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Whole grains and human health

Joanne Slavin

Department of Food Science and Nutrition, University of Minnesota, 1334 Eckles Avenue, St Paul, MN 55108, USA

Epidemiological studies find that whole-grain intake is protective against cancer, CVD, diabetes, and obesity. Despite recommendations to consume three servings of whole grains daily, usual intake in Western countries is only about one serving/d. Whole grains are rich in nutrients and phytochemicals with known health benefits. Whole grains have high concentrations of dietary fibre, resistant starch, and oligosaccharides. Whole grains are rich in antioxidants including trace minerals and phenolic compounds and these compounds have been linked to disease prevention. Other protective compounds in whole grains include phytate, phyto-oestrogens such as lignan, plant stanols and sterols, and vitamins and minerals. Published whole-grain feeding studies report improvements in biomarkers with whole-grain consumption, such as weight loss, blood-lipid improvement, and antioxidant protection. Although it is difficult to separate the protective properties of whole grains from dietary fibre and other components, the disease protection seen from whole grains in prospective epidemiological studies far exceeds the protection from isolated nutrients and phytochemicals in whole grains.

Whole grains: Cancer: Cardiovascular disease: Diabetes mellitus: Obesity

Historical background on whole grains

Whole grains became part of the human diet with the advent of agriculture about 10 000 years ago (Spiller, 2002). For the last 3000–4000 years, a majority of the world's population has relied upon whole grains as a main proportion of the diet. In North America, wheat, oats, barley, and rye were harvested as staple foods as early as the American Revolution. It is only within the past 100 years that a majority of the population has consumed refined grain products. Before this time, gristmills were used for grinding grains. They did not completely separate the bran and germ from the white endosperm and produced limited amounts of purified flour. In 1873, the roller mill was introduced and it more efficiently separated the bran and germ from the endosperm. Widespread use of the roller mill fuelled an increasing consumer demand for refined grain products and was a significant factor in the dramatic decline in whole-grain consumption observed from about 1870 to 1970 (Spiller, 2002).

Health aspects of whole grains have long been known. In the 4th century BC Hippocrates, the father of medicine, recognised the health benefits of wholegrain bread. More recently, physicians and scientists in the early 1800s to mid 1900s recommended whole grains to prevent constipation. The 'fibre hypothesis', published in the early 1970s, suggested that wholefoods, such as whole grains, fruits, and vegetables, provide fibre along with other constituents that have health benefits (Trowell, 1972).

What are whole grains?

The major cereal grains include wheat, rice, and maize, with oats, rye, barley, triticale, sorghum, and millet as minor grains. In the USA, the most commonly consumed grains are wheat, oats, rice, maize, and rye, with wheat constituting 66–75 % of the total. Buckwheat, wild rice, and amaranth are not botanically true grains but are typically associated with the grain family due to their similar composition. All grains have a bark-like, protective hull, beneath which are the endosperm, bran, and germ (Fig. 1). The germ contains the plant embryo. The endosperm supplies food for the growing seedling. Surrounding the germ and the endosperm is the outer covering or bran which protects the grain from its environment, including the weather, insects, moulds, and bacteria.

About 50–75 % of the endosperm is starch, and it is the major energy supply for the embryo during germination of the kernel. The endosperm also contains storage proteins, typically 8–18 %, along with cell-wall polymers. Relatively few vitamins, minerals, fibre, or phytochemicals are located in the endosperm fraction. The germ is a relatively minor contributor to the dry weight of most grains (typically

Abbreviations: DM, diabetes mellitus; GI, glycaemic index.

Corresponding author: Dr J. Slavin, fax +1 612 625 5272, email jslavin@umn.edu

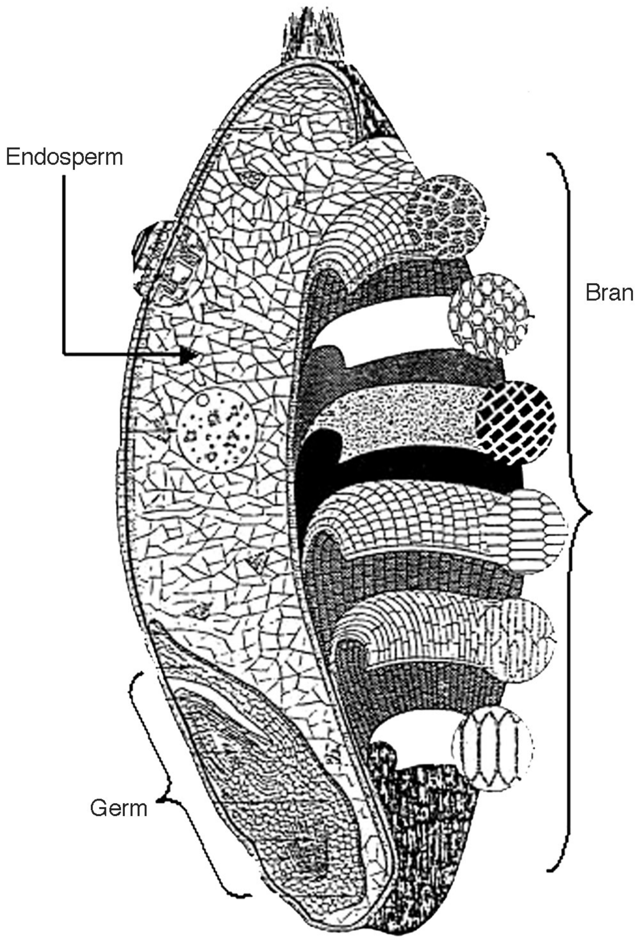

Fig. 1. Structure of a whole grain.

4–5 % in wheat and barley). The germ of maize contributes a much higher proportion to the total grain structure than that of wheat, barley, or oats.

In different parts of the world, various terms are used to describe whole grains, and these differences can complicate the understanding of whole grains. The European phrase 'wholemeal', describes a finely ground wholegrain flour or a wholegrain bread. In the USA, 'whole grain' describes breads, cereal products, and both finely and coarsely ground flour. In an effort to provide a more common understanding of whole grains, whole-grain definitions have been developed.

The American Association of Cereal Chemists has defined a whole-grain ingredient as '…the intact, ground, cracked or flaked caryopsis, whose principal anatomical components, the starchy endosperm, germ and bran, are present in substantially the same relative proportions as they exist in the intact caryopsis'. Thus, for whole-grain ingredients such as flour, the three major components (bran, germ, and endosperm) must be present in the same amounts that occur in the grain's native state. A whole-grain health claim has also been approved in the USA. For a wholegrain food to meet the whole-grain health-claim standards, the food must include 51 % wholegrain flour by weight of final product and must contain 1·7 g dietary fibre.

Who consumes whole grains?

Over the past 20 years, more than a dozen governmental, non-profit health, and industrial and trade groups have encouraged increased whole-grain consumption (Slavin *et al*. 2001*b*). Grain products comprise the base of the US Department of Agriculture's Food Guide Pyramid (United States Department of Agriculture, 1997), which suggests that several of the recommended six to eleven servings of grain products/d should be from whole grains. The 2000 Dietary Guidelines for Americans (United States Department of Agriculture, 2000) established a separate guideline for grains with a particular emphasis on eating more wholegrain foods. It is recommended that at least three servings, or one half of grain foods consumed daily, be whole grain.

Many consumers are unaware of the health benefits of whole grains or of the recommendations regarding increased intake. Also, there is much confusion about which products are truly whole grain. The bran portion of a whole grain may be highly coloured and contain stringent, intensely flavoured compounds that are not always appealing in taste. Other barriers to whole-grain consumption include price, softness, texture, and moisture content.

Americans consume far less than the recommended three servings of whole grains on a daily basis. According to a survey of Americans 20 years and older (Cleveland *et al*. 2000), total grain intake was 6·7 servings/d with only 1·0 of these servings being whole grain. Only 8 % of the study participants consumed the recommended three servings of whole grains on a daily basis. A more recent update of whole-grain intake reported that intake remains at about one serving/d (Kantor *et al*. 2002). A study of US children and teenagers reported that their consumption of whole grains was less than one serving/d (Harnack *et al*. 2003).

Consumers of whole grains were more likely to be male, older, white, more educated, non-smokers, exercisers, vitamin and/or mineral supplement users, not overweight and have a higher income (Cleveland *et al*. 2000). White males and females over the age of 60 years consumed more whole grains/d than any other age group, with males eating 1·3 servings/d and females eating 1·0 servings/d. Black adult males also consumed more servings/d (0·7) than did black females (0·6). Consumers of whole grains had a significantly better nutrient profile than non-consumers.

Whole-grain intake studies in other countries find similar results. Except for parts of Scandinavia where wholegrain breads are the norm, whole-grain consumption is low (Lang & Jebb, 2003). In the UK, the median consumption of whole grains was less than one serving/d (Lang & Jebb, 2003).

Components in whole grains

The bran and germ fractions derived from conventional milling provide a majority of the biologically active compounds found in a grain. Specific nutrients include high concentrations of B vitamins (thiamin, niacin, riboflavin, and pantothenic acid) and minerals (Ca, Mg, K, P, Na, and Fe), elevated levels of basic amino acids (for example, arginine and lysine), and elevated tocol levels in the lipids.

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Numerous phytochemicals, some common in many plant foods (phytates and phenolic compounds) and some unique to grain products (avenanthramides, avenalumic acid), are responsible for the high antioxidant activity of wholegrain foods (Miller *et al*. 2002).

In developed countries, such as the USA and Europe, grains are generally subjected to some type of processing, milling, heat extraction, cooking, parboiling, or other technique before consumption. Commercial cereals are usually extruded, puffed, flaked, or otherwise altered to make a desirable product. Most research finds that the processing of whole grains does not remove biologically important compounds (Slavin *et al*. 2001*a*). The analysis of processed breads and cereals indicates that they are a rich source of antioxidants (Miller *et al*. 2002). Processing may open up the food matrix, thereby allowing the release of tightly bound phytochemicals from the grain structure (Fulcher & Rooney Duke, 2002). Studies with rye find that many of the bioactive compounds are stable during food processing, and their levels may even be increased with suitable processing (Liukkonen *et al*. 2003).

Components in whole grains associated with improved health status include lignans, tocotrienols, phenolic compounds, and antinutrients including phytic acid, tannins and enzyme inhibitors. In the grain-refining process the bran is removed, resulting in the loss of dietary fibre, vitamins, minerals, lignans, phyto-oestrogens, phenolic compounds, and phytic acid. Thus refined grains are more concentrated in starch since most of the bran and some of the germ is removed in the refining process.

Mechanistic studies of whole grains

The wide range of protective components in whole grains and potential mechanisms for protection have been described (Slavin, 2003). To conduct feeding studies in human subjects, whole grains must be fed in a form acceptable to participants. Often feeding studies use processed whole grains for the dietary intervention. Additionally, epidemiological studies find protection with the consumption of processed wholegrain products, such as breads, cereals, and brown rice.

Large-bowel effects of whole grains

Whole grains are rich sources of fermentable carbohydrates including dietary fibre, resistant starch and oligosaccharides. Undigested carbohydrate that reaches the colon is fermented by the intestinal microflora to short-chain fatty acids and gases. Short-chain fatty acids include acetate, butyrate, and propionate, with butyrate being a preferred fuel for the colonic mucosa cells. Short-chain fatty acid production has been related to lowered serum cholesterol and a decreased risk of cancer. Undigested carbohydrates increase faecal wet and dry weight and speed intestinal transit.

Comparing the dietary fibre content of various whole grains, oats, rye and barley contain about one-third soluble fibre with the rest being insoluble fibre. Soluble fibre is associated with cholesterol lowering and an improved glucose response, while insoluble fibre is associated with improved laxation. Wheat is lower in soluble fibre than most grains while rice contains virtually no soluble fibre. The refining of grains removes proportionally more of the insoluble fibre than soluble fibre, although refined grains are low in total dietary fibre.

The disruption of cell walls can increase the fermentability of dietary fibre. Coarse wheat bran has a greater faecal bulking effect than finely ground wheat bran when fed at the same dosage (Wrick *et al*. 1983), suggesting that the particle size of the whole grain is an important factor in determining physiological effect. Coarse bran delays gastric emptying and accelerates small-bowel transit. The effect seen with coarse bran has been shown to be similar to the effect of inert plastic particles, suggesting that the coarse nature of whole grains as compared with refined grains has a unique physiological effect beyond composition differences between whole and refined grains (McIntyre *et al*. 1997).

Not all starch is digested and absorbed during gut transit. Factors that determine whether starch is resistant to digestion include the physical form of grains or seeds in which starch is located, particularly if these are whole or partially disrupted, size and type of starch granules, associations between starch and other dietary components, and cooking and food processing, especially cooking and cooling (Bjorck *et al*. 1994).

Besides dietary fibre and resistant starch, grains contain significant amounts of oligosaccharides. Oligosaccharides are defined as carbohydrates with a low (2–20) degree of polymerisation. Common oligosaccharides include oligofructose and inulin. Wheat flour contains from 1 to 4 % fructan on a dry-weight basis (Van Loo *et al*. 1995). Fructans have also been found in rye and barley with very young barley kernels containing 22 % fructan. Van Loo *et al*. (1995) have estimated that wheat provides 78 % of the North American intake of oligosaccharides. Oligosaccharides have similar effects as soluble dietary fibres in the human gut. Additionally, oligosaccharides have consistently been shown able to alter the human faecal flora. Human studies (Gibson *et al*. 1995) find that the consumption of fructo-oligosaccharides increases bifidobacteria in the gut while decreasing concentrations of *Escherichia coli*, clostridia and bacteroides. Although little research has been conducted directly on whole grains and bowel function, it is well known that dietary fibre from grains such as wheat and oats increases stool weight and speed transit (Marlett *et al*. 2002).

Glucose and insulin changes seen with whole-grain consumption

It is well accepted that glucose and insulin are linked to chronic diseases, especially diabetes mellitus (DM). Whole-grain consumption is part of a healthy diet described as the ‘prudent’ diet. Epidemiological studies consistently show that the risk for type 2 DM is decreased with the consumption of whole grains (Van Dam *et al*. 2002; Murtaugh *et al*. 2003). Whole grains are now recommended by the American Diabetes Association for DM prevention (Franz *et al*. 2002).

Giovannucci (1995) proposed that insulin and colon cancer are linked. He suggests that insulin is an important

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growth factor of colonic epithelial cells and is a mitogen of tumour cell growth *in vitro*. Epidemiological studies find a similarity of factors that produce elevated insulin levels with those related to colon cancer risk, including obesity and low physical activity. Schoen *et al*. (1999) found that incident colon cancer was linked to higher levels of blood glucose and insulin and larger body weight. Hu *et al*. (1999) noted the similarity of lifestyle and environmental risk factors for type 2 DM and colon cancer. They examined the relationship between DM and the risk of colorectal cancer in the Nurses' Health Study and found that they were significantly related, with women with DM having an increased risk of colorectal cancer.

To determine the relationship of whole-grain intake to glucose and insulin metabolism requires biomarkers. Glycaemic index (GI) is one marker used to compare the glycaemic response to foods. The GI is defined as the incremental area under the blood glucose response curve for the test food divided by the corresponding area after an equicarbohydrate portion of white bread, multiplied by 100. It is known that the glycaemic response is affected by many physiological factors. Other factors affecting the response include the form of the food, cooking, processing, fat content of the food, and soluble fibre content of the food.

Wholefoods are also known to slow digestion and the absorption of carbohydrates. Postprandial blood glucose and insulin responses are greatly affected by food structure. Any process that disrupts the physical or botanical structure of food ingredients will increase the plasma glucose and insulin responses. Food structure was found to be more important than gelatinisation or the presence of viscous dietary fibre in determining glycaemic response (Granfeldt *et al*. 1995). Another study found the importance of preserved structure in foods as an important determinant of glycaemic response in diabetics (Jarvi *et al*. 1995). The refining of grains tends to increase glycaemic response and thus whole grains should slow glycaemic response (Jenkins *et al*. 1986).

Intact whole grains of barley, rice, rye, oats, maize, buckwheat and wheat have GI of 36–81 with barley and oats having the lowest values (Jenkins *et al*. 1988). Lower blood glucose levels and decreased insulin secretion have been seen in both normal and diabetic subjects while consuming a low-GI (=67) diet containing pumpernickel bread with intact whole grains, bulgur (parboiled wheat), pasta and legumes compared with a high-GI (=90) diet containing white bread and potato.

Heaton *et al*. (1988) compared glucose responses when subjects consumed whole grains, cracked grains, wholegrain flour, and refined-grain flour. Plasma insulin responses increased stepwise, with whole grains less than cracked grains less than coarse flour less than fine flour. Oat-based meals evoked smaller glucose and insulin responses than wheat- or maize-based meals. Particle size influenced the digestion rate and consequent metabolic effects of wheat and maize, but not of oats. The authors suggest that the increased insulin response to finely ground flour may be relevant to the aetiology of diseases associated with hyperinsulinaemia and to the management of DM.

Some feeding studies have been conducted to evaluate the relationship between whole grains and glucose metabolism. Pereira *et al*. (2002) tested the hypothesis that wholegrain consumption improves insulin sensitivity in overweight and obese adults. Eleven overweight or obese hyperinsulinaemic adults aged 25–56 years consumed two diets, each for 6 weeks. The diets were identical, except that refined-grain products were replaced by whole products. At the end of each treatment, subjects consumed 355 ml of a liquid mixed meal, and blood samples were taken over 2 h. Fasting insulin was 10 % lower during the consumption of the whole-grain diet. The authors conclude that insulin sensitivity may be an important mechanism whereby wholegrain foods reduce the risk of type 2 DM and heart disease.

Juntunen *et al*. (2002) evaluated what factors in grain products affected human glucose and insulin responses. They fed the following grain products: whole-kernel rye bread, wholemeal rye bread containing oat ß-glucan concentrate, dark durum wheat pasta, and wheat bread made from white wheat flour. Glucose responses and the rate of gastric emptying after the consumption of the two rye breads and pasta did not differ from those after the consumption of white wheat bread. Insulin, glucose-dependent insulinotropic polypeptide, and glucagon-like peptide 1 were lower after the consumption of rye breads and pasta than after the consumption of white wheat bread. These results support that postprandial insulin responses to grain products are determined by the form of food and botanical structure rather than by the amount of fibre or the type of cereal in the food.

Other feeding studies have looked at different biomarkers relevant to CVD. Truswell (2002) concluded that enough evidence exists that wholegrain products may reduce the risk of CHD. Katz *et al*. (2001) measured the effect of oat and wheat cereals on endothelial responses in human subjects. They report that month-long, daily supplementation with either wholegrain oat or wheat cereal may prevent the postprandial impairment of vascular reactivity in response to a high-fat meal. In a randomised controlled clinical trial, the consumption of wholegrain and legume powder reduced insulin demand, lipid peroxidation, and plasma homocysteine concentrations in patients with coronary artery disease (Jang *et al*. 2001). Finally, the consumption of wholegrain oat cereal was associated with improved blood pressure control and reduced the need for antihypertensive medications (Pins *et al*. 2002). Thus, clinical studies to date support that whole-grain consumption can improve biomarkers relevant to DM and CVD.

Antioxidant theory for whole-grain protectiveness

The primary protective function of antioxidants in the body is their reaction with free radicals. Free radical attack on DNA, lipids and protein is thought to be an initiating factor for several chronic diseases (Miller, 2001). Cellular membrane damage from free radical attack and peroxidation is thought to be a primary causative factor. Cellular damage causes a shift in the net charge of the cell, changing osmotic pressure, leading to swelling and eventual cell death. Free radicals also contribute to general inflammatory response and tissue damage. Antioxidants also protect DNA from oxidative damage and mutation, leading to cancer. Free radical compounds result from normal metabolic activity as well as from the diet and environment. The body has defence mechanisms to prevent free radical damage and to repair damage, but when the defence is not sufficient, disease may develop. It follows that if dietary antioxidants reduce free radical activity in the body, then disease potential is reduced.

Wholegrain products are relatively high in antioxidant activity. Antioxidants found in wholegrain foods are water-soluble, fat-soluble and approximately one half are insoluble. Soluble antioxidants include phenolic acids, flavonoids, tocopherols, and avenanthramides in oats. A large part of insoluble antioxidants are bound as cinnamic acid esters to arabinoxylan side chains of hemicellulose. Wheat-bran insoluble fibre contains approximately 0·5–1·0 % phenolic groups. Covalently bound phenolic acids are good free radical scavengers. About two-thirds of whole-grain antioxidant activity is not soluble in water, aqueous methanol or hexane. Antioxidant activity is an inherent property of insoluble grain fibre. In the colon, hydrolysis by microbial enzymes frees bound phenolic acids (Kroon *et al.* 1997). Colon endothelial cells may absorb the released phenolic acids and gain antioxidant protection and these phenolic acids may enter the portal circulation. In this manner, wholegrain foods provide antioxidant protection over a long time period through the entire digestive tract.

In addition to natural antioxidants, antioxidant activity is created in grain-based foods by browning reactions during baking and toasting processes that increase total activity in the final product as compared with raw ingredients. For example, the crust of white bread has double the antioxidant activity of the starting flour or crust-free bread. Reductone intermediates from Maillard reactions may explain the increase in antioxidant activity. The total antioxidant activity of wholegrain products is similar to that of fruits or vegetables on a per serving basis (Miller, 2001).

Adom & Liu (2002) suggest that the antioxidant activity of grains reported in the literature has been underestimated since only unbound antioxidants are usually studied. They report that in wheat, 90 % of the antioxidants are bound. Bound phytochemicals could survive stomach and intestinal digestion, but would then be released in the large intestine and potentially play a protective role. When they compared the antioxidant activity of various grains, maize had the highest total antioxidant activity, followed by wheat, oats and then rice.

Phytic acid, concentrated in grains, is a known antioxidant. Phytic acid forms chelates with various metals, suppressing damaging Fe-catalysed redox reactions. Colonic bacteria produce oxygen radicals in appreciable amounts and dietary phytic acid may suppress oxidant damage to the intestinal epithelium and neighbouring cells.

Vitamin E is another antioxidant present in whole grains that is removed in the refining process. Vitamin E is an intracellular antioxidant that protects PUFA in cell membranes from oxidative damage. Another possible mechanism for vitamin E relates to its capacity to keep Se in the reduced state. Vitamin E inhibits the formation of nitrosamines, especially at low pH.

Se is another compound that is removed in the refining process. Its food composition is proportional to the Se content of the soil in which the grain is grown. Se functions as a cofactor for glutathione peroxidase, an enzyme that protects against oxidative tissue damage. It has a suppressive action on cell proliferation at high levels.

Other bioactive compounds in whole grains

Lignans

Hormonally active compounds in grains called lignans may protect against hormonally mediated diseases (Adlercreutz & Mazur, 1997). Lignans are compounds processing a 2,3-dibenzylbutane structure and exist as minor constituents of many plants where they form the building blocks for the formation of lignin in the plant cell wall. The plant lignans secoisolariciresinol and matairesinol are converted by human gut bacteria to the mammalian lignans enterolactone and enterodiol. Limited information exists on the concentration of lignans and their precursors in food. Due to the association of lignan excretion with fibre intake, it is assumed that plant lignans are contained in the outer layers of the grain. Concentrated sources of lignans include wholegrain wheat, wholegrain oats, and rye meal. Seeds are also concentrated sources of lignans including flaxseeds (the most concentrated source), pumpkin seeds, caraway seeds, and sunflower seeds. These compositional data suggest that wholegrain breads and cereals are the best ways to deliver lignans in the diet.

Grains and other high-fibre foods increase urinary lignan excretion, an indirect measure of lignan content in foods (Borriello *et al.* 1985). Mammalian lignan production of plant foods was studied by Thompson *et al.* (1996) using an *in vitro* fermentation method with human faecal microbiota. Oilseeds, particularly flaxseed flour and meal, produced the highest concentration of lignans, followed by dried seaweeds, whole legumes, cereal brans, wholegrain cereals, vegetables and fruits. The lignan concentration produced from flaxseed was approximately 100 times greater than that produced from most other foods.

Differences in metabolism of phyto-oestrogens among individuals have been noted. Adlercreutz *et al.* (1986) found total urinary lignan excretion in Finnish women to be positively correlated with total fibre intake, total fibre intake/kg body weight and grain fibre intake/kg body weight. Similarly, the geometric mean excretion of enterolactone was positively correlated with the geometric mean intake of dietary grain products (kJ/d) of five groups of women (*r* 0·996).

Due to the association of lignan excretion with fibre intake, plant lignans are probably concentrated in the outer layers of the grain. Because current processing techniques eliminate this fraction of the grain, lignans may not be found in processed grain products on the market and would only be found in wholegrain foods.

Serum enterolactone was measured in a cross-sectional study in Finnish adults (Kilkkinen *et al.* 2001). In men, serum enterolactone concentrations were positively associated with the consumption of wholegrain products. Variability in serum enterolactone concentration was great, suggesting that the role of gut microflora in the metabolism of lignans may be important. Kilkkinen *et al.* (2003) also reported that the intake of lignans is associated with serum

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enterolactone concentration in Finnish men and women. They suggested that serum enterolactone is a feasible biomarker of lignan intake. Jacobs *et al*. (2002) found similar results in a US study. Subjects were fed either wholegrain or refined-grain foods for 6 weeks. Most of the increase in serum enterolactone when eating the whole-grain diet occurred within 2 weeks, though the serum enterolactone difference between whole-grain and refined-grain diets continued to increase throughout the 6-week study.

Recent studies find that serum enterolactone is associated with reduced CVD-related and all-cause death in middle-aged Finnish men (Vanharanta *et al*. 2003). The authors suggest that this evidence supports the importance of wholegrain foods, fruits, and vegetables in the prevention of premature death from CVD.

Phytosterols

Plant sterols and stanols are found in oilseeds, grains, nuts and legumes. These compounds are known to reduce serum cholesterol (Yankah & Jones, 2001). Structurally, they are very similar to cholesterol, differing in side-chain methyl and ethyl groups. It is believed that phytosterols inhibit dietary and biliary cholesterol absorption from the small intestine. Phytosterols have better solubility than cholesterol in bile-salt micelles in the small intestine. Phytosterols displace cholesterol from micelles, which reduces cholesterol absorption and increases its excretion (Hallikainen *et al*. 2000). It is required that the sterol is consumed at the same time as cholesterol to inhibit the absorption of dietary cholesterol. The amount of plant sterols and stanols required to have a significant cholesterol-lowering effect is debated. Although a significant effect has been reported for less than 1 g/d, intakes of 1–2 g/d are usually suggested. A dose–response effect is reported for phytosterols that plateaus at about 2·5 g/d. The average Western diet contains an estimated 200–300 mg plant sterols/d. Vegetarians may consume up to 500 mg/d. Increased whole-grain consumption would increase total phytosterol intake and potentially contribute to cholesterol reduction.

Unsaturated fatty acids

Wholegrain wheat contains about 3 % lipids and wholegrain oats are about 7·5 % lipids. Grain lipids are about 75 % unsaturated, comprised of nearly equal amounts of oleic and linoleic acid and 1–2 % of linolenic acid. Palmitate is the main unsaturated fat. There are approximately 2 g unsaturated lipid/100 g whole-wheat and about 5·5 g for whole-oat foods. Both these fatty acids are known to reduce serum cholesterol and are an important component of a heart-healthy diet (McPherson & Spiller, 1995). There has been considerable emphasis on low-fat diets for reduced heart disease. However, the type of fat consumed is important as well as the amount of fat. If the fat is saturated, LDL- and total cholesterol increase, but decrease when the fat is unsaturated. In studies with individual fatty acids, stearic acid, oleic acid and linoleic acid were associated with lowering total and LDL-cholesterol. Other studies show the cholesterol-lowering effect of grain lipids or high-lipid bran products (Gerhardt & Gallo, 1998).

Antinutrients

Antinutrients found in grains include digestive enzyme (protease and amylase) inhibitors, phytic acid, haemagglutinins, and phenolics and tannins. Protease inhibitors, phytic acid, phenolics and saponins have been shown to reduce the risk of cancer of the colon and breast in animals. Phytic acid, lectins, phenolics, amylase inhibitors and saponins have also been shown to lower plasma glucose, insulin and/or plasma cholesterol and triacylglycerols (Slavin *et al*. 1999). In grains, protease inhibitors make up 5–10 % of the water-soluble protein and are concentrated in the endosperm and embryo.

Whole grains and cardiovascular disease

CVD is the number-one cause of death and disability of both men and women in the USA. There is strong epidemiological and clinical evidence linking the consumption of whole grains to a reduced risk for CHD (Anderson, 2002). Morris *et al*. (1977) followed 337 subjects for 10–20 years and concluded that the reduction in heart disease risk was attributable to a higher intake of cereal fibre, while indicating soluble sources such as pectin and guar did not account for the lower CHD. Brown *et al*. (1999) concluded that soluble fibre from different fibre sources was associated with small, but significant decreases in total cholesterol. Other compounds in grains, including antioxidants, phytic acid, lectins, phenolic compounds, amylase inhibitors, and saponins have all been shown to alter risk factors for CHD. It is probable that the combination of compounds in grains, rather than any one component, explains their protective effects in CHD.

Large prospective epidemiological studies have found a moderately strong association between whole-grain intake and decreased CHD risk. Post-menopausal women (*n* 34 492), aged 55–69 years and free of CHD, were followed in the large prospective Iowa Women's Health Study for the occurrence of CHD mortality (*n* 387) between baseline (1986) and 1994 (Jacobs *et al*. 1998*b*). Whole-grain intake was determined by seven items in a 127-item food-frequency questionnaire which was used to divide the participants into quintiles based on mean servings of whole-grain intake/d. The risk reduction in higher whole-grain intake quintiles was controlled for more than fifteen confounding variables, and was not explained by adjustment for dietary fibre intake. This suggests that whole-grain components other than dietary fibre may reduce the risk for CHD.

In a Finnish study, 21 930 male smokers (aged 50–69 years) were followed for 6·1 years (Pietinen *et al*. 1996). A reduced risk of CHD death was associated with an increased intake of rye products. Rimm *et al*. (1996) examined the association between cereal intake and risk for myocardial infarction in 43 757 US health professionals, aged 40–75 years. Cereal fibre was most strongly associated with a reduced risk for myocardial infarction with a 0·71 decrease in risk for each 10 g increase in cereal fibre intake.

The Nurses' Health Study, a large, prospective cohort study of US women followed up for 10 years, was also used to examine the relationship between grain intake and cardio-

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vascular risk (Liu *et al*. 1999). A total of 68 782 women aged 37–64 years without previously diagnosed angina, myocardial infarction, stroke, cancer, hypercholesterolaemia, or DM at baseline were studied. Dietary data were collected with a validated semi-quantitative food-frequency questionnaire. After controlling for age, cardiovascular risk factors, dietary factors, and multivitamin supplement use, the relative risk was 0·77 (95 % CI 0·57, 1·04). For a 10 g/d increase in total fibre intake (the difference between the lowest and highest quintiles), the multivariate relative risk of total CHD events was 0·81 (95 % CI 0·66, 0·99). Among different sources of dietary fibre (cereal, vegetable, fruit), only cereal fibre was strongly associated with a reduced risk of CHD (multivariate relative risk, 0·63; 95 % CI 0·49, 0·81 for each 5 g/d increase in cereal fibre). The authors conclude that higher fibre intake, particularly from cereal sources, reduces the risk of CHD.

Bruce *et al*. (2000) fed a diet high in whole and unrefined foods as compared with a refined diet to twelve hyperlipidaemic subjects. Subjects consumed the refined-food diet for the first 4 weeks of the study and then switched to the phytochemical-rich diet for 4 weeks. The phytochemical-rich diet included dried fruits, nuts, tea, wholegrain products, and more than six servings of fruits and vegetables/d. The wholefood diets significantly lowered serum cholesterol and LDL-cholesterol, improved colon function, and decreased measures of antioxidant defence, all biomarkers of decreased risk of chronic disease.

Food-consumption patterns that include whole grains also appear protective for CVD. Van Dam *et al*. (2003) report that the intake of refined diets which do not include whole grains were associated with higher serum cholesterol levels and lower intakes of micronutrients.

There are many theories as to how whole grains help cut the risk of CVD. Whole grains are rich in compounds such as tocotrienols, a form of vitamin E, which play an important role in disease prevention, including reducing the risk of heart disease (Slavin *et al*. 1999). Whole grains are also a source of plant sterols, such as ß-sitosterol, which can lower cholesterol. And, whole grains are an excellent source of dietary fibre, resistant starch and oligosaccharides, which are fermented by intestinal microflora to short-chain fatty acids, such as acetate, butyrate and propionate. Short-chain fatty acids have been shown to lower serum cholesterol (Hara *et al*. 1999).

Whole grains and blood glucose

Whole grains are known to affect glucose and insulin responses, partly due to their slow digestibility. GI is a way of measuring the blood glucose response to a standard amount of a specific food. Foods with low GI produce small rises in blood sugar and blood insulin. Several studies have shown that cereal-fibre intake is associated with a reduced risk for DM. One recent 7-year study of men and women found a strong relationship between the consumption of whole grains and fasting insulin levels. The greater the intake of whole grains, the lower fasting insulin levels were likely to be (Pereira *et al*. 1998). Wholegrain breads and breakfast cereals were the most commonly consumed wholegrain foods in the study.

Another study comparing the glycaemic response of diabetics to white bread as compared with wholegrain breads found that the consumption of wholegrain breads produced less of a rise in blood glucose in diabetics compared with white bread (Jenkins *et al*. 1988). The intake of fibre from wholegrain cereals has also been found to be inversely related to type 2 DM. In a long-term study of almost 90 000 women (Salmeron *et al*. 1997*b*), and in a similar study of about 45 000 men (Salmeron *et al*. 1997*a*), researchers found that those with higher intakes of cereal fibre had about a 30 % lower risk for developing type 2 DM, compared with those with the lowest intakes. Additionally, the Iowa Women's Health Study found that dietary fibre and whole-grain intake were protective against type 2 DM (Meyer *et al*. 2000). In another study (Liu *et al*. 2000), individuals consuming large amounts of refined grains and small amounts of whole grains had a 57 % higher risk of type 2 DM than did those consuming large amounts of whole grains. In the Health Professional Follow-up Study, an investigation following 42 898 men, a 37 % lower risk of type 2 DM was associated with about three servings of whole-grain intake/d (Fung *et al*. 2002).

Whole grains are good sources of dietary Mg, fibre and vitamin E, which are involved in insulin metabolism. Relatively high intakes of these nutrients from whole grains may prevent hyperinsulinaemia. Whole grains may also influence insulin levels through beneficial effects on satiety and body weight. However, even after adjusting for BMI, studies have found a strong inverse relationship between whole-grain intake and fasting insulin levels.

The effect of substitution of whole grain for refined grain on insulin sensitivity has also been investigated (Pereira *et al*. 2002). Fasting insulin levels were 10 % lower after 6 weeks on the whole-grain diet. This suggests that a change in insulin sensitivity may be responsible for the reductions in insulin levels and risk of type 2 DM reported in epidemiological (population) studies.

Montonen *et al*. (2003) reported an inverse association between whole-grain intake and risk of type 2 DM in a cohort study. Cereal-fibre intake was also associated with a reduced risk of type 2 DM. Liu (2003) pooled data from prospective cohort studies of whole-grain intakes and type 2 DM. The summary estimate of relative risk was 0·70. These studies cannot provide direct causal proof of the effects of whole grains in lowering the risk of type 2 DM since confounding remains an alternative explanation in non-randomised settings.

The synergistic effect of several whole-grain components, such as phytochemicals, vitamin E, Mg, or others, may be involved in the reduction of the risk for type 2 DM. McKeown *et al*. (2002) reported that whole-grain intake was inversely associated with BMI and fasting insulin in the Framingham Offspring Study. Juntunen *et al*. (2003) fed high-fibre rye bread and white-wheat bread to postmenopausal women and measured glucose and insulin metabolism. The acute insulin response increased significantly more during the rye-bread periods than during the wheat-bread period. They suggest that high-fibre rye bread appears to enhance insulin secretion, possibly indicating an improvement of β-cell function. Pereira *et al*. (2002) did

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find improvements in insulin sensitivity with whole-grain consumption.

Whole grains and cancer

There is substantial scientific evidence that whole grains as commonly consumed reduce the risk of cancer. In a meta-analysis of whole-grain intake and cancer, whole grains were found to be protective in forty-six of fifty-one mentions of whole-grain intake, and in forty-three of forty-five mentions after the exclusion of six mentions with design or reporting flaws or low intake (Jacobs *et al.* 1998*a*). Odds ratios were <1 in nine of ten mentions of studies of colorectal cancers and polyps, seven of seven mentions of gastric and six of six mentions of other digestive-tract cancers, seven of seven mentions of hormone-related cancers, four of four mentions of pancreatic cancer, and ten of eleven mentions of eight other cancers. The pooled odds ratio was similar in studies that adjusted for few or many covariates. A systemic review of case–control studies conducted using a common protocol in northern Italy between 1983 and 1996 indicates that a higher frequency of whole-grain consumption is associated with a reduced risk for cancer (Chatenoud *et al.* 1998). Whole grain was consumed primarily as wholegrain bread and some whole-grain pasta in the Italian studies. Other studies have demonstrated a lower risk for specific cancers, such as stomach (Terry *et al.* 2001), mouth and throat and upper digestive tract (Kasum *et al.* 2002), and endometrial (Kasum *et al.* 2001). Epidemiological studies have reported that higher serum insulin levels are associated with an increased risk of colon, breast, and possibly other cancers. The reduction of these insulin levels by whole grains may be an indirect way in which the reduction in cancer risk occurs.

Dietary factors, such as fibre, vitamin B_6 and phyto-oestrogen intake and lifestyle factors such as exercise, smoking and alcohol use, which are controlled for in most epidemiological studies, do not explain the apparent protective effect of whole grains against cancer, again suggesting it is the whole-grain ‘package’ that is effective. Several theories have been offered to explain the protective effects of whole grains. Because of the complex nature of whole grains, there are many potential mechanisms that could be responsible for their protective properties.

Several mechanisms have been proposed for the protective action of the dietary fibre found in whole grains. Increased faecal bulk and decreased transit time allow less opportunity for faecal mutagens to interact with the intestinal epithelium. Secondary bile acids are thought to promote cell proliferation, thus allowing an increased opportunity for mutations to occur and abnormal cells to multiply. The effect of fibre on the actions of bile acids may be attributable to the binding or diluting of bile acids.

Whole grains also provide Se, though the Se content of grains varies depending on soil Se content. One clinical trial using a dose of 200 µg Se/d in 1312 patients, found a 37 % reduction in cancer incidence and a 50 % reduction in cancer mortality, including substantial reductions in lung, prostate and colorectal cancers (Clark *et al.* 1996). Though it was designed only to look at the effect of Se on the recurrence of skin cancer, the study was halted early because of the dramatic effects of Se on the incidence of other cancers. Se functions as a cofactor for glutathione peroxidase, an enzyme that protects against oxidative tissue damage. At high levels, Se can suppress cell proliferation.

Vitamin E, which is found in whole grains, is believed to be a cancer inhibitor that exerts its effect by preventing the formation of carcinogens.

Whole grains also contain several antinutrients, such as protease inhibitors, phytic acid, phenolics and saponins, which until recently were thought to have only negative nutritional consequences. Some of these antinutrient compounds may act as cancer inhibitors by preventing the formation of carcinogens and by blocking the interaction of carcinogens with cells. Other potential mechanisms linking whole grains to a reduced cancer risk include large-bowel effects, antioxidants, alterations in blood glucose levels, weight loss, hormonal effects, and the influence of numerous biologically active compounds.

McIntosh *et al.* (2003) fed rye and wheat foods to overweight middle-aged men and measured markers of bowel health. The men were fed low-fibre cereal-grain foods providing 5 g dietary fibre for the refined-grain diet and 18 g dietary fibre for the whole-grain diet, either high in rye or wheat. This was in addition to a baseline diet that contained 14 g dietary fibre. Both the high-fibre rye and wheat foods increased faecal output by 33–36 % and reduced faecal ß-glucuronidase activity by 29 %. Postprandial plasma insulin was decreased by 46–49 % and postprandial plasma glucose by 16–19 %. Rye foods were associated with significantly increased plasma enterolactone and faecal butyrate, relative to the wheat and low-fibre diets. The authors conclude that rye appears more effective than wheat in the overall improvement of biomarkers of bowel health.

Body-weight regulation

Preliminary studies suggest an association between whole-grain intake and the regulation of body weight (Pereira, 2002). In the Coronary Artery Risk Development in Young Adults Study, whole grains were inversely associated with BMI and waist:hip ratio at baseline and 7 years later (Pereira *et al.* 1998). Although the differences were modest, the risk for weight gain and the development of overweight or obesity could be substantially decreased if the associations are true. A 10-year follow-up to the Coronary Artery Risk Development in Young Adults Study looked at dietary fibre, of which whole grains are a good source. Individuals with the highest dietary fibre intake (>2·51 g/MJ; i.e. >21 g/2000 kcal) gained approximately 3·6 kg (8 lb) less in weight than did those with the lowest intake (<1·43 g/MJ; i.e. <12 g/2000 kcal). Similar results were found for the waist:hip ratio (Ludwig *et al.* 1999).

Whole grains appear to prevent weight gain among middle-aged women (Liu *et al.* 2003*b*). In the Nurses’ Health Study, a prospective cohort of US female nurses, the subjects who consumed more whole grains consistently weighed less than did the women who had lower consumption of whole grains. The women in the highest quintile of dietary fibre intake had a 49 % lower risk of major weight gain than did the women in the lowest quintile.

Several factors may explain the influence of whole grains on body-weight regulation. The high volume, low-energy density and the relatively lower palatability of wholegrain foods may promote satiation (regulation of energy intake per eating occasion through effects of hormones influenced by chewing and swallowing mechanics). Additionally, whole grains may enhance satiety (delayed return of hunger following a meal) for up to several hours following a meal. Grains rich in viscous soluble fibres (for example, oats and barley) tend to increase intraluminal viscosity, prolong gastric emptying time, and slow nutrient absorption in the small intestine. Although preliminary evidence suggests that whole grains may influence body-weight regulation, additional epidemiological studies and clinical trials are needed. Newby *et al*. (2003) report that a healthy eating pattern, including the consumption of whole grains, is associated with smaller gains in BMI and waist circumference in the ongoing Baltimore Longitudinal Study of Aging (Shock *et al*. 1984).

All-cause mortality

Several epidemiological studies suggest that whole grains reduce the risk for all-cause mortality or all-cause death. In the Iowa Women's Health Study, whole grains and cereal fibre lowered all-cause death in post-menopausal women (Jacobs *et al*. 1999, 2000), and a Norwegian study showed a lower mortality rate for men and women with a high wholegrain bread intake (Jacobs *et al*. 2001). Liu *et al*. (2003*a*) reported that both total mortality and CVD-specific mortality were inversely associated with wholegrain but not refined-grain breakfast cereal intake in the Physicians' Health Study.

Conclusion

Whole grains are rich in many components, including dietary fibre, starch, fat, antioxidant nutrients, minerals, vitamin, lignans, and phenolic compounds that have been linked to the reduced risk of CHD, cancer, DM, obesity and other chronic diseases. Most of the protective components are found in the germ and bran, which are reduced in the grain-refining process. Based on epidemiological studies and biologically plausible mechanisms, the scientific evidence shows that the regular consumption of wholegrain foods provides health benefits in terms of reduced rates of CHD and several forms of cancer. It may also help regulate blood glucose levels. More research is needed on the mechanisms for this protection. Also, some components in whole grains may be most important in this protection and should be retained in food processing.

Dietary intakes of whole grains fall short of current recommendations to eat at least three servings daily. The whole-grain health claim should increase the consumption of wholegrain foods in the American population (Marquart *et al*. 2003). This is in keeping with the Food Pyramid educational materials, which recommend that a minimum of six servings of grain foods be eaten daily, with at least one half or three of those servings as whole grains. Efforts to develop health claims for whole grains in Europe are also underway (Richardson, 2003). The successful implementation of these recommendations will require the cooperative efforts of industry, government, academia, non-profit health organisations, and the media. Additional work is needed to confirm the health benefits of whole grains, develop processing techniques that will improve the palatability of wholegrain products, and educate consumers about the benefits of whole-grain consumption.

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