble fiber from certain foods and the risk of CHD.* (1) Cardiovascular disease means diseases of the heart and circulatory system. Coronary heart disease (CHD) is one of the most common and serious forms of cardiovascular disease and refers to diseases of the heart muscle and supporting blood vessels. High blood total cholesterol and low density lipoprotein (LDL)-cholesterol levels are associated with increased risk of developing coronary heart disease. High CHD rates occur among people with high total cholesterol levels of 240 milligrams per deciliter (mg/dL) (6.21 (mmol/L)) or above and LDL-cholesterol levels of 160 mg/dL (4.13 mmol/L) or above. Borderline high risk total cholesterol levels range from 200 to 239 mg/dL (5.17 to 6.18 mmol/L) and 130 to 159 mg/dL (3.36 to 4.11 mmol/L) of LDL-cholesterol. The scientific evidence establishes that diets high in saturated fat and cholesterol are associated with increased levels of blood total- and LDL-cholesterol and, thus, with increased risk of CHD.

(2) Populations with a low incidence of CHD tend to have relatively low blood total cholesterol and LDL-cholesterol levels. These populations also tend to have dietary patterns that are not only low in total fat, especially saturated fat and cholesterol, but are also relatively high in fiber-containing fruits, vegetables, and grain products, such as whole oat products.

(3) Scientific evidence demonstrates that diets low in saturated fat and cholesterol may reduce the risk of CHD. Other evidence demonstrates that the addition of soluble fiber from certain foods to a diet that is low in saturated fat and cholesterol may also help to reduce the risk of CHD.

(b) *Significance of the relationship between diets that are low in saturated fat and cholesterol and that include soluble fiber from certain foods and the risk of CHD.* (1) CHD is a major public health concern in the United States. It accounts for more deaths than any other disease or group of diseases. Early management of risk factors for CHD is a major public health goal that can assist in reducing risk of CHD. High blood total and LDL-cholesterol are major modifiable risk factors in the development of CHD.

(2) Intakes of saturated fat exceed recommended levels in the diets of many people in the United States. One of the major public health recommendations relative to CHD risk is to consume less than 10 percent of calories from saturated fat and an average of 30 percent or less of total calories from all fat. Recommended daily cholesterol intakes are 300 milligrams (mg) or less per day. Scientific evidence demonstrates that diets low in saturated fat and cholesterol are associated with lower blood total- and LDL-cholesterol levels. Soluble fiber from certain foods, when included in a low saturated fat and cholesterol diet, also helps to lower blood total- and LDL-cholesterol levels.

(c) *Requirements.* (1) All requirements set forth in §101.14 shall be met. The label and labeling of foods containing psyllium husk shall be consistent with the provisions of §101.17(f).

(2) *Specific requirements* —(i) *Nature of the claim.* A health claim associating diets that are low in saturated fat and cholesterol and that include soluble fiber from certain foods with reduced risk of heart disease may be made on the label or labeling of a food described in paragraph (c)(2)(iii) of this section, provided that:

(A) The claim states that diets that are low in saturated fat and cholesterol and that include soluble fiber from certain foods "may" or "might" reduce the risk of heart disease.

(B) In specifying the disease, the claim uses the following terms: "heart disease" or "coronary heart disease";

(C) In specifying the substance, the claim uses the term "soluble fiber" qualified by the name of the eligible source of soluble fiber (provided in paragraph (c)(2)(ii)) of this section. Additionally, the claim may use the name of the food product that contains the eligible source of soluble fiber;

(D) In specifying the fat component, the claim uses the terms "saturated fat" and "cholesterol";

(E) The claim does not attribute any degree of risk reduction for CHD to diets that are low in saturated fat and cholesterol and that include soluble fiber from the eligible food sources from paragraph (c)(2)(ii) of this section; and

(F) The claim does not imply that consumption of diets that are low in saturated fat and cholesterol and that include soluble fiber from the eligible food sources from paragraph (c)(2)(ii) of this section is the only recognized means of achieving a reduced risk of CHD.

(G) The claim specifies the daily dietary intake of the soluble fiber source that is necessary to reduce the risk of coronary heart disease and the contribution one serving of the product makes to the specified daily dietary intake level. Daily dietary intake levels of soluble fiber sources listed in paragraph (c)(2)(ii) of this section that have been associated with reduced risk coronary heart disease are:

(*1*) 3 g or more per day of β-glucan soluble fiber from either whole oats or barley, or a combination of whole oats and barley.

(2) 7 g or more per day of soluble fiber from psyllium seed husk.

(ii) *Nature of the substance—Eligible sources of soluble fiber.* (A) Beta (β) glucan soluble fiber from the whole oat and barley sources listed below. β-glucan soluble fiber will be determined by method No. 992.28 from the "Official Methods of Analysis of the AOAC INTERNATIONAL," 16th ed. (1995), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies may be obtained from the AOAC INTERNATIONAL, 481 North Frederick Ave., suite 500, Gaithersburg, MD 20877, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 5100 Paint Branch Pkwy., College Park, MD 20740, or at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202–741–6030, or go to: *http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html* ;

(*1*) *Oat bran.* Oat bran is produced by grinding clean oat groats or rolled oats and separating the resulting oat flour by suitable means into fractions such that the oat bran fraction is not more than 50 percent of the original starting material and provides at least 5.5 percent (dry weight basis (dwb)) β-glucan soluble fiber and a total dietary fiber content of 16 percent (dwb), and such that at least one-third of the total dietary fiber is soluble fiber;

(2) *Rolled oats.* Rolled oats, also known as oatmeal, produced from 100 percent dehulled, clean oat groats by steaming, cutting, rolling, and flaking, and provides at least 4 percent (dwb) of β-glucan soluble fiber and a total dietary fiber content of at least 10 percent.

(3) *Whole oat flour.* Whole oat flour is produced from 100 percent dehulled, clean oat groats by steaming and grinding, such that there is no significant loss of oat bran in the final product, and provides at least 4 percent (dwb) of β-glucan soluble fiber and a total dietary fiber content of at least 10 percent (dwb).

(*4*) *Oatrim.* The soluble fraction of alpha-amylase hydrolyzed oat bran or whole oat flour, also known as oatrim. Oatrim is produced from either oat bran as defined in paragraph (c)(2)(ii)(A)(*1*) of this section or whole oat flour as defined in paragraph (c)(2)(ii)(A)(*3*) of this section by solubilization of the starch in the starting material with an alpha-amylase hydrolysis process, and then removal by centrifugation of the insoluble components consisting of a high portion of protein, lipid, insoluble dietary fiber, and the majority of the flavor and color components of the starting material. Oatrim shall have a beta-glucan soluble fiber content up to 10 percent (dwb) and not less than that of the starting material (dwb).

(*5*) *Whole grain barley and dry milled barley* . Dehulled and hull-less whole grain barley with a β-glucan soluble fiber content of at least 4 percent (dwb) and a total dietary fiber content of at least 10 percent (dwb). Dry milled barley grain products include barley bran, barley flakes, barley grits, pearl barley, barley flour, barley meal, and sieved barley meal that are produced from clean, sound dehulled or hull-less barley grain using standard dry milling techniques, which may include steaming or tempering, and that contain at least 4 percent (dwb) of β-glucan soluble fiber and at least 8 percent (dwb) of total dietary fiber, except barley bran and sieved barley meal for which the minimum β-glucan soluble fiber content is 5.5 percent (dwb) and minimum total dietary fiber content is 15 percent (dwb). Dehulled barley, hull-less barley, barley bran, barley flakes, barley grits, pearl barley, and barley flour are as defined in the Barley Glossary (AACC Method 55–99), published in Approved Methods of the American Association of Cereal Chemists, 10th ed. (2000), pp. 1 and 2, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies may be obtained from the American Association of Cereal Chemists, Inc., 3340 Pilot Knob Rd., St. Paul, Minnesota, 55121, or may be examined at the Center for Food Safety and Applied Nutrition Library, 5100 Paint Branch Pkwy., College Park, MD 20740, or at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202–741–6030, or go to: *http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html* . Barley meal is unsifted, ground barley grain not subjected to any processing to separate the bran, germ, and endosperm. Sieved barley meal is an endosperm cell wall-enriched fraction of ground barley separated from meal by sieving or by air classification.

(*6*) *Barley betafiber* . Barley betafiber is the ethanol precipitated soluble fraction of cellulase and alpha-amylase hydrolyzed whole grain barley. Barley betafiber is produced by hydrolysis of whole grain barley flour, as defined in paragraph (c)(2)(ii)(A)(*5*) of this section, with a cellulase and alpha-amylase enzyme preparation, to produce a clear aqueous extract that contains mainly partially hydrolyzed beta-glucan and substantially hydrolyzed starch. The soluble, partially hydrolyzed beta-glucan is separated from the insoluble material by centrifugation, and after removal of the insoluble material, the partially hydrolyzed beta-glucan soluble fiber is separated from the other soluble compounds by precipitation with ethanol. The product is then dried, milled and sifted. Barley betafiber shall have a beta-glucan soluble fiber content of at least 70 percent on a dry weight basis.

(B)(*1*) Psyllium husk from the dried seed coat (epidermis) of the seed of *Plantago* (*P.*) ovata, known as blond psyllium or Indian psyllium, *P. indica,* or *P. psyllium.* To qualify for this claim, psyllium seed husk, also known as psyllium husk, shall have a purity of no less than 95 percent, such that it contains 3 percent or less protein, 4.5 percent or less of light extraneous matter, and 0.5 percent or less of heavy extraneous matter, but in no case may the combined extraneous matter exceed 4.9 percent, as determined by U.S. Pharmacopeia (USP) methods described in USP's "The National Formulary," USP 23, NF 18, p. 1341, (1995), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies may be obtained from the U.S. Pharmacopeial Convention, Inc., 12601 Twinbrook Pkwy., Rockville, MD 20852, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 5100 Paint Branch Pkwy., College Park, MD 20740, or at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202–741–6030, or go to: *http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html* ;

(2) FDA will determine the amount of soluble fiber that is provided by psyllium husk by using a modification of the Association of Official Analytical Chemists' International (AOAC's) method for soluble dietary fiber (991.43) described by Lee et al., "Determination of Soluble and Insoluble Dietary Fiber in Psyllium-containing Cereal Products," *Journal of the AOAC International,* 78 (No. 3):724–729, 1995, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies may be obtained from the AOAC INTERNATIONAL, 481 North Frederick Ave., suite 500, Gaithersburg, MD 20877, or may be examined at the Center for Food Safety and Applied Nutrition's Library, 5100 Paint Branch Pkwy., College Park, MD 20740 or at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202–741–6030, or go to: *http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html* ;

(iii) *Nature of the food eligible to bear the claim.* (A) The food product shall include:

(*1*) One or more of the whole oat or barley foods from paragraphs (c)(2)(ii)(A)(*1*), (*2*), (*3*), and (*5*) of this section, and the whole oat or barley foods shall contain at least 0.75 gram (g) of soluble fiber per reference amount customarily consumed of the food product; or

(*2*) The food containing the oatrim from paragraph (c)(2)(ii)(A)(*4*) of this section or the barley betafiber from paragraph (c)(2)(ii)(A)(*6*) of this section shall contain at least 0.75 g of beta-glucan soluble fiber per reference amount customarily consumed of the food product; or

(*3*) Psyllium husk that complies with paragraph (c)(2)(ii)(B) of this section, and the psyllium food shall contain at least 1.7 g of soluble fiber per reference amount customarily consumed of the food product;

(B) The amount of soluble fiber shall be declared in the nutrition label, consistent with §101.9(c)(6)(i)(A).

(C) The food shall meet the nutrient content requirement in §101.62 for a "low saturated fat" and "low cholesterol" food; and

(D) The food shall meet the nutrient content requirement in §101.62(b)(2) for a "low fat" food, unless the food exceeds this requirement due to fat content derived from whole oat sources listed in paragraph (c)(2)(ii)(A) of this section.

(d) *Optional information.* (1) The claim may state that the development of heart disease depends on many factors and may identify one or more of the following risk factors for heart disease about which there is general scientific agreement: A family history of CHD; elevated blood total and LDL-cholesterol; excess body weight; high blood pressure; cigarette smoking; diabetes; and physical inactivity. The claim may also provide additional information about the benefits of exercise and management of body weight to help lower the risk of heart disease;

(2) The claim may state that the relationship between intake of diets that are low in saturated fat and cholesterol and that include soluble fiber from the eligible food sources from paragraph (c)(2)(ii) of this section and reduced risk of heart disease is through the intermediate link of "blood cholesterol" or "blood total- and LDL-cholesterol;"

(3) The claim may include information from paragraphs (a) and (b) of this section, which summarize the relationship between diets that are low in saturated fat and cholesterol and that include soluble fiber from certain foods and coronary heart disease and the significance of the relationship;

(4) The claim may specify the name of the eligible soluble fiber;

(5) The claim may state that a diet low in saturated fat and cholesterol that includes soluble fiber from whole oats or barley is consistent with "Nutrition and Your Health: Dietary Guidelines for Americans," U.S. Department of Agriculture (USDA) and Department of Health and Human Services (DHHS), Government Printing Office (GPO);

(6) The claim may state that individuals with elevated blood total- and LDL-cholesterol should consult their physicians for medical advice and treatment. If the claim defines high or normal blood total- and LDL-cholesterol levels, then the claim shall state that individuals with high blood cholesterol should consult their physicians for medical advice and treatment;

(7) The claim may include information on the number of people in the United States who have heart disease. The sources of this information shall be identified, and it shall be current information from the National Center for Health Statistics, the National Institutes of Health, or "Nutrition and Your Health: Dietary Guidelines for Americans," USDA and DHHS, GPO.

(e) *Model health claim.* The following model health claims may be used in food labeling to describe the relationship between diets that are low in saturated fat and cholesterol and that include soluble fiber from certain foods and reduced risk of heart disease:

(1) Soluble fiber from foods such as [name of soluble fiber source from paragraph (c)(2)(ii) of this section and, if desired, the name of food product], as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. A serving of [name of food] supplies ____ grams of the [grams of soluble fiber specified in paragraph (c)(2)(i)(G) of this section] soluble fiber from [name of the soluble fiber source from paragraph (c)(2)(ii) of this section] necessary per day to have this effect.

(2) Diets low in saturated fat and cholesterol that include [____ grams of soluble fiber specified in paragraph (c)(2)(i)(G) of this section] of soluble fiber per day from [name of soluble fiber source from paragraph (c)(2)(ii) of this section and, if desired, the name of the food product] may reduce the risk of heart disease. One serving of [name of food] provides ____ grams of this soluble fiber.

[62 FR 3600, Jan. 23, 1997, as amended at 62 FR 15344, Mar. 31, 1997; 63 FR 8119, Feb. 18, 1998; 66 FR 66742, Dec. 27, 2001; 67 FR 61782, Oct. 2, 2002; 68 FR 15355, Mar. 31, 2003; 70 FR 40880, July 15, 2005; 70 FR 76162, Dec. 23, 2005; 73 FR 9947, Feb. 25, 2008; 73 FR 23953, May 1, 2008]

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Petition to Add to the National List 205.606: "Barley Betafiber"

Appendix 6: Material Safety Data Sheet (MSDS)
Barlív™ Barley Betafiber

MATERIAL SAFETY DATA SHEET

1 PRODUCT AND COMPANY IDENTIFICATION

Product Name: Barliv™ Barley Betafiber

Manufacturer Name:
Cargill France SAS
Rue de Seves
50500 Baupte, France

Emergency Telephone:
1-800-424-9300

Non-emergency Telephone:
1-866-734-2111 (8:00 am-5:00 pm CST)

Intended Use: Food/feed additive

2 HAZARDS IDENTIFICATION

Emergency Overview
Physical State: Powder
Color: White to tan
Odor: Odorless

Low hazard for usual industrial or commercial handling by trained personnel.

Potential Health Effects

Inhalation: Dust may irritate the respiratory system.

Eye Contact: May cause temporary eye irritation.

Skin Contact: None known.

Ingestion: Expected to be a low ingestion hazard. Ingestion may produce a laxative effect.

Chronic Health Effects: This material tested positive for wheat gluten allergy. People allergic to wheat gluten may have an allergic reaction to this product.

OSHA Regulatory Status: This product is not hazardous according to OSHA 29CFR 1910.1200.

3 COMPOSITION / INFORMATION ON INGREDIENTS

General Information: The product contains:

Chemical Name	CAS-No.	Concentration*
(1-3),(1-4)-beta-D-glucan	55965-23-6	100%

* All concentrations are percent by weight unless ingredient is a gas. Gas concentrations are in percent by volume.

4 FIRST AID MEASURES

Inhalation: If symptomatic, move to fresh air. Get medical attention if symptoms persist.

Eye Contact: Any material that contacts the eye should be washed out immediately with water. If easy to do, remove contact lenses. Get medical attention promptly if symptoms occur after washing.

Skin Contact: Wash skin with soap and water. Get medical attention promptly if symptoms occur after washing.

Ingestion: Seek medical advice.

5 FIRE-FIGHTING MEASURES

Extinguishing Media: Extinguish with foam, carbon dioxide, dry powder or water fog.

Unsuitable Extinguishing Media: Not applicable.

Special Fire Fighting Procedures: Self-contained breathing apparatus and full protective clothing must be worn in case of fire.

Unusual Fire & Explosion Hazards: Powdered material may form explosive dust-air mixtures.

Hazardous Combustion Products: Carbon Oxides, Nitrogen Oxides

6 ACCIDENTAL RELEASE MEASURES

Personal Precautions: Wear appropriate personal protective equipment.

Spill Cleanup Methods: Sweep or scoop up and remove.

7 HANDLING AND STORAGE

Handling: Proper sanitation with food grade products is essential. No special precautions are necessary beyond normal good hygiene practices. See Section 8 of the MSDS for additional personal protection advice when handling this product.

Storage: Keep container closed.

8 EXPOSURE CONTROLS / PERSONAL PROTECTION

Exposure Limits:
Engineering Controls: Good general ventilation (typically 10 air changes per hour) should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels to an acceptable level.

Respiratory Protection: If engineering controls do not maintain airborne concentrations below

recommended exposure limits (where applicable) or to an acceptable level (in countries where exposure limits have not been established), an approved respirator must be worn. In the United States of America, if respirators are used, a program should be instituted to assure compliance with OSHA Standard 63 FR 1152, January 8, 1998. Respirator type: High-efficiency particulate respirator.

Eye Protection: Risk of contact: Wear approved safety goggles.

Hand Protection: It is a good industrial hygiene practice to minimize skin contact.

Skin Protection: Apron and long sleeves are recommended. Risk of contact: Use skin protection.

Hygiene Measures: Always observe good personal hygiene measures, such as washing after handling the material and before eating, drinking, and/or smoking. Routinely wash work clothing and protective equipment to remove contaminants.

Environmental Exposure Controls: Environmental manager must be informed of all major spillages.

9 PHYSICAL AND CHEMICAL PROPERTIES

Color: White to tan
Odor: Odorless
Odor Threshold: No data available.
Physical State: Powder
pH: Not applicable
Melting Point: No data available.
Freezing Point: No data available.
Boiling Point: No data available.
Flash Point: No data available.
Evaporation Rate: No data available.
Flammability (Solid): No data available.
Flammability Limit - Upper (%): No data available.
Flammability Limit - Lower (%): No data available.
Vapor Pressure: No data available.
Vapor Density (Air=1): No data available.
Specific Gravity: No data available.
Solubility in Water: Soluble
Solubility (Other): No data available.
Partition Coefficient (n-Octanol/water): No data available.
Autoignition Temperature: 370°C (698°F)
Decomposition Temperature: No data available.
Viscosity: No data available.
Explosive Properties: No data available

10 STABILITY AND REACTIVITY

Stability: Stable.

Conditions to Avoid: Humidity.

Incompatible Materials: Strong oxidizing agents.

Hazardous Decomposition Products: None known.

11 TOXICOLOGICAL INFORMATION

Specified Substance(s)
Acute Toxicity:
Test Results: No test data available for the ingredients.

Listed Carcinogens: None.

Product Information
Acute Toxicity:
Test Results: No test data available for the product.

Other Acute: No additional adverse health effects noted.

Chronic Toxicity: This material tested positive for wheat gluten allergy. People allergic to wheat gluten may have an allergic reaction to this product.

12 ECOLOGICAL INFORMATION

Ecotoxicity: Not expected to be harmful to aquatic organisms.

Mobility: No negative effects on the aquatic environment are known.

Persistence and Degradability: The product is easily biodegradable.

Bioaccumulation Potential: Potential to bioaccumulate is low.

13 DISPOSAL CONSIDERATIONS

General Information: Dispose of waste and residues in accordance with local authority requirements.

Disposal Methods: No specific disposal method required.

Container: Since emptied containers retain product residue, follow label warnings even after container is emptied.

14 TRANSPORT INFORMATION

DOT Not regulated.

TDG Not regulated.

IATA Not regulated.

IMDG Not regulated.

15 REGULATORY INFORMATION

Canadian Controlled Products Regulations: This product has been classified according to the hazard criteria of the Canadian Controlled Products Regulations, Section 33, and the MSDS contains all required information.

WHMIS Classification: This is not a WHMIS controlled product.

Mexican Dangerous Statement: This product is not dangerous according to Mexican regulations.

Inventory Status

This product or one or more component(s) are not listed on the following inventory: DSL, TSCA

US Regulations

CERCLA Hazardous Substance List (40 CFR 302.4): Not regulated.

SARA Title III
Section 302 Extremely Hazardous Substances (40 CFR 355, Appendix A): Not regulated.

Section 311/312 (40 CFR 370):
☐ Acute (Immediate) ☐ Chronic (Delayed) ☐ Fire ☐ Reactive ☐ Pressure Generating

Section 313 Toxic Release Inventory (40 CFR 372): Not regulated.

Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130): Not regulated.

Clean Water Act Section 311 Hazardous Substances (40 CFR 117.3): Not regulated.

Drug Enforcement Act: Not regulated.

TSCA

TSCA Section 4(a) Final Test Rules & Testing Consent Orders: Not regulated.

TSCA Section 5(a)(2) Final Significant New Use Rules (SNURs) (40CFR 721, Subpt. E): Not regulated.

TSCA Section 5(e) PMN-Substance Consent Orders: Not regulated.

TSCA Section 12(b) Export Notification (40 CFR 707, Subpt. D): Not regulated.

State Regulations

California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): Not regulated.

Massachusetts Right-To-Know List: Not regulated.

Michigan Critical Materials List (Michigan Natural Resources and Environmental Protection Act (Act. 451 of 1994)): Not regulated.

Minnesota Hazardous Substances List: Not regulated.

New Jersey Right-To-Know List: Not regulated.

Pennsylvania Right-To-Know List: Not regulated.

Rhode Island Right-To-Know List: Not regulated.

16 OTHER INFORMATION

HAZARD RATINGS

	Health Hazard	Fire Hazard	Instability	Special Hazard
NFPA	0	1	0	NONE

Hazard rating: 0 - Minimal; 1 - Slight; 2 - Moderate; 3 - Serious; 4 - Severe
NFPA Label colored diamond code: Blue - Health; Red - Flammability; Yellow - Instability; White - Special Hazards

	Health Hazard	Flammability	Physical Hazard	Personal Protection
HMIS	1	1	0	--

Hazard rating: 0 - Minimal; 1 - Slight; 2 - Moderate; 3 - Serious; 4 - Severe
HMIS Label colored bar code: Blue - Health; Red - Flammability; Orange - Physical Hazards; White - Special

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Disclaimer: To the best of our knowledge, the information contained herein is accurate. However, neither the above named supplier nor any of its subsidiaries assumes any liability whatsoever or completeness of the information contained herein. Final determination of suitability of any material is the sole responsibility of the user. All materials may present unknown hazards and should be used with caution. Although certain hazards are described herein, we cannot guarantee that these are the only hazards that exist.

Petition to Add to the National List 205.606: "Barley Betafiber"

Appendix 7: Toxicology and Safety Reviews

CBI Start

CBI Deleted

CBI End

Petition to Add to the National List 205.606: "Barley Betafiber"

Appendix 8: Clinical Trials Using Barley Betafiber and Beta-Glucan

Selected articles (additional available on request):

- Keenan, J.M.; Goulson, M.; Shamliyan, T.; Knutson, N.; Kolberg, L.; Curry, L. 2007. The effects of concentrated barley β-glucan on blood lipids in a population of hypercholesterolemic men and women. Br J Nutr 97:1162-8.
- Talati, R,; Baker, W.; Pabilonia, M.; White, M. 2009. The effects of barley-derived soluble fiber on serum lipids. Annals of Family Medicine 7(2): 157-163.
- Behall, K.; Scholfield, D.; Hallfrisch, J. 2006. Barley β-glucan reduces plasma glucose and insulin responses compared with resistant starch in men. Nutrition Research 26: 644 – 650.
- Behall, K.; Scholfield, D.; Hallfrisch, J.; Liljeberg-Elmstahl, H. 2006. Consumption of both resistant starch and β-glucan improves postprandial plasma glucose and insulin in women. Diabetes Care 29(5): 976 – 981.

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The effects of concentrated barley β-glucan on blood lipids in a population of hypercholesterolaemic men and women

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Barley, like oats, is a rich source of the soluble fibre β-glucan, which has been shown to significantly lower LDL-cholesterol (LDL-C). However, barley foods have been less widely studied. Therefore, we evaluated the LDL-C-lowering effect of a concentrated barley β-glucan (BBG) extract as a vehicle to deliver this potential health benefit of barley. In a 10-week blinded controlled study, subjects were randomized to one of four treatment groups or control. Treatment groups included either high molecular weight (HMW) or low molecular weight (LMW) BBG at both 3 and 5 g doses. Treatment was delivered twice per day with meals in the form of two functional food products: a ready-to-eat cereal and a reduced-calorie fruit juice beverage. Levels of total cholesterol, LDL-C, HDL-cholesterol (HDL-C), and TAG were determined at baseline and after 6 weeks of treatment. The study group comprised 155 subjects. All treatments were well tolerated and after 6 weeks of treatment the mean LDL-C levels fell by 15 % in the 5 g HMW group, 13 % in the 5 g LMW group and 9 % in both the 3 g/d groups, versus baseline. Similar results were observed for total cholesterol. HDL-C levels were unchanged by treatment. Concentrated BBG significantly improves LDL-C and total cholesterol among moderately dyslipidaemic subjects. Food products containing concentrated BBG should be considered an effective option for improving blood lipids.

Soluble fibre: Barley: LDL-cholesterol: CVD

CVD is the leading cause of morbidity and mortality for both men and women in the USA with over 1·4 million deaths and 865 000 myocardial infarctions each year (American Heart Association, 2005). The National Cholesterol Education Program's Adult Treatment Panel III (ATP III) has developed guidelines for reducing the risk of CVD which strongly urge lifestyle modification, including dietary changes, as the foundation and initial intervention for persons at risk for CVD (National Cholesterol Education Program, 2001). An important component of the lifestyle modification is a 'heart-healthy' diet, which specifically includes a recommendation for consumption of at least 5–10 g viscous soluble fibre (VSF) per day. As much as 10–25 g/d can provide additional LDL-lowering effects in some individuals. The current average intake of VSF in the USA is well below that at about 3–4 g/d (Bazzano *et al.*, 2003).

The ATP III guidelines emphasize attainment of a healthy level of LDL-C as the primary goal in CVD risk reduction. Clinical trials using VSF treatments have shown the potential for a 10–15 % reduction in LDL-C when it is added to a 'heart-healthy' diet (Bell *et al.*, 1990; Behall *et al.*, 2004*a*, b). VSF is found naturally in some grains, especially oats and barley, in select fruits, such as apples, guava and pears, and in most legumes (e.g. peas and pinto beans). It can also be consumed as a dietary supplement (e.g. psyllium). Despite recommendations for increased intakes of VSF in the diet, most individuals do not meet the recommended levels due, in part, to poor palatability of some fibres and the need to consume a relatively large amount of naturally high-fibre foods in order to achieve the desired level.

In an effort to increase consumption of VSF, concentrated extracts of β-glucan VSF have been added to foods and have been effective in modifying CVD risk (Behall *et al.*, 1997). Recently, a process has been developed for extracting the β-glucan from barley to achieve a barley β-glucan (BBG) concentrate with weight-average molecular weight in the range of 50–400 kDa. This represents a reduction in molecular weight from native (high molecular weight (HMW)) BBG, with weight-average molecular weight of 1000 kDa. This reduction in molecular weight improves BBG sensory properties and performance in foods. Food scientists have successfully incorporated it into foods (e.g. cereals, juices and baked goods) to produce palatable food products which are high in VSF.

The present paper reports the results of a clinical trial of concentrated BBG extract in human subjects. The paper

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Abbreviations: ATP III, National Cholesterol Education Program's Adult Treatment Panel III; BBG, barley β-glucan; HDL-C, HDL-cholesterol; HMW, high molecular weight; LDL-C, LDL-cholesterol; LMW, low molecular weight; VSF, viscous soluble fibre; TAG, triglycerides; CVD, Cardiovascular Disease; CHD, Coronary Heart Disease.

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focuses on the blood lipid results of this intervention. Additional manuscripts are in review or preparation that will report results on insulin sensitivity, adipocytokines, and other CVD risk factors. The aim of the present study was to evaluate the efficacy of a diet augmented with food products (cereal and juice beverage) that were enriched with BBG to increase their VSF content. The study population included subjects at moderate CVD risk who would be considered candidates for the ATP III therapeutic lifestyle changes. The primary variable of interest was the change in LDL-C using two different doses (3 and 5 g) of both low molecular weight (LMW) and HMW forms of BBG. Of particular interest was the percentage of subjects who attained their personal risk-adjusted LDL-C goal using this daily therapy.

Methods

Subjects

The study group comprised men ($n = 75$) and women ($n = 80$) aged 25–73 years who met the National Cholesterol Education Program ATP III criteria for diet therapy due to elevated LDL-C. From September 2003 to October 2004, subjects were recruited from the University of Minnesota-Twin Cities and the greater Twin Cities area. The study was approved by the University of Minnesota Institutional Review Board, and all subjects gave informed consent. Inclusion criteria were: LDL-C between 1300 and 1900 mg/l; TAG < 400 mg/l; fasting glucose < 1260 mg/l. Individuals were excluded if they had diabetes, cancer, secondary hyperlipidaemia, CVD or other chronic medical conditions; TAG > 4000 mg/l; BMI ≥ 40; or a large or unexplained weight change within the previous 6 months. In addition, individuals were excluded if they were taking lipid-altering medications or dietary supplements (2 months prior to screening) which might affect blood lipids; consumed greater than two alcoholic beverages per day on a regular basis; were allergic to aspirin, grain products or any ingredients used in the treatment foods; were following a special diet; or had smoked within the past year. Pregnant and lactating women were also excluded.

Study design

This randomized, double-blind, controlled, five-arm parallel group trial consisted of a 4-week diet stabilization phase followed by a 6-week treatment period. Individuals meeting all inclusion criteria as determined at an initial screening visit were eligible to enter diet stabilization (Fig. 1). These participants attended a group education class in which they were given dietary instruction to consume a diet low in saturated fat and trans-fats (< 10 % of kJ/d) and to discontinue any lipid-altering dietary supplements. Participants who still met all inclusion criteria after the diet period were randomly allocated using a block randomization scheme to receive one of five treatments: low-dose (3 g) LMW BBG, high-dose (5 g) LMW BBG, low-dose HMW BBG, high-dose HMW BBG or control. Subjects were instructed to continue following the low saturated and trans-fat diet and to maintain other lifestyle habits throughout the study. Subjects returned to the clinic for evaluation of side-effects and compliance after 3 and 6 weeks of treatment. Blood pressure, blood lipids, blood apo and other CVD risk markers were evaluated at baseline and at the end of treatment.

Treatment

Two food products were chosen as vehicles to deliver the BBG (Barliv™ barley β-glucan concentrate; Cargill Health and Food Technologies, Wayzata, MN, USA): ready-to-eat cornflakes breakfast cereal and a low-energy tropical juice beverage containing 5 % fruit juice. The foods were formulated such that their nutritional profiles were consistent with FDA heart health claim requirements. Prior to the study, an informal screening exercise was conducted to confirm the sensory acceptability of the treatment foods.

The cereal and juice were packaged in single-serving packages (one cup of cereal or juice per serving) and subjects received a 3-week supply of treatment at baseline and after 3 weeks of treatment. They were instructed to consume two packages of juice beverage and one package of cereal with meals each day (Table 1). Subjects were instructed to save all used and unused cereal and juice containers. These were collected and counted at weeks 3 and 6 as a measure of compliance.

Clinical and laboratory measurements

All visits were conducted at the University of Minnesota General Clinical Research Center. At the screening visit a general medical history was obtained; blood pressure, height and weight were measured; and blood samples were collected to assess fasting chemistry and lipid values. Fasting lipids and lipoproteins were reassessed after the diet stabilization period. Scheduled visits during the treatment period were at baseline and weeks 3 and 6. At all treatment visits, blood pressure and weight were measured and side-effects were assessed. At baseline and week 6, blood was drawn to assess total cholesterol, HDL-C, LDL-C, and TAG.

All blood draws and clinical measurements were performed by University of Minnesota General Clinical Research Center medical staff. Weight and height measurements were obtained with subjects wearing indoor clothing and no shoes. Blood pressure measurements were obtained with an automatic Colin® blood pressure monitor (Press-mate® BP/8800C; Medical Instruments Corp., San Antonio, TX) after subjects had rested in a seated position for at least 5 min. Measurements were repeated four times at 1 min intervals, and the mean of the last three readings was used in analyses. All blood samples were obtained using standard venepuncture techniques after subjects had fasted for 12 h. All laboratory analysis was done using standard automated technology at the Quest Diagnostics® Laboratory (Wood Dale, IL) branch laboratory (certified and accredited laboratory by the Clinical Laboratory Improvement Amendment of 1988 and the College of American Pathologists) or at the University of Minnesota. Specifically, total cholesterol, LDL-C and TAG concentrations were determined using enzymatic methods with Olympus reagents, with automated spectrophotometry performed on Olympus AU5400®. HDL-C was determined directly using Roche reagents on the Olympus AU5400®.

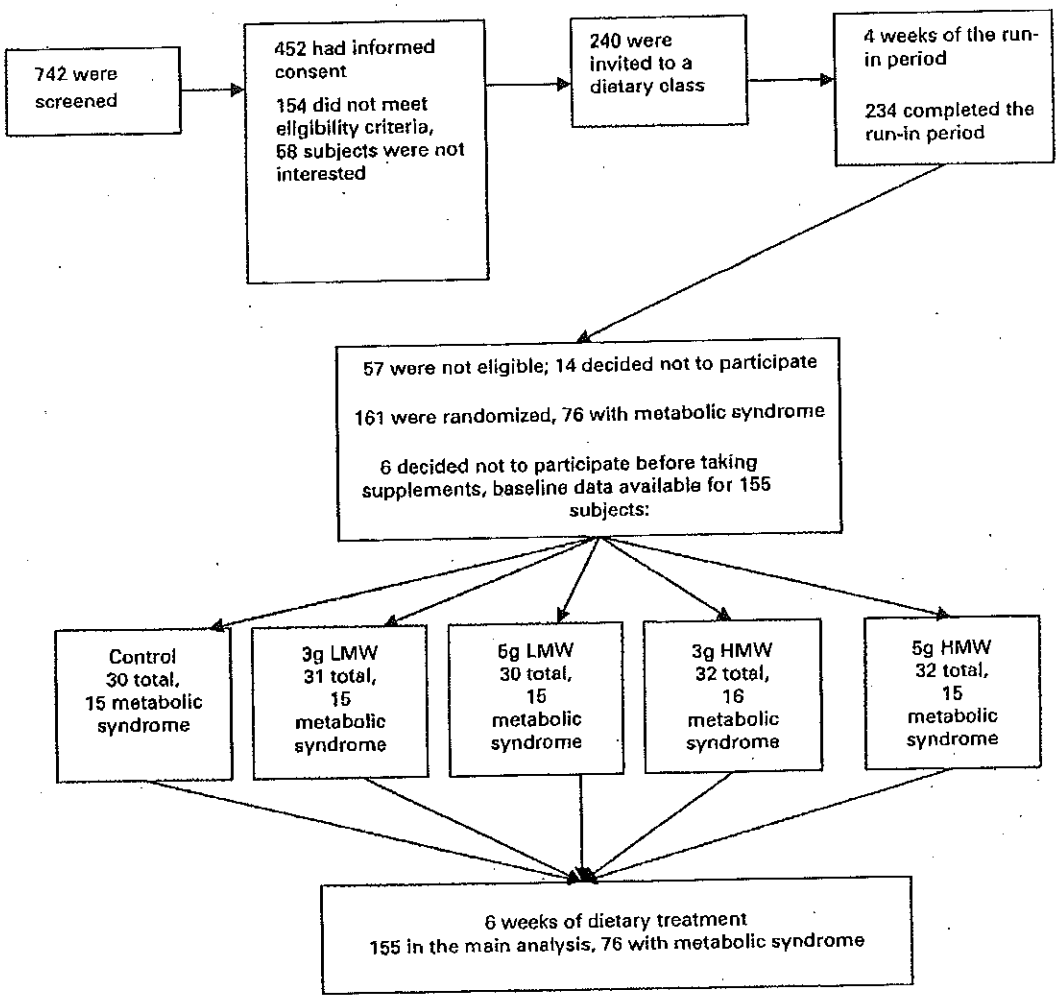

Fig. 1. Flow diagram of study eligibility for concentrated barley β-glucan extract trial. HMW, high molecular weight; LMW, low molecular weight.

Dietary data were collected during the treatment period to monitor diet compliance and consistency. Each subject completed a 3 d food record during the first and last week of treatment and returned them at weeks 3 and 6. Research staff reviewed the records for completeness and clarity during the study visits. Food records were analysed for energy, macronutrient and micronutrient intake using Nutrition Data System for Research software version 5·0_35 (NDS-R; Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN, USA).

Study-related side-effects were assessed by a thirteen-question side-effect questionnaire completed at baseline and subsequent treatment visits. Participants were asked to check the category that best represented their symptoms over the last month at baseline or since their last study visit at each subsequent visit. The categorical options for each symptom were 'Not at all', 'Somewhat', 'Moderately', 'Very much' or 'Extremely'. Frequency counts were used in the analyses and were categorized in two ways: (1) dichotomized as 'Any' *v.* 'No' side-effects or (2) the top two categories were collapsed and were used to indicate the presence of side-effects. Analyses were conducted using both methods of determining side-effects.

Statistical analysis

Differences in baseline demographic and clinical variables among the treatment groups were compared using ANOVA for continuous variables and the χ^2 test for categorical variables. The treatment effect was based on the measurement and comparison of the mean levels of lipids and lipoproteins among treatment groups using ANOVA. The GENMOD procedure of SAS version 8 (SAS Institute Inc., Cary, NC, USA) was used to perform the analyses. In addition, a χ^2 test was performed comparing all side-effect counts (frequencies) at baseline, mid-study and post-study visits. Regression analysis using a general linear model was used to determine the differences in side-effects over time and between the treatment groups and the control group. Test of independent proportions was used to compare the percentage of subjects who attained their LDL-C goal in the treatment groups versus the control

Table 1. Treatment schedule by group

	Juice†		Cereal‡		
Treatment group	Servings consumed	BBG consumed (g)	Servings consumed	BBG consumed (g)	Total BBG consumed (g)
Control (0 BBG/d)	Two cups/d at 0 g BBG/serving	0	One cup/d at 0 g BBG/serving	0	0
High dose HMW (5 g HMW BBG/d)	Two cups/d at 1·0 g BBG/serving	2·0	One cup/d at 3·0 g BBG/serving	3·0	5·0
High dose LMW (5 g LMW BBG/d)	Two cups/d at 1·0 g BBG/serving	2·0	One cup/d at 3·0 g BBG/serving	3·0	5·0
Low dose HMW (3 g HMW BBG/d)	Two cups/d at 0·75 g BBG/serving	1·5	One cup/d at 1·5 g BBG/serving	1·5	3·0
Low dose LMW (3 g LMW BBG/d)	Two cups/d at 0·75 g BBG/serving	1·5	One cup/d at 1·5 g BBG/serving	1·5	3·0

BBG, barley β-glucan; HMW, high molecular weight; LMW, low molecular weight.
† Subjects consumed two juice drinks per day: one with breakfast and the other with their largest meal.
‡ Subjects consumed one cereal per day as part of their breakfast and in lieu of their usual cereal.

group. Statistical significance adjustments were made using Dunnett's test for multiple comparisons.

Results

All baseline variables were similar among the treatment groups (Tables 2 and 3). The mean age overall was 55 years (age range 25–73 years). The ratio of men to women was similar in each treatment arm. The mean BMI between the groups was similar, with each group being borderline obese by National Institutes of Health and WHO standards. The proportion of subjects in each group that had a positive family history of CHD (as defined by the ATP III guidelines) was similar between the treatment groups. Each treatment group was block stratified on metabolic syndrome status resulting in an even distribution of metabolic and non-metabolic syndrome subjects in each group. Metabolic syndrome status was determined according to the ATP III guidelines (elevated TAG, low HDL-C, elevated blood pressure or blood pressure medication, elevated glucose and/or elevated waist girth) and meeting at least three of the five criteria. All study subjects were determined to be generally healthy at baseline and without history of CHD; 38 % had two or more CHD risk factors while 62 % had 0–1 CHD risk factors. For all study participants the mean baseline levels for blood lipids and lipoproteins were as follows (in mg/l): LDL-C, 1540 (range 1100–2200); total cholesterol, 2350 (range 1840–3270); HDL-C, 500 (range 270–1040); TAG, 1600 (range 440–4680).

The mean changes in total cholesterol, LDL-C, TAG and TC/HDL-C for the different treatment groups are shown in Table 3. After 6 weeks of treatment, total cholesterol dropped significantly in all treatment groups compared to control. Specifically, total cholesterol was reduced by 12 % in the 5 g HMW group, a decrease that was slightly more than the other treatment groups: 5 g LMW group, 11 % reduction; 3 g HMW group (−190 mg/l), 8 % reduction; 3 g LMW group, 7 % reduction. LDL-C levels were significantly reduced from baseline in all treatment groups compared to control. The 5 g HMW group experienced a 15 % drop in LDL-C where LDL-C was reduced by 13 % in the 5 g LMW group, 9 % in the 3 g HMW group and 9 % in the 3 g LMW group.

Table 2. Subject characteristics at baseline by treatment group and overall totals†

	Control (n = 30)		5 g, HMW (n = 32)		5 g, LMW (n = 30)		3 g, MW (n = 32)		3 g, LMW (n = 31)		Total (n = 155)	
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age	53·7	12·5	58·6	10·6	52·8	11·9	53·9	10·2	55	10·1	54·8	11·1
BMI	30·8	4·0	28·9	6·7	28·9	5·3	29·6	5·9	28·1	4·3	28·8	5·3
Body weight (kg)	82·8	15·1	81·7	19·8	80·7	16·8	86·4	19·4	80·7	14·9	82·5	17·2
	n	%	n	%	n	%	n	%	n	%	n	%
CHD family history	6	20	11	34·4	9	30	10	31·3	9	29	45	29
Metabolic syndrome‡	15	50	15	46·9	15	50	16	50	15	48·4	76	49
Gender												
Male	17	56·7	15	46·9	11	36·7	16	50·0	16	51·6	75	48·4
Female	13	43·3	17	53·1	19	63·3	16	50·0	15	48·4	80	51·6
Race												
Caucasian	30	100	29	90·6	28	93·3	30	93·8	29	93·5	146	94·2

HMW, high molecular weight; LMW, low molecular weight.
† For details of treatment groups, see Table 1. χ^2 tests of association between groups were performed for gender and ANOVA, F tests were performed for age and BMI. P values were not significant (P>0·09).
‡ Each group was block stratified on metabolic syndrome status as defined by the National Cholesterol Education Program's Adult Treatment Panel III guidelines.

Table 3. Blood lipids results at baseline (Pre) and after 6 weeks of treatment (Post) by treatment group†

	Control ($n = 30$)		5 g, HMW ($n = 32$)		5 g, LMW ($n = 30$)		3 g, HMW ($n = 32$)		3 g, LMW ($n = 31$)	
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
TC										
Pre	234·0	22·7	235·1	25·3	238·0	27·6	233·6	22·8	235·9	23·0
Post	231·3[a]	26·9	205·9*[b]	25·1	211·6*[b]	20·2	214·5*[b]	21·6	218·8*[b]	20·1
TAG										
Pre	153·9	75·4	158·3	79·2	166·7	91·7	164·7	88·7	154·9	61·7
Post	158·8[a]	64·7	133·7*[b]	47·4	145·7*[a]	62·7	152·5[a]	55·8	142·2*[a]	49·2
HDL-C										
Pre	50·5	14·4	50·8	14·2	50·4	13·7	47·9	10·7	49·6	14·8
Post	49·9	13·8	51·9	12·7	49·7	12·8	47·4	11·2	50·8	15·8
TC/HDL-C										
Pre	4·9	1·2	4·9	1·3	5·0	1·4	5·1	1·2	5·0	1·2
Post	5·0[a]	1·4	4·2*[b]	1·0	4·5*[b]	1·2	4·8[a]	1·1	4·6*[b]	1·3
LDL-C										
Pre	152·7	13·9	154·5	16·5	154·6	19·9	152·8	18·1	153·9	15·1
Post	150·9[a]	24·3	132·0*[b]	11·4	134·3*[b]	12·8	138·8*[b]	20·3	140·5*[b]	15·1

HDL-C, HDL-cholesterol; HMW, high molecular weight; LDL-C, LDL-cholesterol; LMW, low molecular weight; TC, total cholesterol.
[a,b] Mean values within a row with unlike superscript letters were significantly different (with adjustments for multiple comparisons; $P < 0.05$).
Mean values were significantly different from those of the baseline (paired Student's *t*-tests): *$P < 0.05$.
† For details of treatment groups, see Table 1. ANOVA *F* tests were done for each variable. No significant differences were found between groups at baseline ($P > 0.60$).

Fasted TAG levels were reduced from baseline in all treatment groups except the 3 g HMW group (Table 3), while the control group experienced a modest increase. However, after adjusting for multiple comparisons only the 5 g HMW group experienced a significant drop in TAG levels compared to control. Fasted TAG level was reduced by 16 % in the 5 g HMW group. There were no significant changes from baseline in any of the treatment groups regarding HDL-C.

Table 3 shows the decrease in the total cholesterol/HDL-C ratio in all the treatment groups at the final study visit. The ratio of total cholesterol/HDL-C was significantly changed by treatment in all the treatment groups except the 3 g HMW group. The 5 g HMW group experienced a 15 % drop in the total cholesterol/HDL-C ratio while this ratio was reduced by 10 % in the 5 g LMW group and 9 % in the 3 g LMW group. The 3 g HMW group also experienced a reduction in the total cholesterol/HDL-C ratio from baseline but this change was not significantly different from the control group after adjusting for multiple comparisons.

Diet was unchaoged throughout the study in both the treatment groups and the control group. All treatment groups (hut not the control group) attained the ATP III guidelines goal of ≥ 10 g VSF/d when the dose of the treatment fibre was added to the background dietary soluble fibre intake. Body weight was unchanged over the duration of the study in all study groups.

The treatment was well tolerated by most subjects, with excellent compliance (average treatment compliance by group: control, 96 %; 5 g HMW, 95 %; 5 g LMW, 97 %; 3 g HMW, 94 %; 3 g LMW, 97 %). The fact that there were no study dropouts further indicates the tolerability of the study treatments. Moreover, adverse events were monitored at all study visits and none were reported. Treatment-related side-effects were also assessed at each study visit. There were no differences in the frequency of side-effects at baseline between any of the study treatment groups or the control group. Additionally, there was no change in the frequency of side-effects from baseline to the mid-study visit or to the final study visit in any of the treatment groups when compared to the control group except for the frequency of intestinal gas. In all groups except the control group the frequency of intestinal gas increased over the first 3 weeks of the study and persisted over the final 3 weeks of treatment. However, the change in frequency of intestinal gas only reached statistical significance in the 5 g HMW group (at week 3 and week 6 of treatment) when all treatment groups were compared to the control group ($P < 0.05$).

Table 4. LDL-cholesterol goal attainment at baseline and week 6 by number of CHD risk factors†

Treatment group	Zero or one CHD risk factors at baseline	Zero or one CHD risk factors at week 6	Two or more CHD risk factors at baseline	Two or more CHD risk factors at week 6
Total ($n = 154$)	66/95	80/95	2/59	20/59
Control ($n = 30$)	19/22	15/22	0/8	0/8
5 g HMW ($n = 32$)	12/17	15/17	1/15	8/15
5 g LMW ($n = 29$)‡	15/21	20/21	0/8	4/8
3 g HMW ($n = 32$)	9/18	15/18	1/14	7/14
3 g LMW ($n = 31$)	11/17	15/17	0/14	1/14
Any BBG treatment ($n = 124$)	47/73	65/73	2/51	20/51

BBG, barley β-glucan; HMW, high molecular weight; LDL-C, LMW, low molecular weight.
† For details of treatment groups, see Table 1. CHD risk factors as defined by National Cholesterol Education Program's Adult Treatment Panel III guidelines.
‡ One subject was left out of analysis (5 g LMW group) because we were unable to get all risk factor data.

The National Cholesterol Education Program ATP III guidelines were applied to each study participant to determine his or her LDL-C goal of therapy based on level of CHD risk (Table 4). A greater percentage of individuals in the treatment groups attained their LDL-C goal compared to the control group. At study conclusion 89 % of those with zero or one CHD risk factors who received any study treatment had attained their LDL-C treatment goal compared to 68 % in the control group. Similarly, among the subjects with two or more CHD risk factors, 39 % (20/51) who received any of the study treatments attained their LDL-C goal compared to 0 % (0/8) in the control group ($P<0.05$).

Discussion

The aim of the present study was to assess the impact of BBG-enriched foods on CVD risk factors, specifically LDL-C and other blood lipid levels, in human subjects with moderate dyslipidaemia. The present study demonstrated that both HMW and LMW BBG, when added at either 3 or 5 g/d, reduced the primary study variable, LDL-C, with significant reductions at both the 3 g and 5 g daily dose. Reductions were 9 % for the 3 g dose and 15 % or 13 % for the 5 g dose (HMW and LMW, respectively). Additionally, total cholesterol was significantly reduced among all treatment groups, while the ratio TC/HDL was more significantly reduced among the 5 g/d groups. The present findings demonstrate that the efficacy of a BBG-enriched diet in modifying blood lipid CVD risk factors is at least comparable to previous clinical trials of VSF-enriched diets. As important, the LMW BBG which has even greater therapeutic potential because of its improved sensory properties and performance in foods demonstrated comparable efficacy to the HMW BBG in blood lipid improvement.

An important study outcome that is a corollary to the LDL-C reduction is the number of subjects who were able to attain their personal LDL-C goal as established by the ATP III guidelines. The ATP III guidelines use a system of assessing core CVD risk factors to establish the LDL level or cut point at which an individual can consider their efforts at risk reduction successful (National Cholesterol Education Program, 2002). If a person does not reach their goal with lifestyle changes, then they will generally need to progress to more aggressive interventions such as pharmacotherapy. It is an additional important measure of the efficacy of the BBG intervention that 69 % of the subjects in the treatment groups were able to attain their LDL-C goal as opposed to 50 % of the control group on a 'heart-healthy' diet alone. Of particular note is the fact that all treatment groups, both the 3 g and 5 g LMW and HMW groups, showed a substantial increase in persons reaching their ATP III goal for LDL-C. The study subjects were only moderately dyslipidaemic; 40 % of the subjects in the treatment groups and 63 % of the control group had already achieved their LDL-C goal on the run-in diet. Nevertheless, LDL-C is a continuous risk variable and additional improvement in LDL-C levels with the BBG intervention further enhanced their CVD risk reduction and maintenance of healthy lipid levels.

Overall compliance with study treatments and the lack of significant study-related side-effects demonstrated excellent acceptance and tolerance of BBG. As is common with an increase in fibre intake, subjects on active treatment did report an initial increase in intestinal gas, but for most subjects this side-effect did not increase over the duration of the study. Three-day food records obtained at baseline and at the end of the study indicated that subjects were generally compliant with overall diet recommendations and there were no significant changes in energy consumption or specific nutrient intake over the 6-week period. Of note, all subjects within the four treatment groups attained the ATP III goal of consumption of 10–25 g VSF/d when the treatment dose of BBG was added to their background VSF consumption on the 'heart-healthy' diet.

To date, most of the human studies investigating the hypocholesterolaemic effects of β-glucan have utilized diets rich in oat and oat products. However, human clinical trials have been conducted using barley foods as the source of β-glucan as well. (McIntosh *et al.* 1991) conducted one of the first trials comparing diets rich in barley versus wheat in a cross-over design. Compared to the wheat period, the barley diet period resulted in a 6 % lower total cholesterol level and a 7 % lower LDL-C level. In 2004, Behall *et al.* reported that adding 6 g soluble fibre from barley per day for 5 weeks in addition to a Step 1 diet resulted in a 24 % reduction in LDL-C (Behall *et al.*, 2004*b*). However, not all studies investigating the cholesterol-altering effects of barley have reported a treatment effect. (Keogh *et al.* 2003) reported that adding β-glucan-enriched barley to the diets of hypercholesterolaemic men containing 38 % of kJ from fat did not significantly reduce total or LDL-C levels.

To date, there have been even fewer studies investigating the cholesterol-altering effects of extracted β-glucan. There have been a few studies showing the benefit of oat β-glucan extract in CVD risk reduction (Behall *et al.*, 1997). However, there has only been one previous study reporting a dietary intervention using β-glucan extracted from oats with molecular weight modification (Frank *et al.*, 2004): the study used 6 g/d oat β-glucan extract (both LMW and HMW) for 3 weeks and failed to show a significant effect on blood lipids, specifically LDL-C. Compared to the findings in the present trial, the results of (Frank *et al.* 2004) would suggest that the extent of the molecular weight reduction of the β-glucan fibre could significantly alter its hypocholesterolaemic action. Additionally, it is apparent from a review of the literature that not all soluble fibre forms and sources have comparable effects on CVD risk factors (Truswell, 1995).

Experts contend that the LDL-C-lowering effects of high-VSF foods, such as oats and barley, are due to the action of VSF in the gastrointestinal tract. VSF has been shown to increase the elimination of bile salts, and secondarily, bacterial fermentation products (SCFA) have been shown to suppress hepatic cholesterol biosynthesis (Marlett *et al.*, 1994). There is a substantial body of knowledge supporting these mechanisms of action, and this persuaded the (US Food & Drug Administration 1993) to grant the first health claim for reduced risk of heart disease in 1993 to foods rich in soluble fibre from oats.

Lowering the molecular weight of β-glucan does improve sensory properties and performance in foods, but it can also reduce the viscosity of the fibre, thus the tradeoff can be a decrease in efficacy. This appears to be the reason that some previous studies of other LMW β-glucans in animals and man had reduced efficacy (Yamada *et al.*, 1999; Frank *et al.*,

2004). In addition, some feel that any β-glucan extract, even a concentrated source, loses some of the important components, such as polyphenolics and antioxidants, present in whole-grain products and thereby may be less effective in overall CVD risk reduction. (Jacobs & Gallaher 2004) have reviewed a number of prospective trials and have concluded that consumption of whole-grain products reduces CVD risk. The present study of foods enriched with extracted BBG demonstrates their efficacy in reducing LDL-C, a major surrogate marker for CVD, and gives support to the position that extracted VSF can significantly reduce CVD risk.

A study of longer duration may be helpful to show maintenance of the benefit. Further, in order to generalize the results to a broader, more diverse population, it may be helpful to study certain subgroups and other population groups over the age of 65.

Conclusion

The present study demonstrates the efficacy and excellent tolerance of a dietary intervention using BBG-enriched foods to reduce CVD risk, specifically LDL-C. All subjects in BBG treatment groups were able to reach the ATP III dietary goal of consumption of 10–25 g/VSF d. An important finding in the present study was that LMW BBG had comparable efficacy gram for gram when compared to native HMW BBG. This is clinically important because the improved sensory properties and performance in foods of LMW BBG make it a more viable food ingredient for broader applications. An additional important outcome of the present study was that a greater number of BBG-treated subjects versus control attained their ATP III goal for LDL-C. The findings of the present study have clear clinical benefits in CVD risk reduction and significant healthcare cost benefits due to reduced need for pharmacotherapy if the results can be sustained long term.

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The Effects of Barley-Derived Soluble Fiber on Serum Lipids

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ABSTRACT

PURPOSE We wanted to determine the association between consumption of barley and changes in plasma lipids in healthy and hypercholesterolemic men and women.

METHODS A systematic literature search was conducted from the earliest possible date through January 2008. Trials were included in the analysis if they were randomized controlled trials of barley that reported efficacy data on at least 1 lipid endpoint. A DerSimonian and Laird random-effects model was used in calculating the weighted mean difference (WMD) and its 95% confidence interval (CI). Statistical heterogeneity was addressed using the I^2 statistic. Visual inspection of funnel plots, Egger's weighted regression statistics, and the trim and fill method were used to assess for publication bias.

RESULTS We found 8 trials (n = 391 patients) of 4 to 12 weeks' duration evaluating the lipid-reducing effects of barley. The use of barley significantly lowered total cholesterol (weighted mean difference [WMD], −13.38 mg/dL; 95% CI, −18.46 to −8.31 mg/dL), low-density lipoprotein (LDL) cholesterol (WMD, −10.02 mg/dL; 95% CI, −14.03 to −6.00 mg/dL) and triglycerides (WMD, −11.83 mg/dL; 95% CI, −20.12 to −3.55 mg/dL) but did not appear to significantly alter high-density lipoprotein (HDL) cholesterol ($P = .07$).

CONCLUSION Barley-derived β-glucan appears to beneficially affect total cholesterol, LDL-cholesterol, and triglycerides, but not HDL-cholesterol.

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INTRODUCTION

According to the guidelines of the National Cholesterol Education Program (NCEP), approximately 30% of Americans have undesirably high serum cholesterol concentrations.[1] High serum lipid levels, including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, are a major cause of coronary atherosclerosis.[1] Any LDL cholesterol concentration above 100 mg/dL appears to be atherogenic and the higher the level, the greater the risk.[1] Although elevated LDL cholesterol plays a role in the development of the coronary plaque instability, lowering LDL cholesterol stabilizes plaques and reduces the likelihood of acute coronary syndromes.[1] Lowering serum cholesterol reduces the risk of coronary heart disease.

The effect of dietary fiber on cholesterol metabolism has been studied extensively.[2,3] Barley and oats have a similar concentration of soluble fibers called β-glucan (3.5%-5.9% of the dry matter), whereas wheat and rice do not posses this constituent type of fiber.[4] Unlike wheat and rice,[5-10] a diet high in β-glucan has been shown to slow gastric emptying, digestion, and absorption.[11] These effects are associated with increased excretion of bile acids and neutral sterols, increased catabolism of cholesterol, and reduced absorption of cholesterol and fat.[12,13]

Although the antihyperlipidemic effects of oats have been extensively studied, there are fewer barley studies, and findings have shown more

apparent inconsistency in cholesterol effects.[14,15] Some reasons for inconsistencies in the barley studies may be explained by differences in the β-glucan dose, the molecular size of β-glucan, the composition of dietary food, the process of food preparation, and the initial variation in cholesterol level. Even though several clinical trials[10,16-29] have investigated the impact of barley β-glucan on total cholesterol, LDL cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides, a meta-analysis assessing these effects has not been published. We therefore sought to perform a meta-analysis of randomized controlled trials of barley to better characterize its effect on various lipid parameters.

METHODS

Was conducted a systematic literature search of MEDLINE, EMBASE, CINAHL, Web of Science, the Cochrane Library, and the Natural Medicines Comprehensive Database from the earliest possible date through January 2008. Our search strategy used the Medical Subject Headings (MeSH) and text key words: "β-glucan," "barley" and "lipids," "serum cholesterol," "total cholesterol," "low-density lipoproteins," "high-density lipoproteins," "LDL," "HDL," "triglycerides," or "hypercholesterolemia." This search was then limited to clinical trials in humans. We also performed a manual search of references from retrieved articles. When applicable, we made an effort to contact investigators for clarification or additional data (although no additional data were acquired).

To be included in this meta-analysis, studies had to be randomized controlled trials of barley and report data on at least 1 of the following lipid parameters: total cholesterol, LDL cholesterol, HDL cholesterol, or triglycerides. Both parallel and crossover trials were eligible for inclusion; however, crossover trials had to have at least a 4-week washout period. If this criterion was not met, when possible, we included only the first phase of each crossover trial.

A more detailed description of the methods can be found in the Supplemental Appendix, available online at http://www.annfammed.org/cgi/content/full/7/2/157/DC1.

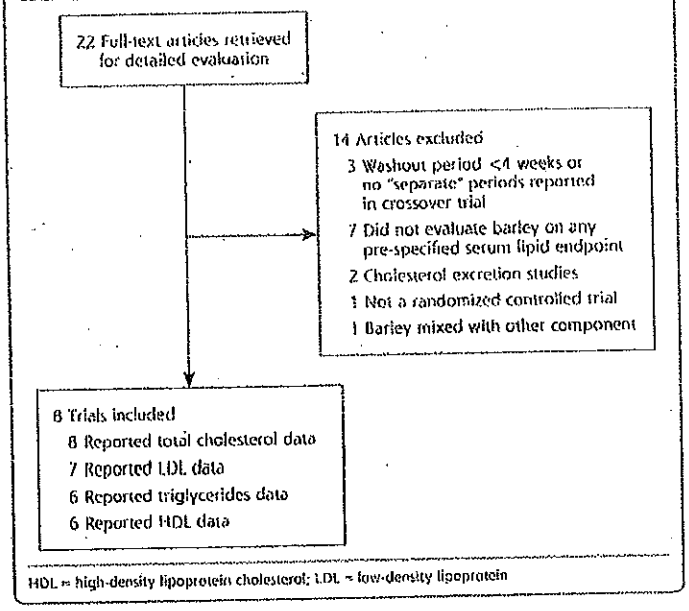
We treated the mean change in lipid parameters from baseline as a continuous variable, and the weighted mean difference (WMD) and its 95% confidence interval (CI) were calculated as the difference between the mean in the β-glucan and control groups using a DerSimonian and Laird random-effects model.[30] For parallel trials, we calculated net changes in each of these study parameters as the difference (β-glucan minus control) of the changes (baseline minus follow-up) in the mean values (also referred to as the change score). For crossover trials, we calculated net changes as the mean difference in values at the end of the β-glucan and control periods. Standard statistical methods were used to impute change scores, as suggested by Follman and colleagues.[31]

Statistical heterogeneity was addressed using the I^2 statistic. Visual inspection of funnel plots, Egger's weighted regression statistics, and the trim and fill method was used to assess for the presence of publication bias.[32] Sensitivity analysis was conducted to assess the impact of double-blinding, the use of crossover methodology ,and the use of a fixed-effects model (Mantel-Haenszel methodology).[33] Additionally, subgroup analyses were conducted to assess the effect of using or not using concurrent dietary modifications and to asses the effect on only hypercholesterolemic patients. Statistics were performed using StatsDirect statistical software, version 2.4.6 (StatsDirect Ltd, Cheshire, England). A P value of $<.05$ was considered statistically significant for all analyses.

RESULTS

The initial search yielded a total of 22 studies for full-text review. For reasons depicted in Figure 1, 14 of

Figure 1. Flow diagram of trial identification, inclusion, and exclusion.



HDL = high-density lipoprotein cholesterol; LDL = low-density lipoprotein

the 22 studies were excluded; therefore, a total of 8 randomized controlled trials[10,16-22] (evaluating 391 participants) were included in this meta-analysis (Table 1). Five of the studies[10,16-18,20] were conducted using a parallel study design, whereas 2 studies[19,22] used a crossover design with a 4-week washout period, and 1 study[21] used a crossover design with no washout period and was treated as a parallel trial by taking into account only the first phase of the study data.

Each study enrolled relatively few participants (median sample size, 30 participants; range, 10-155 participants) and had a short duration of treatment (median duration, 4 weeks; range, 4-12 weeks). The dosage of β-glucan reported in included studies ranged from 3 to 10 g/d (median dose, 7 g/d) and was administered in various forms, including pearled barley, barley bran flour, oil extracts in capsules, barley concentrates, barley-containing beverages, and gelling agents. Only 2 studies[17,20] administered barley along with some type of dietary modification. Of the 8 studies, 6 were not double-blind.[10,18,22] Three of the 8 studies were industry funded.[10,17,22]

Upon meta-analysis, participants consuming barley had significantly greater reductions in total cholesterol, LDL cholesterol, and triglycerides, but not HDL cholesterol compared with control participants (Table 2, Figure 2). No statistical heterogeneity was observed in any of these analyses (I^2 = 0% for all). Visual inspection of funnel plots (not shown) suggested a low likelihood of publication bias. This finding was further supported by Egger's weighted regression statistic *P* values, which also suggested that publication bias was unlikely for all analyses except total cholesterol ($P = .02$). After recalculating effect size estimates using trim and fill methods, barley's effect was not significantly altered for triglycerides. For total cholesterol, LDL cholesterol, and HDL cholesterol, the trim and fill analysis suggests that as many as 4 studies for total cholesterol and 3 studies for LDL cholesterol and HDL cholesterol could potentially exist for each endpoint; however, barley still had a significant, although reduced, effect when these theoretically "missing" studies were imputed for total cholesterol and LDL cholesterol. For HDL cholesterol, the original analysis did not show significance, but after imputing the 3 "missing" studies from the trim and fill, it was statistically significant for this endpoint.

Upon subgroup and sensitivity analysis, similar results were seen for all of the study endpoints when crossover or non–double-blinded studies were excluded, except the effect of barley on triglycerides lost statistical significance (Table 2). When a fixed-effects model was used, the results did not change. When studies evaluating barley in only hypercholesterolemic patients were analyzed, the effect of barley on triglycerides lost statistical significance but still

Table 1. Characteristics of Included Randomized Controlled Trials of Barley

Reference	Design	Type of Patient	Double-Blinding	N[a]	Duration of Treatment (wk)	Preparation of Barley	β-Glucan Intake per Day	Concurrent Diet Modification
Shimizu et al,[16] 2007	Parallel	Hypercholesterolemic	Yes	39	12	Pearled barley	7 g	None
Keenan et al,[17] 2007	Parallel	Hypercholesterolemic	Yes	155	6	Barley concentrate in cereal and juice	3 or 5 g of either HMW or LMW	Low saturated (<10%) & low trans unsaturated fat diet
Björklund et al,[18] 2005	Parallel	Hypercholesterolemic	No	55	5	Barley concentrate as beverage	5 or 10 g	None
Keogh et al,[19] 2003	Crossover	Hypercholesterolemic	No	18	4	Naturally extracted barley β-glucan as a gel	9.9 g	None
Li et al,[21] 2003	Crossover	Healthy	No	10	4	Barley bran in whole grain	NR	None
Lupton et al,[20] 1994	Parallel	Hypercholesterolemic	No	79	4	Barley bran flour or oil extract in capsules	NR	Step I diet
McIntosh et al,[22] 1991	Parallel[b]	Hypercholesterolemic	No	21	4	Barley grain (bran and flakes)	8 g	None
Newman et al,[10] 1989	Parallel	Healthy	No	14	4	Barley grain flour in cereal and baked goods	4.5 g	None

HMW or LMW = high or low molecular weight β-glucan; NR = not reported; step I diet = diet consisting total fat to ≤30% of total calories, saturated fat to ≤10% of total calories, and cholesterol to 300 mg/d.

[a] Number of patients evaluated.

[b] Crossover trial treated as parallel trial with only the first phase of the study data taken into account.

Table 2. Results of the Meta-Analysis of Randomized Controlled Trials Evaluating Effect of Barley Cholesterol Levels

Study Type	Total Cholesterol mg/dL (95% CI)	LDL Cholesterol mg/dL (95% CI)	HDL Cholesterol mg/dL (95% CI)	Triglycerides mg/dL (95% CI)
All studies	−13.38 (−18.46 to −8.31) [8 studies]	−10.02 (−14.03 to −6.00) [7 studies]	0.99 (−0.09 to 2.06) [6 studies]	−11.83 (−20.12 to −3.55) [6 studies]
Fixed-effects model	−13.38 (−18.46 to −8.31) [8 studies]	−10.02 (−14.03 to −6.00) [7 studies]	0.99 (−0.09 to 2.06) [6 studies]	−11.83 (−20.12 to −3.55) [6 studies]
Excluding crossover studies	−13.75 (−19.24 to −8.26) [6 studies]	−9.76 (−14.64 to −4.88) [5 studies]	−0.97 (−3.31 to 1.36) [4 studies]	−13.68 (−12.74, 0.39) [4 studies]
Excluding studies not double-blind	−17.39 (−26.05 to −8.74) [2 studies]	−13.43 (−20.58 to −6.29) [2 studies]	0.85 (−4.71 to 6.41) [1 studies]	−22.45 (−50.65 to 5.76) [1 studies]
Excluding studies in patients without hypercholesterolemia	−12.56 (−17.89 to −7.24) [6 studies]	−9.38 (−14.13 to −4.63) [5 studies]	1.08 (−0.01 to 2.17) [4 studies]	−11.06 (−24.97 to 2.85) [4 studies]
Trim and fill	−10.49 (−15.09 to −5.89) [+4 studies]	−8.45 (−12.21 to −4.69) [+3 studies]	1.34 (0.31 to 2.37) [+3 studies]	−11.83 (−20.12 to −3.55) [+0 studies]
Studies evaluating barley with diet modification	−17.14 (−25.02 to −9.23) [2 studies]	−14.57 (−21.69 to −17.45) [2 studies]	1.53 (−2.98 to 6.05) [2 studies]	−17.36 (−40.66 to 5.94) [2 studies]
Studies evaluating barley without diet modification	−10.75 (−17.36 to −4.12) [6 studies]	−7.89 (−12.75 to −3.04) [5 studies]	−0.16 (−2.33 to 2.02) [4 studies]	−11.03 (−19.90 to −2.17) [4 studies]

CI = confidence interval; LDL = low-density lipoprotein; HDL = high-density lipoprotein; + = analysis-imputed missing studies.

Note: All results reported as weighted mean differences.

trended toward a reduction. When studies using and not using dietary modification were assessed separately, the effect of barley on serum lipids qualitatively appeared more robust when combined with dietary modifications.

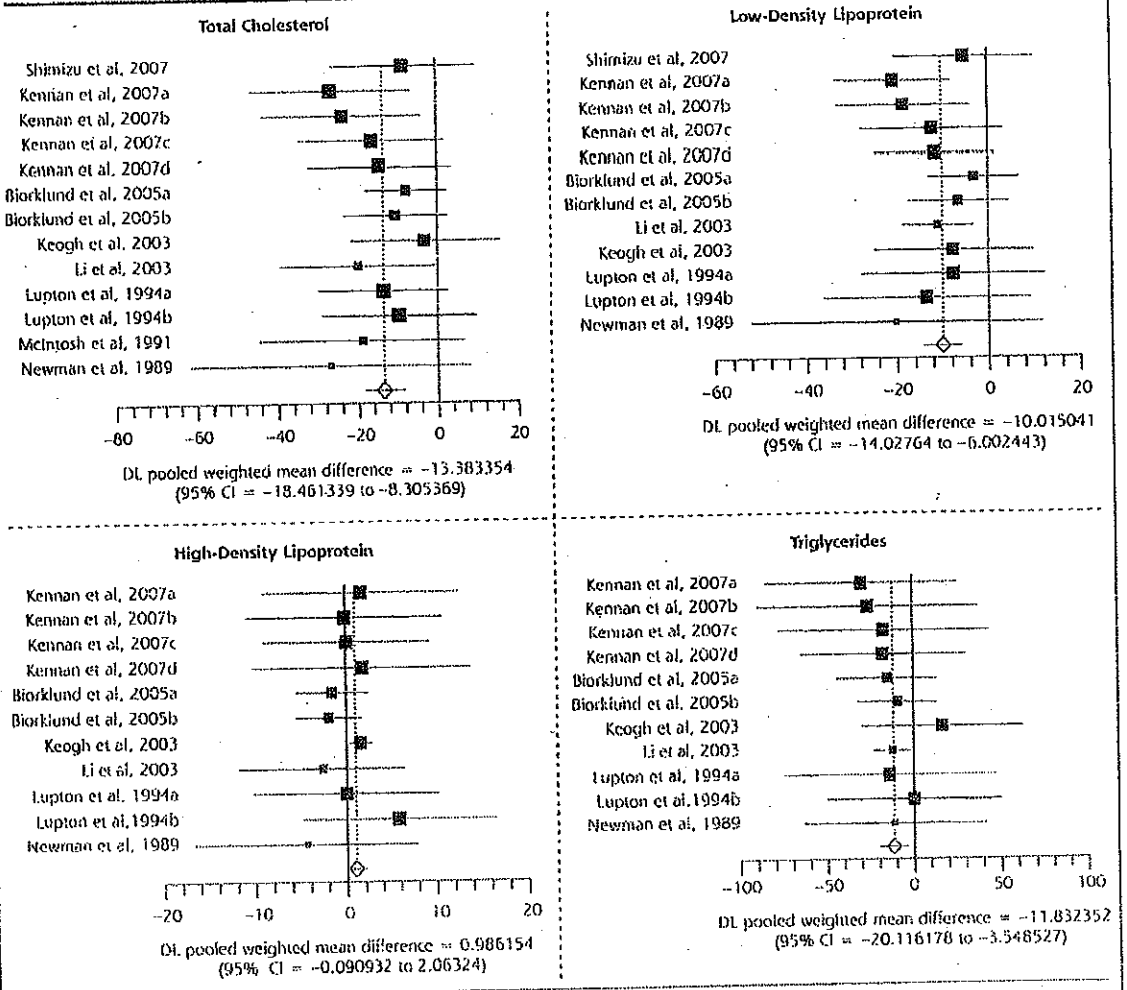
DISCUSSION

In our meta-analysis of 8 randomized controlled trials, participants receiving barley had statistically significant reductions in total cholesterol (−13 mg/dL), LDL cholesterol (−10 mg/dL), and triglycerides (−12 mg/dL) compared with control group participants. Because studies have shown that for each milligram per deciliter reduction in a patient's LDL cholesterol level, their relative risk of having a coronary heart disease event is decreased by 1%, this modest reduction in LDL cholesterol observed with barley is likely clinically significant as well.[34]

This reduction in total cholesterol and LDL cholesterol is in line with that found for oat-derived β-glucan. In a meta-analysis of oats containing 2 to 10 g/d of β-glucan, there was a net change resulting from soluble fiber ingested of −3.1 mg/dL to −15.5 mg/dL for total cholesterol, and −2.9 mg/dL to −14.3 mg/dL for LDL cholesterol.[35] Barley and oats have similar concentrations of β-glucans (3.5%-5.9% of the dry matter), the proposed active ingredient in both soluble fibers, so a similar magnitude of total cholesterol or LDL cholesterol reductions is plausible.[4] In the meta-analysis of oats by Brown and colleagues, however, changes of −0.08 to −0.4 mg/dL were noted for HDL cholesterol, and changes of 1.06 to 5.3 mg/dL were noted for triglycerides, which is in contrast to our meta-analysis, in which with barley-derived β-glucan we saw a nonsignificant increase of 1 mg/dL for HDL cholesterol and a significant reduction of 12 mg/dL in triglycerides compared with a control group.[35] In addition, Brown and colleagues found a dose-response relationship when evaluating studies of soluble fibers in the practical dose range (<10 g/d).[35] That review, however, included 67 clinical trials evaluating a variety of soluble fibers (not including barley). Thus, their analysis was appropriately powered to evaluate dose response. In comparison, our meta-analysis included 8 studies, only 6 of which reported a β-glucan dose (75% of total patient population), making it difficult to conduct a dose-response analysis. At least 10 studies are recommended to provide adequate power.[36]

The Food and Drug Administration (FDA) has stated that daily intakes of 3 g or more of soluble fiber

Figure 2. Impact of barley on serum lipids.



DL = DerSimonian and Laird random-effects model.

(β-glucan) in whole oats or barley may reduce the risk of heart disease by its ability to lower total cholesterol and LDL cholesterol.[37,38] Our meta-analysis results support this FDA decision, because 3 to 10 g of β-glucan from various forms of barley lowered total cholesterol, LDL cholesterol, and triglycerides in the study participants. Furthermore, a significant reduction in total cholesterol and LDL cholesterol was found regardless of whether a low-fat or step I diet was mandated equally in both arms of the studies. This finding is important because of the potential for a dietary substitution effect. If study participants are replacing their normal foods (eg, eggs, bacon, sausage) with barley, it may be difficult to discern whether the improvements in cholesterol resulted from the healthier diet or from barley. That significant reductions in total cholesterol and LDL cholesterol were seen regardless of whether diet modifications were mandated equally in both study groups helps guard against the issue of dietary substitution and strengthens the beneficial effects of barley use.

There are some limitations to this meta-analysis that should be noted. First, we included crossover and parallel studies. Crossover studies have methodological advantages compared with parallel studies, because patients act as their own controls; however, an adequate washout period is necessary. As such, we did not include trials that did not explicitly state the presence and duration of the washout period or trials that had a washout period of fewer than 4 weeks, in which case, we only included the first phase of the

study when possible. The only noteworthy change seen upon conducting a sensitivity analysis excluding crossover studies was loss of statistical significance in the triglycerides endpoint.

Second, as with any meta-analysis, the potential for publication bias is a concern. Although visual inspection of our meta-analysis' funnel plot could not rule out the possibility of publication bias, review of Egger's weighted regression statistics and trim and fill analyses showed that it was unlikely that publication bias significantly affected our study results. Finally, we did not evaluate the potential for harms with barley. Based upon available data, barley appears to be well tolerated, with flatulence and abdominal discomfort being reported as the most common adverse effects, but there is not adequate power to look for other less common adverse effects.[17]

The results of our study support the routine use of soluble fibers in the diets of adult patients with and without hypercholesterolemia. Barley adds another source of soluble fibers, in addition to oats, psyllium, pectin, and guar gum that patients can consume as part of a healthy diet.[35] Larger randomized clinical trials are warranted to better characterize the potential for a dose-response relationship with barley β-glucan. Health practitioners should feel comfortable recommending barley β-glucan to their patients to help reduce total cholesterol and LDL cholesterol concentrations as recommended by the NCEP guidelines.[1]

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Key words: Barley; beta-glucans; dietary fiber; lipids; meta-analysis

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Barley β-glucan reduces plasma glucose and insulin responses compared with resistant starch in men

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Abstract

Glucose and insulin responses have been reported to be lowered by acute consumption of soluble oat fiber or high amylose cornstarch. This study sought to determine if barley β-glucan and preformed resistant starch reduced glucose and insulin responses in men independently or if a synergism exists between the two carbohydrate sources. A total of 20 men (10 control, 10 overweight; average body mass index, 23.8 vs 29.0) were fed a controlled diet for 2 days before each treatment containing 75 g available carbohydrate. Fasting subjects consumed 10 treatments consisting of glucose or 1 of 9 muffins containing 3 levels of resistant starch (0.1, 6.1, or 11.6 g/tolerance) and 3 levels of β-glucan (0.1, 3.1, or 5.8 g/tolerance) in a Latin square design. Plasma glucose and insulin responses were determined over 4 hours after each treatment. Compared with controls, overweight subjects had significantly higher mean glucose (5.5 vs 6.0 ± 0.1 mmol/L) ($P < .003$) and insulin (153 vs 285 ± 21 mmol/L) ($P < .0001$) concentrations. Glucose ($P < .001$) and insulin ($P < .003$) responses were lower and returned to fasting quicker in the controls than in overweight subjects. The highest β-glucan level was the most effective in lowering glucose ($P < .001$) and insulin responses ($P < .0001$). Average glucose ($P < .025$) and insulin ($P < .0001$) areas under the curve were lowest after the muffins containing the high β-glucan. Resistant starch content was less effective than β-glucan in reducing glucose or insulin response. Acute consumption of barley β-glucan, but not resistant starch, in muffins was effective in reducing glucose and insulin responses in men who were mildly insulin-resistant.

Keywords: Amylose; Insulin; Glycemic response; Insulin resistance; Soluble fiber; Human

1. Introduction

Elevated glucose and insulin concentrations are the primary indicators for insulin resistance and type 2 diabetes [1,2]. Insulin resistance is associated with obesity, hypertension, dyslipidemia, glucose intolerance [1,3,4], and type 2 diabetes [1,2]. Abnormal carbohydrate metabolism, especially with respect to elevated glucose or insulin concentrations in the blood, occurs with increasing age and weight [3,5]. Obesity is associated with decreased ability of the body to control blood glucose with normal levels of insulin [6]. This may also be an early step in the development of non–insulin-dependent diabetes mellitus [6]. Insulin resistance increases as weight increases [3] and is more prevalent in obese subjects (up to 46% in obese subjects compared with 4% in a control population) [4]. It has been estimated that occurrence of insulin resistance increases nearly 20% for each 5% increase in weight over the reported weight at age 20 [3]. Delaying the delivery of glucose through dietary means may assist in the management of insulin resistance [7,8].

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Table 1
Baseline characteristics of control and overweight men (mean ± SEM) as selected for the study

	Control (n = 10)	Overweight (n = 10)
Age (y)	42.2 ± 2.3[a]	41.5 ± 2.9[a]
Height (cm)	177.5 ± 1.8[a]	179.3 ± 2.8[a]
Weight (kg)	75.3 ± 1.8[a]	93.1 ± 3.3[b]
BMI[b]	23.8 ± 0.4[a]	29.0 ± 1.0[b]
Body fat (%)	18.0 ± 1.2[a]	25.2 ± 2.1[b]

[a] Means within a row with different superscripts are significantly different ($P < .05$) based on least-mean squares.
[b] BMI measured as weight/height^2 (kg/m^2).

Consumption of foods containing soluble fiber or resistant starch (RS) reduces the risk of chronic disease. Risk factors include reductions in blood glucose and insulin [7-9] and improvement of glycemic control in normoglycemic and diabetic subjects [1,7-10] after consumption of soluble fiber or RS. Glucose and insulin responses (peak and/or area under the curve) have been reported to be lower after a test meal containing soluble fiber, including pectin, Oatrim (oat fiber extract), guar gum, gum tragacanth, and methyl cellulose fibers, when compared with the meal without the soluble fiber [8-12]. Consumption of foods high in amylose or RS decreased postprandial glucose and insulin responses in people with normal as well as those with impaired glucose tolerance [13-15]. The amount of soluble fiber or high amylose starch/RS fed in the acute meal tolerances has varied greatly.

Because both soluble fiber and RS modulate postprandial glucose and insulin response, this study evaluated the postprandial glycemic responses of normal-weight and overweight or obese men after consumption of several levels of RS (from high-amylose comstarch) and soluble fiber (β-glucan from barley) singularly and combined in the same food product. Barley β-glucan has not been evaluated for its ability to reduce glycemic parameters, and the potential synergism between RS and barley β-glucan has not been examined in men.

2. Methods and materials

2.1. Subjects and study design

The study was approved by the Institutional Review Board of The Johns Hopkins University Bloomberg School of Public Health. Medical supervision was provided by Dr Benjamin Caballero, Division of Human Nutrition, The Johns Hopkins University. A total of 20 men, 25 to 56 years of age, were selected for the study after clinical analysis of fasting blood and urine samples and a medical evaluation of their health history (Table 1). The protocol and purpose of the study were explained to the subjects both orally and in writing. Selection criteria included (1) weight stable for 6 months before the study, (2) normotensive, (3) normal fasting glucose, (4) no history of disease affecting carbohydrate metabolism, (5) taking no medication known to affect glucose or lipid metabolism, and (6) no current disease found by a routine urinalysis and blood screen. Half of the subjects had a body mass index (BMI) lower than 25; the other half had a BMI greater than 27. Control and overweight men were paired for age.

An equilibration diet containing 30% fat, 55% carbohydrate, and 15% protein was fed for 2 days before the day of sample collection to be sure all of the subjects were eating a moderately high carbohydrate diet before the acute meal tests. The menu was designed to exclude foods known to lead to colonic gas production. The menu was identical before each acute test. Body weight was used to determine the energy level given to the subjects, and subjects consumed the same amount of energy during all 10 periods.

Table 2
Carbohydrate composition (g) of the treatments as consumed

	Total carbohydrate[a]	Total fiber[a]	Available carbohydrate	β-glucan[b]	RS[c]
Glucose	75	0	0	0	0
Low β-glucan (spent malt barley)[d]					
Low RS	94.6	19.5	75.1	0.67	0
Mid RS	100.6	25.5	75.1	0.72	6.28
High RS	105.9	30.8	75.1	0.66	12.67
Medium β-glucan (whole barley flour)[d]					
Low RS	80.3	5.4	74.9	3.12	0
Mid RS	86.1	11.2	74.9	3.47	6.07
High RS	90.6	16.4	74.2	2.84	11.51
High β-glucan (whole barley flour plus barley β-glucan extract)[d]					
Low RS	81.8	6.8	75.0	5.32	0
Mid RS	87.3	12.3	75.0	5.27	5.85
High RS	92.2	17.2	75.0	5.26	11.13

[a] Total carbohydrates and fibers were determined by Covance Laboratories Inc.
[b] β-Glucan content of the flours and muffins was determined enzymatically using the American Association of Cereal Chemists method 32-23 [16,17].
[c] Analysis of the RS added to the muffins was provided by National Starch Co.
[d] Ingredient used to prepare muffins in addition to the spent malt barley, whole barley flour, barley β-glucan extract and resistant starch listed previously: wheat flour, baking powder, baking soda, skim milk, corn oil, egg white, and artificial sweetener.

Subjects were weighed before breakfast in the Human Studies Facility 2 days before each acute test. After breakfast, subjects were given prepacked lunch and dinner. They were required to consume all foods and beverages given to them and nothing else unless approved by the principal investigators. Subjects were to record all additional items such as water, noncaloric beverages, salt, and pepper. Blood was collected after a 10-hour fast. Each treatment, glucose solution or test muffins, contained 75 g available carbohydrate (total carbohydrate minus fiber and RS). Three types of muffin varying in β-glucan content were made with either (1) spent malt barley, (2) standard barley flour, or (3) a standard barley flour plus added barley β-glucan extract. Each type of muffin was made with no added RS (Novelose 260, National Starch and Chemical, Bridgewater, NJ) or Novelose calculated to provide 6 or 12 g of RS per 75-g available carbohydrate for a total of 9 muffin preparations. Carbohydrate content of the muffins as eaten is listed in Table 2. All 10 treatments (glucose alone and 9 muffin types) were consumed by all subjects, and the order of consumption was randomized in a Latin square design. The spent malt barley was provided by DeGroeu's Micro-brewery, Baltimore, Md. Barley flour was provided by National Barley Foods Council (Spokane, Wash), and the barley extract was provided by Vau Drunen Farms (Momence, Ill).

2.2. Sample collection and laboratory analyses

Blood samples were collected before treatment and at 0.5, 1, 2, 3, and 4 hours after the treatment was consumed. Glucose was determined on an automated spectrophotometric system (Dade Bering Instruments). Insulin (Diagnostics Products Corporation, Los Angeles, Calif) was determined by radioimmunoassay. Two-hour response arcas under the curve (AUCs) were calculated by using the method of Gannon and Nutall [10]. Analyses of the flours' nutrient compositions (total carbohydrate, total and soluble fiber) were determined by Covance Laboratories Inc (Madison, Wis). The β-glucan content of the flours and muffins was determined enzymatically by AACC method 32-23 [16,17]. Analysis of the RS added to the muffins was provided by National Starch Co.

2.3. Data calculations and statistical analyses

Insulin resistance was calculated using the homeostasis model assessment (HOMA = $\text{insulin}^{\text{uU/mL}} \times \text{glucose}^{\text{mmol/L}}/22.5$) [18]. In addition, a method using fasting insulin (I) and triacylglycerol concentrations and an index of glucose disposal rates (M) corrected for fat-free mass (ffm) based ($\text{Mffm} = \text{EXP}[2.63\text{-}0.28 \times (\log \text{insulin}^{\text{nmol/L}}) - 0.31 \times (\log \text{triacylglycerol}^{\text{mmol/L}})]$) [19] was also used to determine insulin resistance. Data were analyzed statistically with a mixed-models procedure for repeated-measures analysis of variance (ANOVA; PCSAS, version 8.0, SAS Institute, Cary, NC). Data were evaluated for the main effects of treatment (glucose or level of RS and β-glucan), group (control vs overweight men), time, and interactions among the main effects. Insulin data were log-transformed before statistical analysis because of nonhomogeneity of variance. Data reported are least-squares means and SEM.

3. Results

Plasma glucose responses were significantly different between the groups (control vs overweight; $P = .003$), but no group-by-treatment interaction ($P < .455$) was observed. Significant differences were observed at specific times in plasma glucose concentrations after the 10 loads were consumed (time, $P < .001$; treatment-by-time interaction, $P < .001$) (Table 3). Overweight men maintained plasma glucose above fasting concentrations longer than did the control men (group-by-timc interaction, $P < .001$). Overweight subjects had significantly higher mean glucose concentrations compared with control concentrations at 0.5, 1, 2, and 3 hours. Both groups' glucose concentrations

Table 3
Glucose responses (mmol/L) after glucose and 9 muffins containing 3 levels of RS and 3 levels of β-glucan consumed in a Latin square[1]

Treatment	Fasting	30 min	60 min	120 min	180 min	240 min
Glucose	5.21 ± 0.20	8.36 ± 0.20^{a}	7.55 ± 0.20^{a}	4.67 ± 0.20^{c}	4.20 ± 0.20^{d}	4.73 ± 0.20^{ad}
Low β-glucan						
Low RS	5.29 ± 0.20	7.71 ± 0.20^{b}	6.98 ± 0.20^{ab}	5.29 ± 0.20^{bd}	4.65 ± 0.21^{a}	4.74 ± 0.20^{ad}
Mid RS	5.16 ± 0.20	7.51 ± 0.20^{b}	6.94 ± 0.20^{ab}	5.19 ± 0.20^{bd}	4.87 ± 0.20^{abe}	4.88 ± 0.20^{abd}
High RS	5.26 ± 0.20	7.31 ± 0.20^{bc}	6.80 ± 0.20^{b}	4.95 ± 0.20^{bc}	4.67 ± 0.20^{a}	4.90 ± 0.20^{abc}
Medium β-glucan						
Low RS	5.19 ± 0.20	7.38 ± 0.20^{bd}	7.54 ± 0.20^{a}	5.88 ± 0.20^{a}	4.89 ± 0.20^{abc}	4.78 ± 0.20^{ad}
Mid RS	5.22 ± 0.21	7.31 ± 0.21^{bd}	7.30 ± 0.21^{ab}	5.45 ± 0.21^{ab}	4.83 ± 0.21^{abce}	4.87 ± 0.21^{abd}
High RS	5.13 ± 0.19	7.29 ± 0.19^{bd}	6.80 ± 0.20^{b}	5.43 ± 0.19^{ab}	4.63 ± 0.19^{a}	4.67 ± 0.19^{d}
High β-glucan						
Low RS	5.14 ± 0.20	6.85 ± 0.20^{e}	6.83 ± 0.20^{b}	5.21 ± 0.20^{bd}	5.11 ± 0.20^{bc}	5.06 ± 0.20^{bc}
Mid RS	5.22 ± 0.20	7.04 ± 0.20^{d}	6.67 ± 0.20^{b}	5.62 ± 0.20^{ad}	5.20 ± 0.20^{ce}	5.07 ± 0.20^{c}
High RS	5.24 ± 0.22	7.20 ± 0.21^{bd}	6.81 ± 0.21^{b}	5.37 ± 0.21^{ab}	5.26 ± 0.21^{c}	5.12 ± 0.21^{c}
ANOVA within a collection time	$P = .712$	$P < .001$	$P < .049$	$P = .002$	$P < .001$	$P = .001$

[1] Mean SEM of 10 normal and 10 overweight men. Overall ANOVA: treatment, $P = .179$; time, $P < .0001$; treatment-by-time, $P < .0001$. Means with different superscripts within a column (a-c) are significantly different ($P < .05$). Low, medium and high β-glucan averaged 0.1, 3.1, or 5.8 g/tolerance, respectively. Low, mid, and high RS averaged 0.1, 6.1, or 11.6 g/tolerance, respectively.

Table 4
Insulin responses (pmol/L) after glucose and 9 muffins containing 3 levels of RS and 3 levels of β-glucan consumed in a Latin square[1]

Treatment	Fasting	30 min	60 min	120 min	180 min	240 min
Glucose	80 ± 8[†]	495 ± 32[a]	506 ± 65[a]	169 ± 33[c]	79 ± 19[b]	53 ± 28[c]
Low β-glucan						
Low RS	70 ± 8	434 ± 46[ab]	477 ± 65[a]	242 ± 33[abd]	124 ± 19[ac]	59 ± 28[ac]
Mid RS	68 ± 8	411 ± 46[ab]	464 ± 65[a]	275 ± 33[ad]	137 ± 19[ac]	115 ± 28[b]
High RS	76 ± 8	383 ± 46[b]	475 ± 65[a]	295 ± 33[ab]	130 ± 19[ac]	78 ± 28[ac]
Medium β-glucan						
Low RS	78 ± 8	333 ± 46[bc]	455 ± 65[a]	294 ± 33[ab]	135 ± 19[ac]	95 ± 28[ab]
Mid RS	68 ± 8	344 ± 46[bc]	462 ± 65[a]	238 ± 33[abd]	167 ± 19[a]	80 ± 28[abc]
High RS	65 ± 8	424 ± 46[ab]	422 ± 65[a]	245 ± 33[b]	107 ± 19[c]	75 ± 28[ac]
High β-glucan						
Low RS	59 ± 8	263 ± 46[c]	360 ± 65[b]	181 ± 33[bd]	121 ± 19[abc]	79 ± 28[ac]
Mid RS	80 ± 8	255 ± 46[c]	338 ± 65[b]	224 ± 33[ab]	142 ± 19[ac]	101 ± 28[ab]
High RS	75 ± 8	289 ± 46[c]	345 ± 65[b]	207 ± 33[bd]	132 ± 19[ac]	87 ± 28[ab]
ANOVA within a collection time	$P = .794$	$P < .001$	$P < .001$	$P < .020$	$P = .079$	$P = .035$

[1] Mean SEM of 10 normal and 10 overweight men. Overall ANOVA: treatment, $P < .001$; time, $P < .0001$; treatment-by-time, $P < .0001$. †Means with different superscripts within a column (a-c) are significantly different based on log transformed evaluation ($P < .05$). Low, medium, and high β-glucan averaged 0.1, 3.1, or 5.8 g/tolerance, respectively. Low, mid, and high RS averaged 0.1, 6.1, or 11.6 g/tolerance, respectively.

at 0.5 and 1 hour were significantly higher than at all other collection times. Plasma glucose concentrations at 0.5 hour after the glucose treatment were significantly higher and at 2 and 3 hours were significantly lower than concentrations observed after all muffin treatments. The lowest glucose concentrations at 1 hour after the loads were observed after the high β-glucan or high RS treatments.

Insulin responses were significantly affected by group ($P < .001$), treatment ($P < .001$), time ($P < .0001$), group-by-treatment interaction ($P < .04$), group-by-time interaction ($P < .001$), and treatment-by-time interaction ($P < .001$). Overweight men had higher plasma insulin concentrations and maintained them above fasting longer than did the control men. Overweight subjects had significantly higher mean concentrations compared with control concentrations at 0.5, 1, 2, and 3 hours. Overweight subjects had significantly lower mean insulin following the high β-glucan compared with other treatments, whereas the insulin reduction observed in controls did not reach significance. Plasma insulin concentrations were significantly higher at 0.5 and 1 hour than at other times, the response after glucose resulting in the highest concentrations (Table 4). Insulin concentrations at 0.5 and 1 hour after all the high β-glucan loads were significantly lower than concentrations after the other treatments. Plasma insulin concentrations 2, 3, and 4 hours after the muffin treatments were higher than after the glucose load, but a distinct pattern between the different tolerances was not observed.

Differences in the β-glucan and RS content of the loads resulted in a significant difference in glucose AUC (treatment, $P < .004$) and insulin AUC (treatment $P < .0001$) (Fig. 1). Both glucose and insulin AUCs were lowest after the treatments containing the highest β-glucan (high β-glucan/low RS, high β-glucan/mid RS, and high β-glucan/high RS). The insulin AUCs after muffins containing the midrange of β-glucan were lower than after the low β-glucan muffins, but the differences were not significant. The insulin AUCs of overweight men were higher than that of the control men ($P < .0001$). However, no tolerance-by-group interaction was observed for either glucose ($P < .75$) or insulin ($P < .35$). No differences in AUC were observed with varying RS content.

Overweight men had significantly higher mean triacylglcyerol concentrations compared with the control subjects (166.6 vs 74.2 mmol/L, respectively; $P < .006$). Although there were significant differences in treatment ($P < .027$), group-by-treatment ($P < .001$), and group-by-time ($P < .001$), no pattern due to the β-glucan or RS content of the different tolerances was observed. No differences in free fatty acids were observed by group treatment or time.

Insulin resistance calculations resulted in a significant difference between groups with the MFFM method (overweight, 7.6 ± 0.22; control, 9.1 ± 0.22; $P < .0001$) or with HOMA (overweight, 3.0 ± 0.28; control, 1.7 ± 0.28; $P < .002$). When the fasting insulin values were evaluated based on fasting insulin above or below 87.5 mmol/L [19], 8 of the overweight subjects and 1 control subject were responsible for almost all of the higher values. The HOMA calculations based on grouped fasting insulin rather than weight or BMI resulted in a distinct separation ($P < .0001$) in insulin resistance; the lower average fasting insulin (62.4 mmol/L) had a value of 1.6, whereas the higher average insulin (125.4 mmol/L) had a value of 4.2.

4. Discussion

Glucose and insulin responses have been reported to be improved (lowered or flattened) after a test meal containing a soluble gum, including pectin, Oatrim, guar gum, gum tragacanth, and methyl cellulose fibers, as compared with the meal without the gum fiber [7-9] or insoluble fibers, such as wheat [20]. The addition of soluble fiber from oats [21-24] or guar gum [13] to the diet of adults with type 2 diabetes was beneficial in lowering insulin requirements and/or significantly lower blood glucose concentrations or

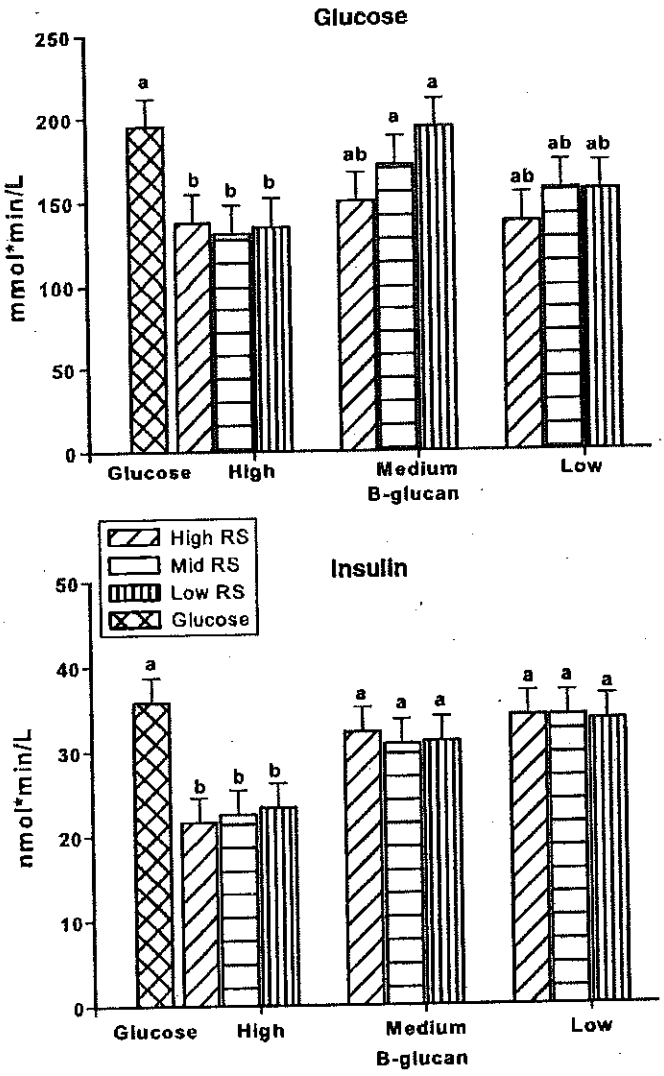

Fig. 1. Areas under the curve for glucose and insulin by treatment after glucose and 9 muffins containing 3 levels of RS and 3 levels of β-glucan consumed in a Latin square. Least-square means ± SEM. Area under the curve based on 0- to 120-minute plasma glucose or insulin concentrations. Bars with different superscripts are significantly different ($P < .05$). Glucose ANOVA: group, $P = .13$; treatment, $P < .004$; group-by-treatment, $P = .75$. Insulin ANOVA: group, $P = .0001$; treatment, $P < .0001$; group-by-treatment, $P = .35$.

postprandial AUCs. In few studies, oat-containing foods have been fed, and glucose and insulin concentrations have not been significantly lowered in normal and hypercholesterolemic subjects [25,26].

Barley has been used in fewer studies as a source of soluble fiber. Lower glucose and insulin responses have been reported after acute consumption of barley pearls, bread, and pasta in normoglycemic [27-29] and type 2 diabetic subjects [30]. The insulin requirement was reduced for some type 2 diabetic subjects when barley was consumed [30]. The amount of soluble fiber consumed in the barley meal affects the postprandial responses. Porridge made with high-fiber barley, but not common barley, significantly lowered glucose and insulin responses compared with white bread [25]. In a study similar to the one presented here but with women [31], glucose and insulin AUC decreased as the β-glucan content increased; the highest β-glucan content resulted in significant decreases compared with the low-β-glucan–low RS muffins.

Tappy et al [21] reported a linear inverse relation between the β-glucan content and the glucose plasma peak and AUC after consumption of 4.0, 6.0, or 8.4 g oat β-glucan. Insulin response did not appear to be dose-dependent. However, Wood et al [32] reported significant reductions in postprandial glucose and also in insulin responses that were inversely linear with the amount (1.8-7.2 g) consumed and with the logarithm of the viscosity of the meals. Delayed or reduced carbohydrate absorption from the gut and not the effects of fermentation was suggested as the mechanism of action of β-glucan in postprandial glucose metabolism [33].

Reductions in postprandial glucose and insulin responses after foods containing 5.8 to 18.4 g of RS have been reported in control, overweight, hyperinsulinemic, and type 2 diabetic subjects [15,34-40]. Behall et al [37] reported a significant reduction of postprandial glucose and insulin concentrations after the consumption of breads containing more than 8 g of RS from high amylose cornstarch. Granfeldt et al [35] reported significantly lower glucose and insulin response curves and AUCs after products containing 12.2 or 18.9 g of RS compared with responses after the standard corn product (2.0 g RS); responses after the 2 high-RS products (different in total and available carbohydrate) were not significantly different. No effect on postprandial glucose, insulin, free fatty acid, or triacylglycerol concentrations occurred after meals containing 0%, 2.7%, 5.4%, or 10.7% of the carbohydrate as RS from high amylose maize [41]. Yamada et al [42] reported significantly smaller postprandial increases in both blood glucose and insulin when subjects with borderline high-fasting glucose (111 mg/dL) consumed bread containing 6 g of RS from tapioca. The postprandial responses of the normal group after the 2 breads were not different [42]. None of the subjects reported here had fasting glucose greater than 111 mg/dL during the study. This may have contributed to the lack of response after the different levels of RS in the men.

In a previous study [31], 20 women (10 control, 10 overweight) consumed muffins containing varying amounts of oat β-glucan (assayed to contain 0.7, 3.2, or 8.1 g per average tolerance) and high amylose cornstarch (assayed to contain 0.8, 3.8, or 8.8 g of RS per average tolerance) alone and combined similar to the study reported here. Compared to the muffins containing the lowest amounts of β-glucan and RS, glucose and insulin AUC decreased when β-glucan (17.3% and 40.9%, respectively) or RS (20.2% and 25.4%, respectively) content increased. Unlike the men reported here, the reduction in glycemic response in the women was enhanced by combining RS and soluble fiber, although they consumed less RS. The greatest AUC reduction occurred after meals containing both high β-glucan and high RS (28% and 49% lower AUC for glucose and insulin, respectively). Men had the lowest glucose and insulin AUCs after the muffins

containing the high β-glucan regardless of RS content. Controlling the amount of RS in a product is more difficult when high amylose cornstarch or cornmeal is used than with commercially available preparations using preformed RS. The differences between the men and women may have been due in part to the source of the RS. Evaluation of the 2 RS sources in the same subjects would be needed to determine if more preformed RS is needed to match glycemic reduction observed with high amylose corn.

Consumption of 60 g preformed RS (Novelose 260) (rather than high amylose maize cornstarch) for 1 day before an RS/fiber-free tolerance test resulted in significantly lower postprandial plasma glucose and insulin compared with responses after prefeeding the menu without RS [43]. Calculated postprandial insulin sensitivity and C-peptide-to-insulin molar ratio was significantly increased following the high-RS diet. No RS effect was observed on plasma triacyglycerol. When a self-selected diet of subjects was supplemented with 30 g of RS (from High-Maize 260) per day, fasting plasma glucose and insulin, as well as glucose AUC after the diets with and without RS, were not different. Insulin AUC was significantly lower, and C-peptide/insulin AUC and total glucose uptake by the adipose tissue were significantly higher after the diet with added RS [44]. No reduction in postprandial glucose or insulin was observed after 30 g of acid denatured crystalline RS mixed with glucose compared with responses after glucose alone [45]. Prefeeding the RS in the diet appears to potentiate a greater postprandial glycemic reduction in a later meal. Improvement of insulin sensitivity occurred after a test breakfast containing at least 6.8 g of RS [36] and chronic RS consumption [43]. Estimates of daily intake of RS range from 3 to 6 g/d in Europe and Australia with similar but inconsistent data for the United States [46].

Similar to soluble fiber, a minimum intake of RS (approximately 5 g or more) appears to be needed, and chronic consumption appears to improve beneficial reductions in postprandial glucose and/or insulin response. Improvement in insulin sensitivity may require more than 7 g of RS or chronic consumption of this type of starch. Current intake estimates of American and European RS consumption are below this level. It appears that more RS than is currently consumed should be included in the diet for these health benefits. Individuals who would benefit the most are those who are overweight, have elevated glucose and insulin, or have reduced insulin sensitivity. Beneficial reductions in glucose and insulin can result when sufficient soluble fiber from isolates or grain sources such as oats or barley is consumed. Consumption of food sources containing adequate levels of β-glucan and RS should reduce the rise of type 2 diabetes.

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Consumption of Both Resistant Starch and β-Glucan Improves Postprandial Plasma Glucose and Insulin in Women

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OBJECTIVE — Consumption of a meal high in resistant starch or soluble fiber (β-glucan) decreases peak insulin and glucose concentrations and areas under the curve (AUCs). The objective was to determine whether the effects of soluble fiber and resistant starch on glycemic variables are additive.

RESEARCH DESIGN AND METHODS — Ten normal-weight (43.5 years of age, BMI 22.0 kg/m^2) and 10 overweight women (43.3 years of age, BMI 30.4 kg/m^2) consumed 10 tolerance meals in a Latin square design. Meals (1 g carbohydrate/kg body wt) were glucose alone or muffins made with different levels of soluble fiber (0.26, 0.68, or 2.3 g β-glucan/100 g muffin) and three levels of resistant starch (0.71, 2.57, or 5.06 g/100 g muffin).

RESULTS — Overweight subjects had plasma insulin concentrations higher than those of normal-weight subjects but maintained similar plasma glucose levels. Compared with low β-glucan–low resistant starch muffins, glucose and insulin AUC decreased when β-glucan (17 and 33%, respectively) or resistant starch (24 and 38%, respectively) content was increased. The greatest AUC reduction occurred after meals containing both high β-glucan–high resistant starch (33 and 59% lower AUC for glucose and insulin, respectively). Overweight women were somewhat more insulin resistant than control women.

CONCLUSIONS — Soluble fiber appears to have a greater effect on postprandial insulin response while glucose reduction is greater after resistant starch from high-amylose cornstarch. The reduction in glycemic response was enhanced by combining resistant starch and soluble fiber. Consumption of foods containing moderate amounts of these fibers may improve glucose metabolism in both normal and overweight women.

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A variety of fiber components, especially soluble fiber and resistant starch, have beneficial effects on glucose tolerance in people with normal as well as impaired glucose tolerance (1,2). These effects include reductions in blood glucose and insulin (1,3) and improvement of glycemic control in diabetes (2). Glucose and insulin responses improved (decreased) after test meals containing soluble fibers, including pectin, Oatrim (oat fiber extract), guar gum, gum tragacanth, and methyl cellulose fibers, when compared with meals without soluble fiber (1,4).

Increased amylose or resistant starch (high amylose versus amylopectin) decreased postprandial glucose and insulin responses in people with either normal glucose tolerance or impaired glucose tolerance (3,5–8). Different amounts of resistant starch or high-amylose starch consumed in the meals as well as different recipes and storage conditions make direct comparison of studies difficult (3,8).

Hyperinsulinemia, an indication of insulin resistance, is one indicator of the potential to develop type 2 diabetes (9,10). Abnormal carbohydrate metabolism, especially with respect to elevated glucose or insulin concentrations in the blood, occurs with increasing age and weight (10,11). Insulin resistance (abnormal glucose metabolism and/or hyperinsulinemia) increases as weight increases and is more prevalent in obese subjects (up to 46% in obese subjects compared with 4% in a control population) (12).

Objectives of this study include assessment of the effect of various levels of resistant starch (from high-amylose cornstarch) and soluble fiber (β-glucan from Oatrim) on the improvement of glycemic response and insulin sensitivity in normal-weight and overweight or obese adults and determination of whether an interaction between the two carbohydrate sources might retard or improve glycemic response. The hypothesis of the study is that the effects of β-glucan and resistant starch are additive.

RESEARCH DESIGN AND METHODS

— Twenty women were selected for the study after clinical analysis of fasting blood and urine samples and a medical evaluation of their health history. Subjects were selected based on the following criteria: 1) weight stable for 6 months before the study, 2) normotensive, 3) nondiabetic fasting glucose, 4) no history of disease affecting carbohydrate metabolism, 5) taking no medication known to affect glucose or lipid metabolism, and 6) no current disease found by a routine urinalysis and blood screen. Control subjects averaged 43.4 years old, 61.6 kg, with BMI 22.0 kg/m^2, 29.7% body fat, fasting glucose 4.92 mmol/l, and triglycerides 0.98 mmol/l. Overweight women were paired for age with control subjects and averaged 43.3 years old, 81.7 kg, with BMI 30.4 kg/m^2, 37.6% body fat, fasting glucose 5.01 mmol/l, and triglycerides 1.20 mmol/l. The design and purpose of the study were explained to the subjects both orally and in writing. The

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Abbreviations: AUC, area under the curve; HOMA, homeostasis model assessment.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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study was approved to include both men and women by the institutional review board of The Johns Hopkins University Bloomberg School of Public Health. Due to facility and staff limitations, women were studied first.

Subjects were given a standard equilibration diet containing 30% fat, 55% carbohydrate, and 15% protein for 2 days before and the day of sample collection. Body weight was used to determine energy intake for the controlled diet, and subjects consumed that same amount of energy during all 10 periods. The menu was identical before each tolerance. Subjects consumed their self-selected diets between tolerance meals.

Blood was collected after a 10 h fast. Subjects then consumed 1 g carbohydrate/kg body wt either as a glucose solution plus 100 g water or a test muffin containing an equal amount of total carbohydrate plus water equal to that in the glucose tolerance. Nine muffin types were made that contained either 1) standard cornstarch, 2) a 50/50 blend of standard and high-amylose cornstarches, or 3) high-amylose cornstarch providing 0.71, 2.57, or 5.06 g resistant starch/100 g muffin, respectively. Each of the three starches was combined with Oatrim (1, 2.5, or 10% β-glucan by weight) providing 0.26, 0.68, or 2.3 g β-glucan/100 g muffin, respectively. The 10 meal tests were performed in a Latin square design. The starches were provided by American Maize-Product Company (Hammond, IN). The Oatrims were provided by Quaker Oats (St. Louis, MO) and ConAgra (Omaha, NE). In addition to the starch and Oatrim, muffins contained baking powder, salt, gluten, egg, milk, oil, and sweetener.

Sample collection and analyses

Blood samples were collected before treatment and at 1, 2, 3, and 4 h after the meal was given. Glucose was determined on an automated spectrophotometric system (Baker Instruments, Allentown, PA). Insulin (Diagnostics Products, Los Angeles, CA) was determined by radioimmunoassay. Two-hour postprandial response areas under the curve (AUCs) were calculated using the trapezoid method.

The amount of resistant starch in the muffins was determined using AOAC (Association of Official Analytic Chemists) method 991.43 (13) with and without pretreatment with DMSO. Starch was calculated from the glucose content in enzyme hydrolysate as determined by high-performance anion exchange chromatography (13). The β-glucan content of the Oatrim was determined enzymatically by AACC (American Association of Cereal Chemists) method 32-23 (14).

Data calculations and statistical analyses

Power analysis for sample size has determined that a 10% difference in insulin response, a critical variable in testing the hypothesis, can be detected with $n = 8$ in each group with a significance level of $P < 0.05$. However, to ensure power to reach desired statistical outcomes and allow for voluntary withdrawal, we increased the number of subjects to 10 per group. When samples were analyzed after the study, one control and one overweight woman were found to have abnormal glucose concentrations. Analyses were rerun eliminating the data from these women. Insulin resistance was calculated using the homeostasis model assessment (HOMA = insulin$^{\mu U/ml}$ × glucose$^{mmol/l}$/22.5) (15) and a method using a published index of glucose disposal rates corrected for fat-free mass (FFM) based on fasting insulin and triglyceride concentrations {MFFM = EXP[2.63 − 0.28 × (log insulin$^{nmol/l}$) − 0.31 × (log triglyceride$^{nmol/l}$)]} (16). All fasting data were utilized for these analyses. Data were analyzed statistically with a mixed-models procedure for repeated-measures ANOVA (PCSAS, version 8.0; SAS Institute, Cary, NC). Data were evaluated for the main effects of treatment (glucose or level of amylose and β-glucan), group (control versus overweight women), time, and interactions among the main effects. Insulin data were log transformed before statistical analysis because of no homogeneity of variance. Data reported are least-squares means ± SE. When effects were statistically significant, mean comparisons were done with Sidak-adjusted P values so that the experiment-wise error was $P < 0.05$.

RESULTS — β-Glucan intake averaged 0.3, 0.9, and 3.7 g β-glucan for the low–, mid–, and high–β-glucan meals, respectively. Resistant starch intake averaged 0.9, 3.4, and 6.5 g for the low–, mid–, and high–resistant starch meals, respectively. Because overweight women consumed a higher amount of total carbohydrate, they consumed more β-glucan and resistant starch. Mean differences between the groups of control and overweight women were ~0.08, 0.2, and 1.0 g for the three levels of β-glucan, respectively and 0.2, 0.8, and 1.6 for the three levels of resistant starch, respectively. These differences in intake do not appear to have affected results, since there were minimal differences between the groups.

Significant differences were observed in plasma glucose concentrations (Table 1) after the 10 meals were consumed (time, $P < 0.001$; treatment-by-time interaction, $P < 0.009$). Since there was no statistically significant group ($P = 0.869$), group by treatment ($P = 0.089$), or group by time ($P = 0.746$), the two groups of women were combined. Plasma glucose concentrations of the combined weight groups after the glucose were higher at 2 h and lower at 3 h than after the test meals. Glucose concentration at 2 h after the high–β-glucan/high–resistant starch meal was significantly lower than after meals with low or medium β-glucan. Glucose concentrations at 1 h after the meals were lowest after the high–β-glucan/high– and mid–resistant starch meals.

Insulin responses (Table 2) were significantly affected by treatment ($P < 0.001$), time ($P < 0.0001$), and treatment-by-time interaction ($P < 0.04$). Mean fasting 3- and 4-h insulin concentrations were not significantly different among treatments. Insulin concentrations at 30 min and 2 h after the high–β-glucan /high–resistant starch meals were lowest. At 1 h after the meals, the high β-glucan with high or medium resistant starch significantly lowered insulin levels. There were significant differences by group ($P < 0.017$) and group-by-treatment interaction ($P < 0.006$) in plasma insulin responses. Overweight women had significantly higher mean insulin compared with control. Overweight women had the lowest insulin concentrations within a β-glucan level when the meal contained the highest amount of β-glucan. Mean insulin concentrations of control women were less affected by treatment.

Differences in the β-glucan and resistant starch content of the meals resulted in a significant difference in glucose area under the curve (AUC) by treatment ($P = 0.05$) (Fig. 1) but not by group ($P = 0.774$) or treatment by group ($P = 0.661$). Glucose AUCs were significantly reduced only after the meals with high or moderate resistant starch and high β-glucan. Compared with low–β-glucan/low–

Table 1—*Glucose responses (mmol/l) after glucose and nine meals containing three levels of resistant starch and three levels of β-glucan*

	Time					
Treatment	Fasting	30 min	1 h	2 h	3 h	4 h
Glucose	5.99	9.11*	7.54*†	6.05	5.06‡	5.30
Low β-glucan						
Low RS	6.11	8.92*†	7.75*†	6.39	5.88*†	5.60
Mid RS	5.90	8.08‡	7.37†	6.31	6.31*	5.44
High RS	6.03	8.04‡	7.32*†	5.79	5.93*†	5.53
Medium β-glucan						
Low RS	6.11	8.56*†‡	8.13*	6.30	5.58†‡	5.62
Mid RS	5.93	8.29†‡	7.15†	6.10	5.59†‡	5.66
High RS	6.13	8.10‡	7.46*†	6.18	5.99*†	5.87
High β-glucan						
Low RS	5.95	7.87‡§	7.28†	6.44	6.22*	5.91
Mid RS	6.11	7.75‡§	6.67‡	6.43	6.24*	5.82
High RS	5.65	7.33§	6.50‡	6.34	5.86*†	5.68
SE by time	±0.24	±0.40	±0.54	±0.32	±0.23	±0.17
ANOVA by time	$P = 0.83$	$P < 0.008$	$P < 0.028$	$P = 0.76$	$P < 0.003$	$P = 0.23$

Data are mean SE of 9 normal and 9 overweight women. Overall ANOVA: group, $P = 0.8690$; treatment, $P = 0.248$; group by treatment, $P < 0.089$; time, $P < 0.0001$; group by time $P = 0.746$; treatment by time, $P < 0.016$; group by treatment by time, $P = 0.999$. Means with different symbols within a column are significantly different ($P < 0.05$). Low, medium, and high β-glucan intake averaged 0.3, 0.9, and 3.7 g/meal, respectively. Low, mid, and high resistant starch averaged 0.9, 3.4, and 6.5 g/meal, respectively. RS, resistant starch.

resistant starch muffins, glucose AUC decreased when β-glucan (17%) or resistant starch (24%) content was increased. High β-glucan/high resistant starch reduced AUC by 33% compared with the low β-glucan/low resistant starch.

Insulin AUC was also significantly affected by treatment ($P = 0.0001$) but not by group ($P = 0.165$) or group by treatment ($P = 0.531$) (Fig. 1). The high–β-glucan/high–resistant starch meal resulted in the lowest insulin AUC. Compared with the low–β-glucan/low–resistant starch meal, insulin AUC decreased when β-glucan (33%) or resistant starch (38%) content was increased. High β-glucan/high resistant starch reduced AUC by 59% compared with the low–β-glucan/low– resistant starch meal.

Insulin resistance calculations resulted in a significant difference between groups with the MFFM method (overweight group 8.1 ± 0.14, control group 8.5 ± 0.15; $P < 0.05$) but not HOMA ($P = 0.11$). Values calculated by the MFFM method were above the value (6.3) suggested by McAuley et al. (16), indicating insulin resistance. HOMA calculations based on grouped fasting insulin rather than weight or BMI resulted in a

Table 2—*Insulin response (pmol/l) after glucose and nine meals containing three levels of resistant starch and three levels of β-glucan*

	Time						Group	
Treatment	Fasting	30 min	1 h	2 h	3 h	4 h	Control	Overweight
Glucose	72	318*†	314*	163†‡	106	68	168	178‡
Low β-glucan								
Low RS	63	401*	393*†	225*†	105	126	156*	282*
Mid RS	69	321*†	347*†	164†‡	91	109	159*	208†‡
High RS	82	352*†	292*†	129‡	94	73	171*	169‡§
Medium β-glucan								
Low RS	67	346*†	345*†	191*	120	101	160*	229†
Mid RS	77	340*†	303*†	176†‡	107	104	157*	212†‡
High RS	64	319*†	297*†	150‡	103	122	149*	202†‡
High β-glucan								
Low RS	96	322†‡	302*†	148†‡	105	108	130*	229†
Mid RS	77	328*†	258†	140‡	100	111	146*	192†‡
High RS	68	234‡	170‡	105§	97	125	122*	144§
SE by time	±8	±46	±65	±33	±19	±28	±25	±24
ANOVA	$P = 0.22$	$P < 0.048$	$P < 0.003$	$P < 0.012$	$P = 0.99$	$P = 0.73$		

Data are mean SE of 9 normal and 9 overweight women. Overall ANOVA: group, $P < 0.017$; treatment, $P < 0.01$; group by treatment $P < 0.001$; time, $P < 0.0001$; treatment by time, $P < 0.040$; group by time, $P = 0.274$; group by treatment by time, $P = 0.875$. Means with different symbols within a column are significantly different based on log-transformed evaluation ($P < 0.05$). Means within the group (control and overweight) columns with different symbols are significantly different. Low, medium, and high β-glucan intake averaged 0.3, 0.9, and 3.7 g/meal, respectively. Low, mid, and high resistant starch (RS) averaged 0.9, 3.4, and 6.5 g/meal, respectively. RS, resistant starch.

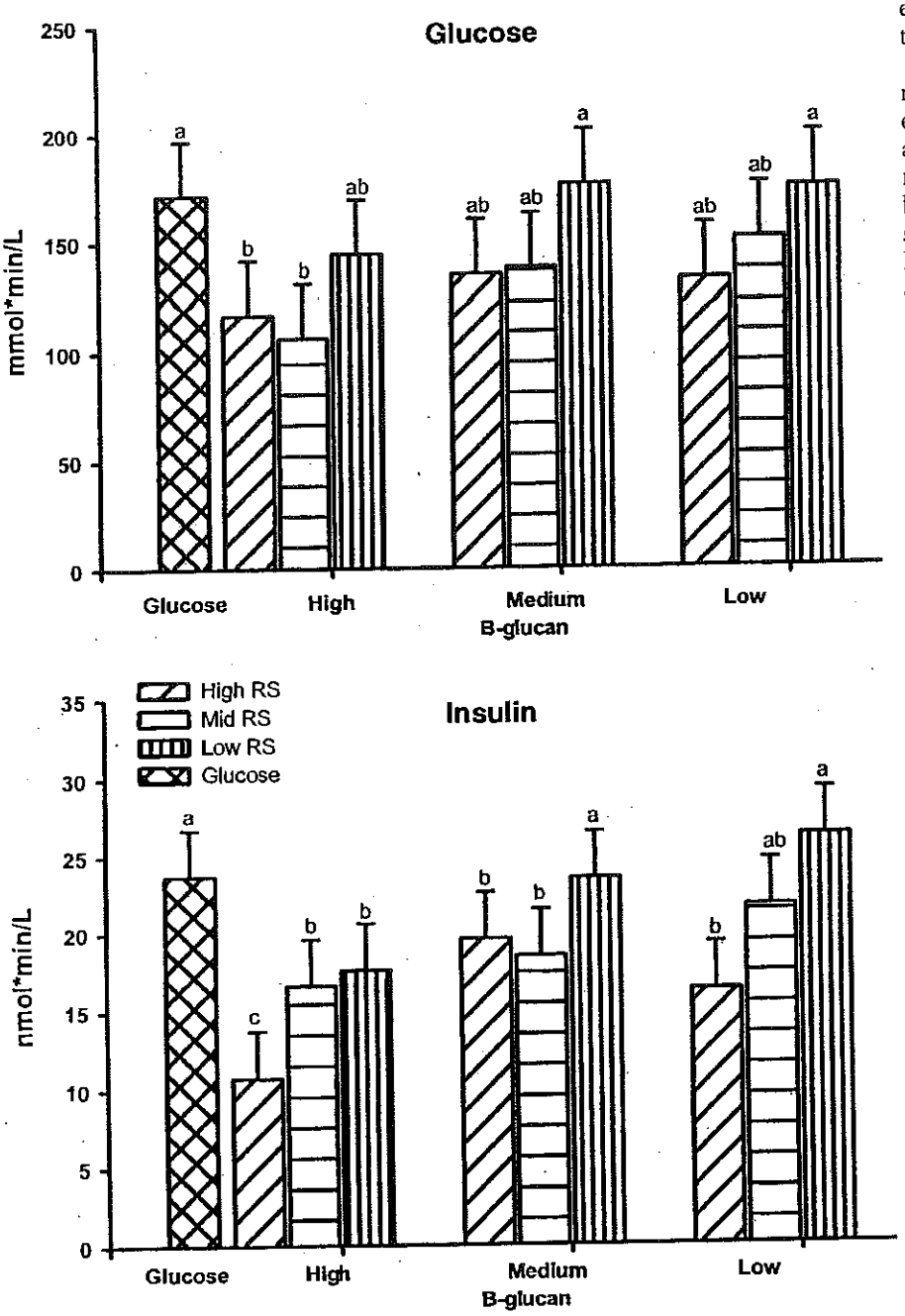

Figure 1—*AUCs for glucose and insulin by treatment after glucose and nine meals containing three levels of resistant starch and three levels of β-glucan. Data are least-square means ± SE. AUC based on 0- to 2-h plasma glucose or insulin concentrations. Bars with different superscripts are significantly different ($P < 0.05$). Glucose ANOVA: group, $P = 0.465$; treatment, $P < 0.038$; group by treatment, $P = 0.631$. Insulin ANOVA: group, $P = 0.165$; treatment, $P < 0.0003$; group by treatment, $P = 0.532$.*

distinct separation ($P < 0.0001$) in insulin resistance; the lower average fasting insulin (62.4 mmol/l) had a value of 2.3, whereas the higher average insulin (125.4 mmol/l) had a value of 4.9.

CONCLUSIONS — This study demonstrates that consumption of a moderate amount of either resistant starch or β-glucan can improve (lower) the glucose and insulin responses of both normal and overweight women. Results of this study can be used in the control of glucose responses in both normal and insulin-resistant subjects. The amount of β-glucan or resistant starch required to effect this improvement can be achieved through diet (Table 3).

Although a variety of fiber components, especially soluble fibers, have generally been reported to decrease glucose and insulin responses (1–4,6–8) in normoglycemic and diabetic subjects, none has compared both sources used in this study. Soluble fibers (found in oats, barley, and citrus fruits) are more effective in controlling glucose and insulin than predominantly insoluble fibers such as wheat (1,2). Glucose and insulin responses were significantly lower after barley pasta containing 12 g β-glucan (17) or barley bread (18) than after wheat pasta or bread, respectively. This level of soluble fiber is higher than that consumed in our study (averaging 3.7 g/meal). Numerous studies have reported inverse relationships between β-glucan and glucose and/or insulin responses after subjects consumed amounts comparable to those consumed in our study (19–21). Suggested mechanisms for these results include viscosity of the soluble fibers resulting in delayed or reduced carbohydrate absorption from the gut (22).

A few studies have not found glucose and insulin concentrations to be significantly lowered (1,18) with soluble fiber, but these studies used lower amounts than consumed by subjects in our study. Studies that reported little or no decrease in glucose or insulin response to the meal may have had soluble fiber contents near or below the threshold needed to reduce glycemic response. None of these studies combined β-glucan with resistant starch.

High-amylose starches are less digestible than standard starches in part because of the presence or development of resistant starch. Similar to soluble fibers, resistant starch is digested by colonic bacteria. Improvement in glycemic response after foods containing high-amylose starch or resistant starch has been reported in a few studies (5–8,23,24). Krezowski et al. (6) reported significantly lower postprandial glucose and insulin responses of subjects with type 2 diabetes after high-amylose muffins compared with concentrations after corn flakes or low-amylose muffins. Significantly lower insulin and AUC has been reported in normal, hyperinsulinemic, and overweight hypertriglyceridemic subjects after high-amylose than after low-amylose cornstarch muffins or bread averaging 5.8 vs. 1.3 g resistant starch (23), 13 vs. <1.0 g resistant starch (5), or 18.4 vs. 2.4 g resistant starch (24). Behall et al. (8) re-

Table 3—*Approximate fiber* and resistant starch† of some food sources as eaten*

	Amount	Total fiber (g)	Soluble fiber (g)	Resistant starch (g)
Cereals				
Oatmeal	2 c cooked	2	1	0.15
Barley	2 c cooked	4	1	2.25
Corn flakes	1 c	1	0	0.3
Wheat bran flakes	3/4 c	5.5	0.5	0.2
Grain Products				
Whole wheat bread	1 slice	2.5	0.5	0.1
English muffin	1 muffin	2	0.5	0.6
Spaghetti	1 c	2	0.5	0.3
White rice	1/2 c	0.5	0	0.6
Other starch sources				
Potato, baked	Medium	3	1	0.3
Potatoes, mashed	1/2 c	1.4	0.5	2.4
Legumes (beans)	2 c cooked	6–7	1–3	2–3.5
Lentils	2 c cooked	7	1	2.8
Fruit (1 medium fruit)				
Apple		4	1	0
Bananas (varies with ripeness)		3	1	4.9
Citrus fruits		2–3	2	0
Peaches		2	1	0
Plums		1.5	1	0

*Total fiber (26–28), *†soluble fiber (26–28), and †resistant starch (27–29).

ported a significant reduction of glucose and insulin responses after the consumption of breads containing 8–13.4 g resistant starch. Subjects consuming 12.2–18.9 g resistant starch also had significant reductions in glucose and insulin responses (7). Our highest level of resistant starch was ~8–10 g. Responses after two different levels of total and available carbohydrate were not significantly different (7). In the current study, the β-glucan combined with resistant starch, especially both high β-glucan and resistant starch, resulted in a greater reduction in glucose and insulin concentrations than might have been expected with only the resistant starch.

Similar to soluble fiber, a minimum intake of resistant starch (~5–6 g) appears to be needed in order for beneficial reductions in insulin response to be observed. Estimates of daily intake of resistant starch range from 3–6 g/day (averaging 4.1 g/day) in Europe and Australia with similar but inconsistent data for the U.S. (25). It appears that more resistant starch than currently is consumed should be included in the diet for the health benefits related to diabetes and cardiovascular disease. Consumption of at least one serving each of cooked barley flakes, lentils, English muffin, and a citrus fruit in a day would contain ~4.5 g soluble fiber and 5.65 g resistant starch (Table 3).

Our study found the overweight women to be somewhat more insulin resistant than the normal-weight women, as would be expected. Overweight subjects in this study had higher fasting insulin concentrations. Insulin resistance is associated with obesity, hypertension, dyslipidemia, glucose intolerance, and hyperinsulinemia (9,12). It has been estimated that occurrence of insulin resistance increases nearly 20% for each 5% increase in weight over the reported weight at age 20 years. Insulin resistance occurs in 4% of a nonobese population but up to 46% in obese subjects and may be the initiating step in the development of type 2 diabetes (12). McAuley et al. (16) reported that fasting insulin of >87.5 mmol/l (12.2 μU/dl) was as accurate at predicting insulin resistance in a normoglycemic population as was HOMA, insulin-to-glucose ratio, or the Bennett index.

Increased incidences of abnormal carbohydrate metabolism, especially with respect to elevated glucose or insulin concentrations in the blood, are reported with increasing age and weight. Our study used a simple food to provide a combination of levels of soluble fiber and resistant starch. The combination of resistant starch with β-glucan resulted in a greater decrease in glucose and insulin than the same amounts consumed individually and as great a decrease as that reported elsewhere with larger amounts of resistant starch or β-glucan consumed alone. Beneficial reductions in glucose and insulin can result if sufficient soluble fiber, resistant starch, or both are consumed. Consumption of foods containing moderate amounts of these fibers may improve glucose metabolism in both normal and overweight women.

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Petition to Add to the National List 205.606: "Barley Betafiber"

Appendix 9: Example of Label for Product Using Barley Betafiber

- Bolthouse Farms -- Heart Healthy Pear Merlot Juice Blend

MULTI-COLOR MCSD084
450ml BOLTHOUSE

4.0mm clear | Radius | Radius | Radius | 238mm Slit Width | Radius | .5mm Clear

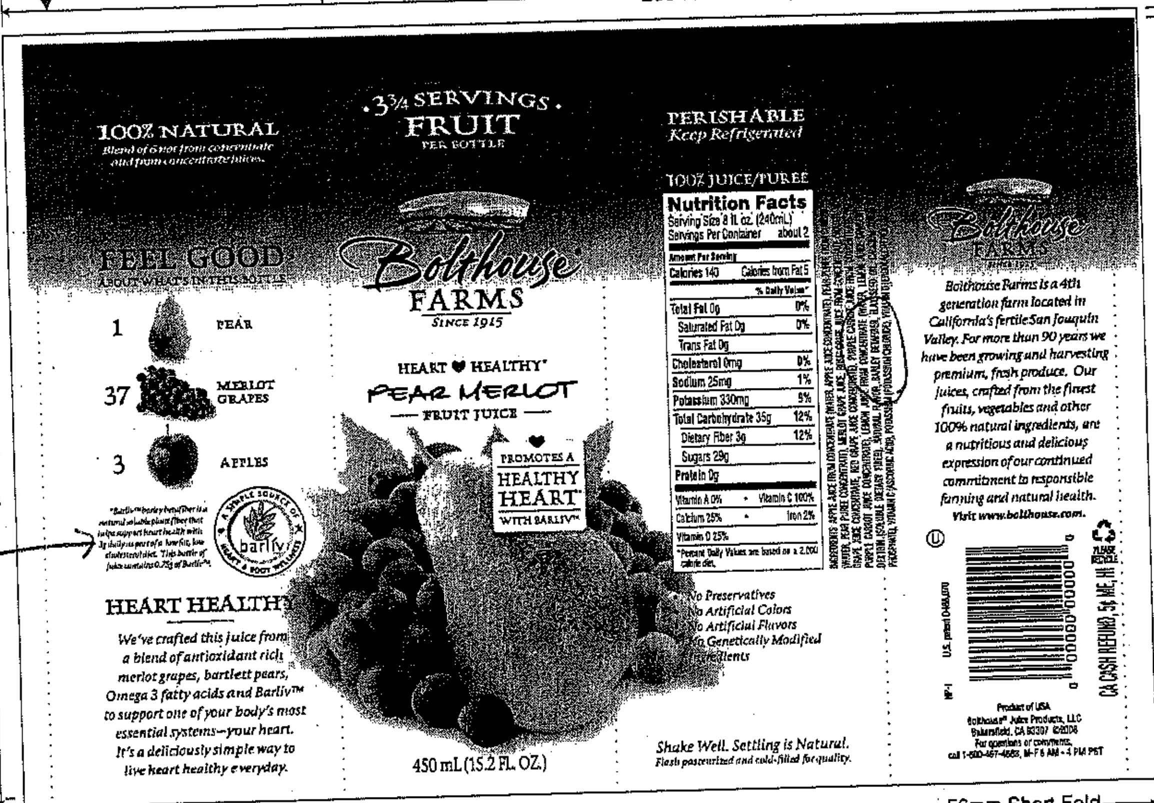
Barley beta fiber

2mm clear

shoulder

161mm Cut Length

health claim



2mm clear

6mm Copy-Free Zone. Graphics OK | 67mm Long Fold | 115mm Lay Flat | 56mm Short Fold | 6mm Copy-Free Zone. Graphics OK

UPC CODE: 0 71464- XXXXX X
UPC CODE PLACED AT 90%

HMS DESIGN

Bolthouse	12/12/08	BHF178	BHF178_PM450US_v3.ai	4 CH	0 71464- XXXXX X
Pear Merlot 450ml 1.5	Illustrator CS	AG	Gary	v1	HP-1

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DESIGNER X | PRODUCTION X | GRAPHICS DIRECTOR X | PROOFREADER X

Petition to Add to the National List 205.606: "Barley Betafiber"

Appendix 10: Additional Reference Articles and Information

- Conway, J.; Behall, K. 2005. Health Effects of Barley Consumption.
- USDA NHANES Nutrient Intakes from Food, 2005 – 2006.
- USDA Nutrient Intakes, 1994 - 96

Health Effects of Barley Consumption

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Agricultural Research Center, United States Department of Agriculture
Beltsville, MD 20705

Obesity has reached epidemic proportions within the American population, such that 65% of Americans are classified by the Centers for Disease Control (CDC) as overweight or obese (1). The diseases associated with this epidemic include: type 2 diabetes, cardiovascular disease (heart disease and stroke), osteoarthritis, high blood pressure, some cancers, sleep apnea and gall bladder disease. Furthermore scientists have shown that people with the Metabolic Syndrome, those with at least three of the following risk factors: a large waist, high blood pressure, high triglycerides and cholesterol, low HDL cholesterol, glucose and insulin irregularities, have increased risk for diabetes and cardiovascular disease (2).

By necessity resolution of this health crisis in America will require multi-faceted interventions on the national level that focus on the prevention of obesity, the development of effective long-term weight loss strategies, the reduction of risk factors for disease in those who are already overweight, and the prevention of regain of weight in those who have achieved a weight reduction. All of these goals require dietary changes as part of total lifestyle changes.

Benefits of consuming grains

Consumption of diets high in whole grains has been recommended in the 2005 Dietary Guidelines for Americans (3) and are reported to have a number of beneficial health effects including reduced risk of cancer (4), cardiovascular disease (5,6), and type 2 diabetes (7,8), which are leading causes of death in the USA. These results have been attributed to the effects of the soluble and insoluble fiber content of whole grain foods on risk factors for these diseases including blood glucose (9), insulin (10), and cholesterol (11,12). Other more general beneficial physiological effects of consumption of whole grains include reduced transit time which may reduce risk of colon cancer (13,14), and reduced rate of absorption of energy containing nutrients (15, 16) which may reduce glucose and insulin responses and risk of obesity (17). Numerous studies have demonstrated that whole grains that are high in soluble fibers, such as beta-glucan, found in oats and barley are more effective in lowering blood cholesterol than those in which fibers are predominantly insoluble such as wheat or rice (18-21). Health claims that consumption of oats or oat products effectively lower blood cholesterol concentrations have been approved by the Food and Drug Administration (22). This claim states that consumption of oats or oat products containing a total of at least 3 grams of beta-glucan per day is necessary to observe a health benefit.

Benefits of Barley Consumption – Studies at BHNRC

Because cardiovascular disease (1 in 4 people) and diabetes (1 in 18 people) are among the leading causes of morbidity and mortality in the USA, we have focused our research on the ability of soluble fiber from oats and more recently from barley on the

expression of the risk factors for these diseases. These factors include fasting plasma lipids, i.e., total cholesterol, triglycerides, the glucose and insulin response to a carbohydrate challenge, and blood pressure.

Plasma Lipids

Compared to oats, barley has been utilized as the beta-glucan source in few studies. Work conducted in this laboratory (23-28) indicates that consumption of a diet rich in barley results in as great or even greater reduction in plasma cholesterol and other blood lipids. Data from these studies are currently being used as support for an application to the FDA for a health claim for barley similar to that for oats.

The long-term studies were conducted in adults who consumed each of the 4 study diets in a random order. The meal plans consisted of 1) the American Heart Association Step 1 diet, 2) a control diet containing 30% fat, 15% protein and 55% carbohydrate with no added soluble fiber (beta-glucan), 3) a moderate beta-glucan diet of 3 grams per day, and 4) a high beta-glucan diet of 6 grams per day. The food used to vary the beta-glucan content of the diets included granola, muffins, spiced cake, cookies, steamed grains, and tabouleh salad. The experimental food products were made with either whole wheat flour or flakes, with a 50/50 mixture of barley and wheat flour or flakes, or barley flour or flakes. Plasma total cholesterol and triglycerides decreased significantly in men with moderate and high beta-glucan intakes from barley and total cholesterol and LDL cholesterol decreased in post-menopausal women (Figure 1).

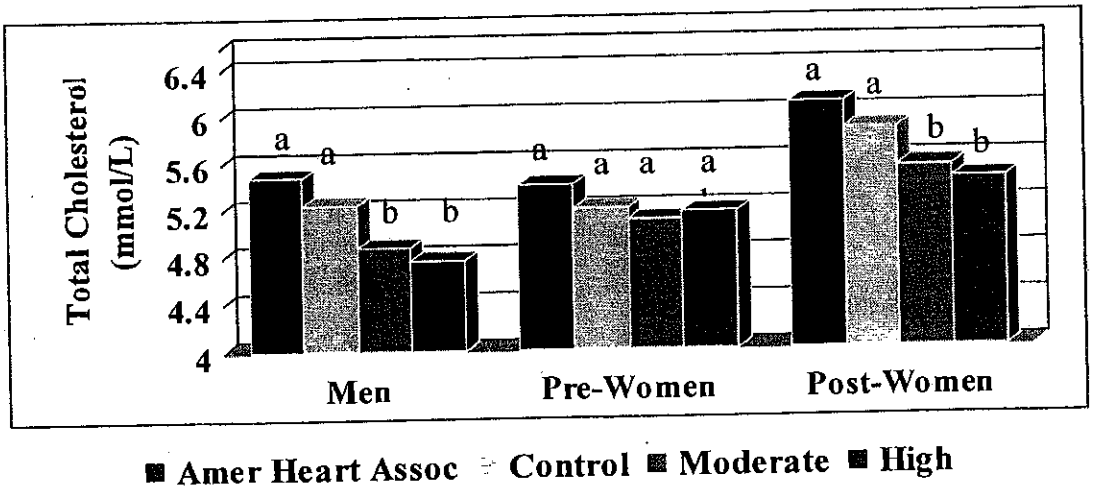


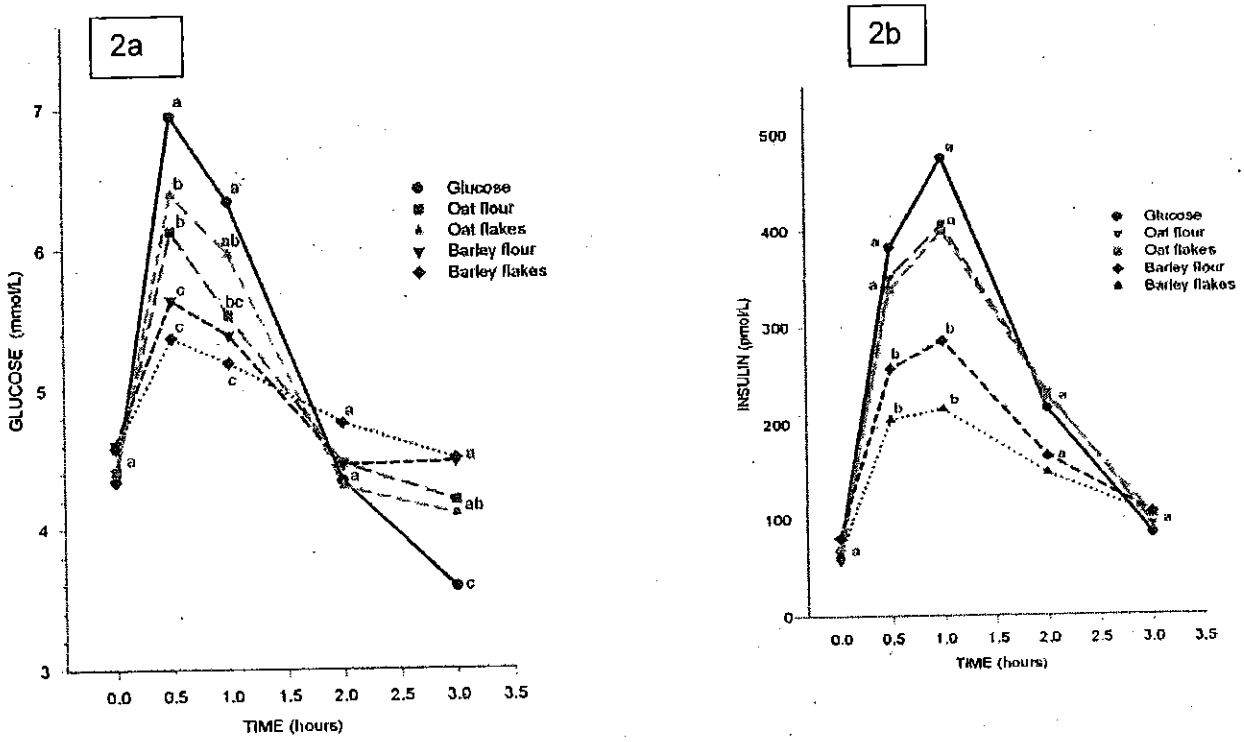
Figure 1. Total cholesterol response to the American Heart Association's Step 1 diet, to a control diet low in beta-glucan and diets containing moderate and high levels of beta-glucan from barley. Pre-women = pre-menopausal women; Post-women = post-menopausal women. For dietary comparisons, within gender groups, treatments with different letters are different.

In studies comparing the response of plasma cholesterol and triglycerides to diets rich in oats or barley, barley appeared to be more effective in lowering plasma cholesterol than oats, perhaps because of its higher beta-glucan content.

Plasma glucose and insulin

In acute studies where volunteers were fed carbohydrate containing meals the glucose responses to oats, barley, and extracts of both grains were significantly lower than responses to the glucose solution (23). Insulin responses for the barley extract were lowest and were significantly lower than after the glucose solution. Oat and barley extracts retain the beneficial effects of the grains from which they are extracted. Barley, which is high in the soluble fiber beta-glucan, is more effective than standard oats. Barley, as a whole grain or as an extract, can serve as a fat replacer in food products and can provide a useful addition to menus to control plasma glucose responses.

The effect of acute barley consumption on post-meal glucose and insulin values (Figures 2a and 2b) was similar to that of the other grains tested in that there was a blunted post-meal glucose and insulin response in comparison to the response after a glucose load (25).



Figures 2a and 2b. Comparison plots of glucose (2a) and insulin (2b) response to carbohydrate test meals containing glucose, oat flour and flakes and barley flour and flakes. Glucose or insulin values with different letters at each time point are different.

The analyses are ongoing from a long-term study of barley intake on glucose and insulin responses.

In a review of the effect of fiber-rich carbohydrates on features of the Metabolic Syndrome, Davy and Melby (29) report that consumption of 20-35 g/day of total dietary fiber and at least 3 g/day of soluble fiber, as recommended by the American Dietetic

Association, results in a reduction in risk factors for cardiovascular disease and diabetes.

Soluble Fiber Intakes

The typical American diet contains less than half the amount of soluble fiber or total dietary fiber recommended to provide health benefits. The median reported total dietary fiber intake for men and women in the U. S. was 17.0 and 13.8 g/d, respectively (30). This is approximately half the level of intake suggested by many health organizations (29) and the National Academy of Sciences, Institute of Medicine's Dietary Reference Intakes (30). The recommended intake for total fiber for adults 50 years and younger is set at 38 grams for men and 25 grams for women, while for men and women over 50 it is 30 and 21 grams per day, respectively, due to decreased food consumption. It is essential to determine ways to increase intake of total fiber and, especially, soluble fibers. Increasing the intake of whole grain products such as barley would increase both total and soluble dietary fiber in the diet and most likely would result in decreasing the risk factors for disease even in men and women already overweight.

Dietary Fiber, Satiety, and Body Weight Regulation

Few studies have been conducted on the short or long term effect of the soluble fiber beta-glucan on satiety or the feeling of fullness after a meal. Howarth et al. (32) conducted a pilot study of the effect on body weight of dietary fiber supplementation (to an *ad libitum* diet for 3 weeks) which compared a methylcellulose supplement with a pectin/beta-glucan (2:1 ratio) supplement. No significant effect on food intake, assessed by 24 h recalls, or on body weight was found.

In a position paper for The American Dietetic Association on the health implications of dietary fiber, Marlett et al, (33) provide support to the hypothesis that meals rich in fiber are processed more slowly thereby promoting satiety and potentially reduce overall energy intake. Pereira and Ludwig (34) reviewed the literature on dietary fiber and body-weight regulation and concluded that many short term and epidemiological studies support the role of dietary fiber in body-weight regulation. Further they suggested an increase in fiber intake as a means of preventing obesity in children. They also note that there is a need for further research and for long-term dietary intervention studies.

Acute satiety studies

A study (Figure 3) is currently underway to test the effect of cooked whole grain barley and a barley or oat extract containing beta-glucan on satiety. Twenty men and women who are at risk for the Metabolic Syndrome have been recruited to consume a "breakfast" test meal of 75 g of glucose or a food product, such as yogurt or whole grain cereal containing doses of soluble fiber, as beta-glucan, varying from 0 to 3 grams. Blood glucose and Visual Analogue Scales (VAS) are measured at -¼, 0, ¼, ½, 1, 2, 2½ hours to test hunger, satiety, desire to eat, nausea, drowsiness, etc. A standardized lunch offering of a casserole containing approximately 2000 kcal is fed at 2 hours after the breakfast test meal. Satiety is evaluated based on the VAS results and on the amount of energy consumed at lunch.

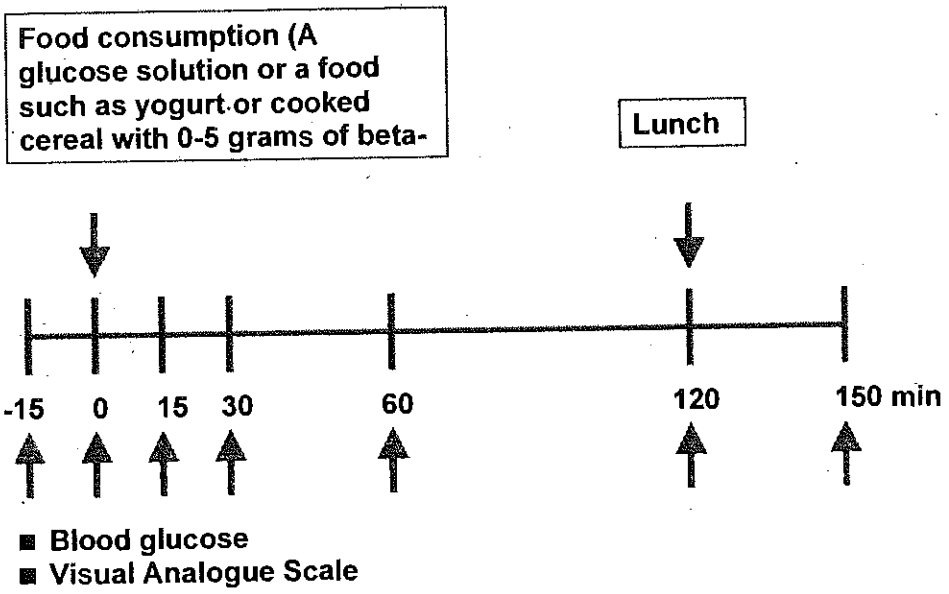


Figure 3. The time course of an acute satiety study underway at USDA, ARS, BHNRC, DHPL.

Planned Long-term Studies

Future studies will examine the effect of supplementation of the diet in people who have successfully lost weight with high soluble fiber food items. The metabolic measurements that are planned include resting metabolic rate, body weight, body fat, fasting plasma glucose, insulin, triglycerides and cholesterol, insulin sensitivity, blood pressure, body composition, measures of satiety, and behavioral measures. These studies will be long-term and will take place over a period of time of at least 6 months to one year.

Conclusion

Consumption of soluble fiber improves risk factors for cardiovascular diseases and diabetes mellitus. It also provides satiety value. Soluble fiber reduces plasma cholesterol concentrations, lowers postprandial plasma glucose and insulin concentrations and ameliorates insulin resistance. Most research on soluble fiber has focused on oats. Barley, another excellent soluble fiber source, has received little attention. Many forms of barley or barley extracts have not been investigated in human subjects. Thus, research is needed to assess the health effects of human consumption of barley and barley products including germinated barley foodstuff, barley co-products, and barley Nutrim. This paper describes research that uses controlled feeding of human subjects to determine the ability of barely and barley products to affect risk factors for cardiovascular disease and diabetes in normal weight and overweight adults. Moreover, the research will assess the ability of diets high in soluble fiber to aid in weight loss and maintenance of weight-reduced subjects. The proposed research will extend the number of barley products and extracts examined for health benefits.

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NHANES

Table 1. Nutrient Intakes from Food: Mean Amounts Consumed per Individual, One Day, 2005-2006

Gender and age (years)	N	Food energy (kcal)	Protein (g)	Carbo-hydrate (g)	Total sugars (g)	Dietary fiber (g)	Total fat (g)	Saturated fat (g)	Mono-unsaturated fat (g)	Poly-unsaturated fat (g)	Choles-terol (mg)
Males:											
2 - 5.....	442	1641	56.3	228	122	11.0	58.4	21.4	21.4	10.8	174
6 - 11.....	489	2092	70.9	280	142	14.1	79.4	28.3	29.1	15.4	223
12 - 19.....	1052	2707	99.1	352	177	15.2	100.9	35.6	37.5	19.1	320
20 - 29.....	388	2821	106.2	344	160	16.6	100.6	33.7	37.9	20.2	340
30 - 39.....	371	2978	118.0	342	153	18.9	114.1	38.7	42.5	22.9	406
40 - 49.....	382	2753	106.6	313	141	18.2	104.9	35.2	39.2	21.4	388
50 - 59.....	303	2597	97.4	307	143	18.3	102.3	33.3	38.1	22.2	350
60 - 69.....	320	2202	88.3	258	114	17.5	84.2	27.9	30.7	18.2	314
70 and over.....	399	1984	76.9	239	109	16.8	77.3	25.8	28.5	16.3	306
20 and over...	2163	2638	101.9	310	141	17.8	100.1	33.4	37.3	20.7	358
Females:											
2 - 5.....	460	1486	51.9	207	112	10.4	52.2	19.1	18.7	10.0	164
6 - 11.....	523	1879	63.4	251	124	12.0	71.6	25.4	26.4	14.0	237
12 - 19.....	1063	1906	64.2	253	124	12.3	72.3	24.6	26.2	15.5	189
20 - 29.....	582	1959	72.2	246	118	12.9	73.9	25.6	26.8	15.2	238
30 - 39.....	406	1923	75.4	231	104	14.6	74.5	24.4	27.6	16.2	238
40 - 49.....	390	1873	75.9	221	103	14.4	71.6	24.3	25.6	15.5	255
50 - 59.....	301	1718	70.3	205	90	14.9	67.6	22.7	24.5	14.6	245
60 - 69.....	315	1598	63.5	194	85	14.3	63.1	21.0	22.9	13.8	224
70 and over.....	363	1495	57.2	192	90	13.6	56.1	19.2	19.9	12.4	205
20 and over...	2357	1785	70.1	217	100	14.1 *	68.7	23.2	24.9	14.8	237
Males and females:											
2 and over...	8549	2157	81.8	265	124	15.1 *	81.9	27.8	30.1	17.0	278

DV (daily value) = 25g

NOTES: # indicates an estimate with a relative standard error greater than 30%.
* indicates a non-zero value too small to print.
[1]SFA = saturated fatty acid.
[2]MFA = monounsaturated fatty acid.
[3]PFA = polyunsaturated fatty acid.

DATA SOURCE: What We Eat in America, NHANES, 2005-2006, individuals 2 years and over (excluding breast-fed children), Day 1 dietary intake data, weighted.
CITATION: U.S. Department of Agriculture, Agricultural Research Service. 2008. Nutrient Intakes from Food: Mean Amounts Consumed per Individual, One Day, 2005-2006. Available: www.ars.usda.gov/ba/bhnrc/fsrg.

Table 1.--Nutrient Intakes: Mean amount consumed per individual, by sex and age, 1 day, 1994-96--continued USDA

Sex and age (years)	Total carbohydrate	Dietary fiber	Vitamin A	Carotenes	Vitamin E	Vitamin C	Thiamin
	Grams		Micrograms retinol equivalents		Milligrams alpha-tocopherol equivalents	Milligrams	
Males and females:							
Under 1	106.8	3.4	855	217	11.9	108	.90
1-2	175.9	8.8	717	263	4.6	99	1.11
3-5	215.6	10.7	789	274	5.4	96	1.34
5 and under	188.3	9.1	772	264	5.9	98	1.21
Males:							
6-11	276.3	13.6	950	291	6.9	101	1.76
12-19	366.1	17.4	1,086	411	9.3	119	2.13
20-29	344.9	18.3	994	432	10.0	120	2.04
30-39	322.3	19.4	1,069	529	10.9	107	2.01
40-49	294.7	18.3	1,134	546	9.5	105	1.89
50-59	273.1	18.5	1,194	590	9.7	110	1.80
60-69	252.5	18.5	1,281	666	9.4	105	1.76
70 and over	231.2	17.7	1,356	632	8.6	101	1.63
20 and over	298.8	18.6	1,133	544	9.9	109	1.90
Females:							
6-11	247.3	12.2	816	285	6.4	94	1.47
12-19	261.9	13.0	798	333	7.0	95	1.44
20-29	241.6	13.2	855	448	7.1	93	1.37
30-39	218.8	13.6	895	500	7.1	83	1.36
40-49	213.8	14.0	903	511	7.7	90	1.33
50-59	201.5	14.5	932	523	7.2	95	1.32
60-69	188.7	14.2	977	531	6.8	94	1.28
70 and over	183.5	14.2	1,099	567	6.4	95	1.24
20 and over	211.7	13.9	930	508	7.1	91	1.33
All individuals	255.4	15.1	982	463	8.0	100	1.59

DV = 74%

DV = 58%

Excludes breast-fed children.

DV = daily value = 25g

Continued

DATA TABLES:

Results from USDA's
1994-96 Continuing Survey of Food Intakes by Individuals
and
1994-96 Diet and Health Knowledge Survey

Table Set 10

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