Potential Health Benefits of Whole Grain Wheat Components

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Whole grain foods are associated with reduced risk of several chronic diet-related diseases. Wheat is a staple in the Western diet and has been linked to these health effects and yet has received minimal attention for its health properties compared with other plant foods, such as oats or fruit and vegetables. Wheat should now be reexamined as a potential protective food against diet-related diseases, as whole grain wheat contains a multitude of compounds with reputed health benefits. Research has shown that consumption of wheat fiber leads to increased laxation, decreased gut transit time, and a potential reduction in the risk of colorectal cancer. Colonic fermentation of nondigestible carbohydrates may lead to favorable changes in the gut microflora and increase the production of beneficial compounds such as short-chain fatty acids. However, in addition to the effects of fibre, wheat contains numerous other components that may play a role in health and disease risk reduction, such as polyphenols, carotenoids, vitamin E, and phytosterols. The additive and synergistic effects of these compounds may contribute to the health benefits of whole grain consumption. This article provides an overview of the major components in whole grain wheat and reviews their associated health benefits. Nutr Today. 2012;47(4):163–174

Whole grain wheat may be a protective food against the development of chronic diet-related diseases. Large cohort studies have reported a marked reduced risk of cardiovascular disease (CVD),[1–3] type 2 diabetes,[4,5] and some forms of cancer[6,7] with increased consumption of whole grains, and wheat has been flagged as a key food in producing these effects.[5] Despite this intriguing connection, wheat is often perceived as a source of starch and energy with little added nutritional value[8] and has gained little attention for its health properties compared with other plant foods such as oats and even fruit and vegetables.[9,10]

However, wheat should be recognized for its contribution to health, as wheat is a core food in the Western diet and when consumed in whole grain form contains a variety of compounds, which may assist in the prevention of chronic disease.[11,12] Wheat fiber is well recognized for its role in health, through stimulating laxation, increasing fecal weight, and decreasing gut transit time, leading to a potential reduction in the risk of colorectal cancer.[13] Other components found in wheat are emerging as potentially significant to health, such as wheat polyphenols, which display strong antioxidant activity in vitro,[14] and wheat germ phytosterols, which have been found to reduce cholesterol levels in health subjects;[15] a risk factor for CVD. Furthermore, the additive and synergistic physiological effects of these compounds may exert health benefits greater than the effects of individual compounds.[11,16] However, many of the proposed mechanisms have not been substantiated by clinical studies involving whole grain wheat, and future research is needed to investigate the effects of wheat consumption on biomarkers of health and disease.

Given the prominence of wheat in the Western diet and the gaps in our understanding of the precise contribution of wheat to health and disease risk reduction, attention should now be shifted to wheat as a priority for research. Examining the compounds in wheat and their respective health effects may allow for an appreciation of the variety of health benefits potentially provided by whole grain wheat consumption. With this in mind, this review examines the components of whole grain wheat and their associated health effects.

WHOLE GRAIN WHEAT COMPOSITION

There has been renewed interest in examining the composition of whole grain wheat, in order to identify health-promoting compounds and better understand the potential role of wheat in health and disease prevention.[17] To this end, several analytical studies have investigated the phytochemical profile of whole grain wheat, and a literature review has exhaustively characterized its composition.[12] Wheat (*Triticum aestivum* L) is a complex food, consisting of a single-seeded fruit, encompassed by multiple outer layers.[17] It contains a variety of components with reputed health benefits including dietary fiber (DF), phenolic acids (PAs), alkylresorcinols, flavonoids, carotenoids, lignans, sterols, magnesium, selenium, tocopherols, and B-complex vitamins.[8,17–22] Whereas other whole grains may contain similar components, the contribution of wheat to the

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intake of these compounds is potentially greater due to its prominence in the diet.[9,23] The majority of these compounds are concentrated in the bran and germ fractions of the kernel, and thus whole grain foods, which contain all components of the grain, contain more potentially beneficial compounds than refined-grain foods.[22] The Table shows the content of bioactive compounds in whole-wheat bran, germ, and endosperm. Readers and referred to the article by Fardet[12] for a further indepth characterisation of the range of compounds found in whole grain wheat and its fractions. Several variables are known to influence the composition of wheat foods, including environmental conditions where the grain was cultivated, the processing and storage of the grain, and ripeness of the grain at harvest, as well as genetics and breeding techniques.[30,31] A study examined the effect of wheat genotype and environment on the DF and phytochemical composition in 26 wheat cultivars grown in Europe.[32] Significant variations were found in the content of phytochemical compounds, dependent on the genotype and the environmental conditions of growth. The results suggest that wheat varieties have different nutritional characteristics, and potential exists to manipulate environmental variables to optimize the nutritional quality of wheat foods.[17,32]

TABLE Phytochemical Content of Whole Grain Wheat and Fractions of Wheat[abc]

Wheat Compound	Whole Grain Wheat	Bran/Germ	Endosperm
Total phenolic acid,[de] μmol/100g	709.9–859.96	Bran and germ: 2867–3120	176–195
Phytosterols,[f] mg/100g	69–70	Bran: 197–200, germ: 344	28
Carotenoids,[d] μg/100 g	Lutein: 26.41–143.46, zeaxanthin: 8.70–27.08, β-cryptoxanthin: 1.12–13.28	Bran and germ: lutein: 164.1–191.7, zeaxanthin: 19.36–26.15, β-cryptoxanthin: 8.91–10.03	Lutein: 36.9–70.7, zeaxanthin: 1.58–2.71, β-cryptoxanthin: 3.48–4.41
Vitamin E,[g] mg/100 g	0.8	Bran: 1.1, germ: 11.96	0.62
Alkylresorcinols,[h] μg/g	123.18–587.67	Bran: 2369.78	11.93–41.19
Lignan,[i] μg/100g	210	Bran: 3629.5–7046.5	27
Flavonoids,[dj] μmol/100 g	105.85–148.93	Bran and germ: 740–940	60–80
Dietary fiber,[g] g/100 g	11.3	Bran: 44.7, germ: 18.3	3.8
Folate,[gk] μg/100 g	47	Bran: 252, germ: 356	17
Magnesium,[g] mg/100 g	103	Bran: 490, germ: 276	34
Selenium,[g] μg/100g	15	Bran: 21, germ: 24.9	13

[a]Data adapted from References 19, 20, 22, 24–29.

[b]When values are expressed as ranges, they represent the lowest and highest values from the selected references.

[c]All values are expressed as fresh weights (FW), unless otherwise specified. Where data were reported on a dry weight (DW) basis, values were converted to fresh weights using a conversion factor previously applied in the literature [μg/g FW = μg / g DW x[1.0 − (%moisture / 100)].[12] Where moisture content values were not reported in the literature, moisture values of 11% for whole-meal wheat flour, 11.6% for white wheat flour, 10.3% for wheat bran, and 11% for wheat germ were applied, based on data from the Australian nutrient database NUTTAB 2010.[28]

[d]Phytochemical content was determined by analyses of laboratory-milled whole grain wheat and wheat fractions.[19,22]

[e]Phenolic acid content expressed as mol of gallic acid equivalents per 100 g of grain.[19,22]

[f]Phytosterol content was determined by analyses of commercial wheat products, including crushed whole grain wheat, whole-meal flour, white (refined) wheat flour, wheat bran, and wheat germ.[26]

[g]Nutrient contents derived from analyses of commercial wheat products, including whole-meal wheat flour, white (refined) wheat flour, wheat bran, and wheat germ.[28]

[h]Alkylresorcinol content was determined by analyses of whole grain and white (refined) wheat, and commercial wheat bran products. Alkylresorcinol content was originally reported as 2672 μg/g in bran, 138.4 to 660.3 μg/g in whole grain wheat, and 13.5 to 46.6 μg/g in white (refined) wheat flour, on a dry-weight basis.[27,29]

[i]Lignan content was derived from analyses of commercial samples of whole-meal wheat flour and white (refined) wheat flour, and wheat bran obtained from laboratory-milled whole grain wheat.[20,25] Data pertaining to wheat bran were originally reported as 42.7 to 82.9 μg/g, on a dry-weight basis.[25]

[j]Flavonoid content expressed as μmol of catechin equivalents per 100 g of wheat.[19,22]

[k]Folate content refers to folate found naturally in wheat and does not include folic acid.[28]

Food manufacturing practices such as milling and baking may also impact the composition, bioavailability, and physiological effects of wheat foods. Anson and colleagues[33] investigated the effect of bioprocessing wheat bran in whole-wheat bread on the bioavailability of phenolics, antioxidant activity, and inflammation, in the postprandial phase. Bread that contained the finer-particle-size bran had a greater bioavailability of phenolics and reduced inflammation to a greater extent than the control bread. Another study found that increasing baking temperature of whole-wheat pizza crusts from 204°C to 288°C increased the antioxidant properties of the food by up to 82%.[34] These studies suggest that food processing may improve the nutritional quality and health effects of wheat foods.

Incorporating whole grain wheat into the diet is one way to increase the intake of a range of potentially beneficial dietary compounds. Furthermore, future opportunities to benefit from whole grain wheat consumption may come with the development of wheat foods with enhanced nutritional properties.

WHEAT COMPOUNDS AND HEALTH

Wheat has an important position in the Western diet, as a core component of a wide range of common foods such as breads and breakfast cereals.[16] Consumption of whole-grain wheat may benefit health, as whole grains have been associated with reduced risk of CVD,[1–3] type 2 diabetes,[4,5] and some forms of cancer.[6,7] In The Adventist Health Study, consumption of whole-wheat bread was associated with a significant reduced risk of myocardial infarction.[35] A relative risk of 0.56 (85% confidence interval, 0.35–0.89) was reported for nonfatal myocardial infarction when comparing whole-wheat bread consumption with white wheat bread, suggesting a significant protective effect of whole grain wheat against CVD. Other studies support these findings and suggest that wheat may be an important component of the protective eating pattern linking whole grains to reduced risk of disease.[5,36] The bulk of evidence comes from observational studies, which do not prove causality, and future studies are needed to delineate the contribution of individual grains such as wheat to the observed health effects. However, the consistent findings demonstrating health benefits associated with whole grain consumption suggest that whole grains including wheat are an important component of the diet and lifestyle approach to disease risk reduction.[37]

Although the precise mechanisms are not known, it is hypothesized that the compounds found in grains contribute to health benefits of whole grain consumption through additive and synergistic physiological effects.[38] Examining the individual components and their associated health effects allows for an appreciation of the variety of physiological responses possible as a consequence of consuming the compounds found in grains. Furthermore, identifying individual components and their associated health effects may enable the building of hypotheses around the protective mechanisms involved.[12] The following section provides an overview of some of the components of whole grain wheat and their associated health effects.

NUTRIENTS IN WHEAT

Dietary Fiber

Dietary fiber refers to the indigestible component of edible plants, extracts of plants, or synthetic analogs that resist digestion and absorption in the small intestine and are partially or completely fermented by anaerobic bacteria in the colon.[39] Dietary fiber potentially promotes beneficial physiological function including stimulating laxation, reducing blood cholesterol levels, or moderating blood glucose levels.[40]

Whole grain wheat is known to be a good source of DF, contributing to a significant proportion of the total cereal and insoluble fiber intakes in Western populations.[1,41,42] The physiological effects of fiber consumption depend on the type of fiber consumed. Wheat fiber is predominantly insoluble, with a minor soluble component, and may also contain fermentable carbohydrates and resistant starch, depending on the variety of wheat, its starch composition, and methods of food production.[43,44] Insoluble fiber facilitates bowel function by increasing stool weight, which promotes laxation and decreases gut transit time, whereas soluble fiber is known to decrease postprandial glycemia and reduce serum cholesterol.[45] Resistant starch refers to the starch component of grains that escapes digestion and is delivered to the colon.[46] This fiber component is highly fermentable and through its prebiotic effect in the large bowel, may result in the formation of short-chain fatty acids (SCFAs), which may also benefit health.[46,47]

Wheat fiber has diverse functions in the body that may impact several physiological processes linked to improved health and disease risk reduction. The following section discusses cardiovascular and bowel health—2 key health areas where wheat fiber and whole grain wheat have been linked to health.

Wheat Fiber, CVD, and Type 2 Diabetes

Large cohort studies suggest cereal fiber may protect against the development of type 2 diabetes and CVD.[48] Furthermore, insoluble fiber has been associated with reduced risk of CVD.[42] Wheat has been linked to these effects, as wheat is reported to be the primary source of cereal and insoluble fiber in the Western populations studied.[1,41,42] The mechanisms to explain this effect are not clear, as nonviscous and insoluble sources of fiber are not considered effective at modifying conventional disease biomarkers such as gastric emptying, blood glucose levels, or blood lipids, unlike soluble and viscous fibers.[48]

A limited number of experimental studies have investigated the effect of wheat fiber on CVD risk factors. Wheat fiber powder was demonstrated to decrease blood pressure, improve blood glucose levels, and improve the lipid profile, in patients with dysmetabolic cardiovascular syndrome.[49] Other studies have demonstrated improvements in triglycerides[50] and cholesterol[51,52]; demonstrating the possibility that wheat fiber may favorably modulate blood lipids. Contrary to this, the addition of 36 g of wheat fiber raised cholesterol levels slightly in a sample of healthy volunteers who took a fiber supplement for 2 weeks,[53] and studies of wheat bran have been inconsistent in demonstrating a reduction of serum lipids.[10]

Although wheat fiber is not considered an effective agent at reducing serum cholesterol, it is notable that a recent study found whole-meal wheat to be effective at reducing fasting plasma cholesterol and low-density lipoprotein (LDL) cholesterol levels, compared with refined grain wheat, in healthy individuals.[54] In this 3-week crossover study, the diets were isoenergetic, with a similar macronutrient composition, except for the higher content of wheat fiber in the intervention diet (23.1 g), compared with the control diet (9.8 g). Wheat fiber was suggested as the agent responsible for the improved cholesterol levels, but the effect may also relate to other aspects of the grain such as food structure or the effects of other bioactive compounds. Future studies are needed to investigate the impact of wheat fiber and whole grain wheat consumption on lipid metabolism and determine which factors modify their effectiveness.

Modulation of gut microflora and colonic fermentation of DF, including its component of resistant starch, are another proposed mechanism linking whole grains to reduced risk of CVD and type 2 diabetes.[47,55,56] When nondigestible carbohydrates enter the colon, they are fermented by bacteria and produce a number of byproducts such as SCFAs.[47,57] Short-chain fatty acids such as butyrate may increase insulin sensitivity by increasing hepatic glycolysis, reducing hepatic glucose production and improving postprandial glycemia.[58,59] Furthermore, SCFAs may decrease gastric emptying and increase serum polypeptide YY, leading to reduced uptake of glucose into the bloodstream.[12] More research is needed to determine whether consumption of whole grain foods leads to improvements in glucose and insulin metabolism through a mechanism of colonic fermentation.

A small number of human intervention studies have demonstrated the ability of whole grain wheat and wheat fiber to initiate beneficial alterations in gut microbiota.[47,56] One study found that increased wheat fiber consumption of 20 g/d, in the form of wheat bran, over 9 to 12 months, led to an increased production of butyrate and GLP-1.[47] This effect was partly attributed to the increase in starch delivered to the colon, which would favor fermentation and lead to the increased production of SCFAs. This study was the first to map the time course of effects of wheat fiber intake on plasma SCFAs and GLP-1 and suggests that fermentation of wheat fiber may increase over time, as the colonic microflora adapt to the sustained increase in carbohydrate delivered to the colon.[47] Studies are now needed to determine whether wheat fermentation leads to improvements in biomarkers of CVD and type 2 diabetes, through the modification of gut microflora or increased production of fermentation byproducts.

Experimental studies of whole grains have tended to be of short duration and have scarcely examined the role of gut microbes or colonic fermentation as a potential mechanism for health effects. Studies designed to measure byproducts of fermentation, such as SCFAs and GLP-1, may need to be conducted over a long time frame to allow for colonic adaptation. Studies characterizing the composition of indigestible carbohydrates in wheat foods and the associated fermentation activity in parallel with biomarkers of disease may be a useful step forward to understanding the potential contribution of whole grain wheat and its fermentable fiber components to disease risk reduction.

Wheat Fiber, Bowel Function, and Cancer

Wheat fiber may reduce the risk and severity of conditions such as hiatus hernia,[60] diverticular disease,[61] hemorrhoids,[62] and constipation[63,64] by stimulating laxation,[65] increasing stool weight,[66] and decreasing gut transit time.[67,68] Observational studies have also linked wheat fiber to reduced risk of colorectal cancer, which may relate to the fecal bulking properties of wheat fiber, leading to the dilution and absorption of fecal carcinogens and their reduced exposure to the intestinal epithelium.[39,69,70] Fecal bulking also leads to a decrease in gut transit time, which hastens the removal of contaminants from the luminal environment, further reducing their exposure to the epithelium.[71,72] Other proposed mechanisms of protection against colorectal cancer include slowing the growth and inducing apoptosis of cancer cells and up-regulating detoxification enzymes, which assist with elimination of carcinogenic substances.[73] In a study, 38 individuals at increased risk of developing colorectal cancer were given 10.5 g wheat fiber or 60 mL lactulose daily for 12 weeks and measured for rectal mucosal proliferation, a biomarker of colorectal cancer risk, before and after treatment.[70] Wheat fiber produced an antiproliferative effect, suggesting a protective effect of wheat fiber consumption against colorectal cancer.[70]

Colonic fermentation of indigestible carbohydrates leads to the proliferation of beneficial bacteria and the production SCFAs, which reduce colonic pH and decrease the concentration of pathogenic bacteria in the colon.[74] The SCFA butyrate is believed to be particularly important for bowel health, because of its ability to inhibit cancer cell proliferation, promote normal differentiation of colonic cells, and induce apoptosis of cells with damaged DNA.[39] Resistant starch may provide additional benefits to colon health, as it has a superior capacity to produce butyrate compared with nonstarch polysaccharides and may reduce colonic pH; lower harmful substances present in the colon, such as ammonia and bile acids; and provide nourishment to the intestinal epithelium.[75,76] However, future research is needed as large cohort studies have been inconsistent in demonstrating a relationship between fiber consumption and colorectal cancer.

Wheat fiber appears to be a health-promoting component of whole grain wheat. The health benefits may be related to the modulation of disease risk factors through nonconventional disease pathways such as changes in colonic microflora and fermentation. It is prudent to recommend the consumption of whole grain wheat or wheat fiber for the promotion of health and reduced risk of disease. Future research is needed to better understand how fiber components interact with the luminal environment including microflora to promote bowel health and reduce the risk of adenomas and carcinogenesis.

VITAMINS AND PROVITAMINS IN WHEAT

Vitamin E

Tocopherols and tocotrienols (vitamin E) are powerful membrane antioxidants that protect cell membrane polyunsaturated fatty acids from lipid peroxidation in vitro.[77] Whole grain wheat kernels were reported to contain between 27.6 and 79.7 μg/g (dry matter) of tocopherols and tocotrienols, with significant variation between genotypes.[78] The total amount of vitamin E in wheat is minor compared with other foods; however, whole grains are considered an important dietary source because of the high quantity of grains consumed as part of the human diet.[78]

Vitamin E is hypothesized to play a role in reducing mortality, cancer, and CVD[79] and may also reduce the risk and ameliorate the complications of type 2 diabetes,[80] optimize cognitive function,[81] and protect against cognitive decline in the elderly.[82] However, a recent study linked vitamin E supplementation to increased risk of prostate cancer, suggesting that food is the safest means to obtain the recommended intake of this nutrient.[83]

Some epidemiological evidence suggests that minor components of grains such as vitamin E contribute to the health benefits of whole grain consumption. A prospective study examining the effects of whole grain consumption on risk of type 2 diabetes found that dietary factors, including vitamin E, slightly attenuated the effects of whole grain consumption on type 2 diabetes risk.[78] This suggests that the minor components of grains, including vitamin E, may contribute to the health effects of whole grain consumption.[84]

B-Complex Vitamins

Whole grain wheat is a good source of B vitamins with diverse functions in the human body. In the Australian National Nutrition Survey, consumption of regular bread and bread rolls contributed 12% to 14% of the total folate intake consumed by Australians,[85] suggesting that wheat may be an important source of this vitamin. A recent study determined the content of thiamine (vitamin B_1), riboflavin (B_2), niacin (B_3), and pyridoxine (B_6) in the whole-meal flour of 24 winter wheat varieties.[86] On a dry weight (dw) basis, wheat was found to contain vitamins B_1 (5.53–13.55 μg/g), B_2 (0.77–1.40 μg/g), vitamin B_3 (0.16–1.74 μg/g), and B_6 (1.27–2.97 μg/g). As with most compounds found in whole grains, B vitamins are concentrated in the outer layers of the grain, and thus consuming whole grain foods delivers more of these nutrients than refined grain foods.[86]

The B-complex vitamins are known for their role in converting dietary carbohydrates, fat, and protein into energy, which is subsequently used to fuel cellular metabolic processes in the body.[87] Deficiencies of these important nutrients are known to compromise energy metabolism.[87] Other functions of B-complex vitamins relate to the maintenance of gastrointestinal tract muscle tone, the nervous system, connective tissues, and liver metabolism.[12] Much attention has been given to the B vitamin folate, which is essential to the process of DNA synthesis and regulation of gene expression.[88] Deficiencies may lead to genomic instability,[89] anemia,[90] and hyperhomocysteinemia, a risk factor for CVD.[91] Folate is known for its role in preventing neural tube defects[92] and certain cancers.[93] However, recent evidence suggests that high intakes of folate, particularly in the form of supplemental folic acid, may increase the risk of breast cancer in women who carry a particular genetic polymorphism.[94]

New evidence suggests that B vitamins such as folate, thiamine, nicotinic acid, pyridoxine, and pantothenic acid may also play a role in mental health, as they are involved in the synthesis of neurotransmitters essential to the maintenance of optimal brain function.[12] This suggests an exciting possibility that whole grain foods such as wheat may contribute to the optimization of brain and cognitive function, but future studies are needed to investigate this further.

Carotenoids

Carotenoids are the pigments that give plants their colors such as yellow, orange, and red.[95] There are hundreds of carotenoids in plants, of which approximately 40 are consumed as part of the human diet.[96] Carotenoids in wheat include lutein, zeaxanthin, β-cryptoxanthin, and β-carotene, which are concentrated in the germ fraction of the grain.[22] The contribution of wheat to the dietary intake of carotenoids is quite low, as modern varieties of wheat have been bred to contain low levels of carotenoids, in order to meet consumer demand for cereal products that are white in colour.[97]

Consumption of carotenoid-rich foods is associated with reduced risk of some types of cancer,[98] CVD,[99] and a number of eye conditions, notably age-related macular degeneration.[100] Lutein and zeaxanthin, found in wheat, are concentrated in the lens and macula of the retina and have been found to promote eye health by offering protection against age-related macular degeneration[100,101] and cataracts,[102] as well as improving visual acuity in patients with retinitis pigmentosa.[103] The protective mechanisms may involve their antioxidant activity and their ability to filter blue light.[96] Additionally, some carotenoids such as β-cryptoxanthin, β-carotene, and α-carotene have vitamin A activity, which has the function of promoting normal growth and development of the eye and visual pathways and promoting immune function.[104,105] Current research is focused on developing varieties of wheat with enhanced carotenoid content as an option to address vitamin A deficiencies in developing nations.[97]

Dietary carotenoids may also have antigenotoxic activity. A study found that a diet rich in carotenoids, from fruit and vegetable sources, reduced genetic damage in lymphocytes, decreased DNA strand breakage, and reduced oxidized DNA damage.[106] The authors conclude that a diet rich in carotenoids from plant sources may offer protection against cancer.[106] However, contrary to this, supplementation of carotenoids has been linked to increased cancer. A recent meta-analysis found that supplementation with β-carotene increases the incidence of lung and stomach cancer, particularly in smokers and asbestos workers; furthermore, it offered no protection against lung, pancreatic, colorectal, prostate, breast, skin, or total cancer incidence.[107]

The evidence supports the recommendation to obtain dietary carotenoids through consumption of a balanced diet inclusive of a range of plant foods such as fruit, vegetables, and whole grains, rather than as a supplement.

MINERALS IN WHEAT

Magnesium

Magnesium is an abundant intracellular cation distributed in the skeleton and intracellular and extracellular fluids throughout the human body.[108] Grains are an important source of magnesium, contributing up to 25% of the total dietary intake of magnesium in US women.[109] Average magnesium levels in wheat have been reported to range from 630 to 1261 mg/kg, with significant variations between wheat varieties based on the genotype and location of growth.[110]

Magnesium has been recognized as a key nutrient in mediating the effect of whole grains on insulin sensitivity and chronic lifestyle-related diseases.[111] Pereira and colleagues[112] conducted a 6-week crossover study in obese hyperinsulinemic subjects, to compare diets consisting of 6 to 10 servings of whole grain or refined grain wheat, on markers of insulin sensitivity. The diets were energy controlled and differed in terms of fiber but also their magnesium content, with the whole grain diet providing ~30% more magnesium than the refined diet. Areas under the curve and insulin infusion rate reflected greater insulin sensitivity after the whole grain diet. It has been hypothesized that, in addition to the potential effect of fiber, magnesium may have contributed to the improvements in insulin metabolism.[111]

This theory is supported by large cohort and prospective epidemiological studies showing inverse associations between dietary and supplemental magnesium intake and insulin sensitivity,[113] type 2 diabetes,[114] hypertension,[115] coronary heart disease,[116] hyperlipidemia, and metabolic syndrome.[117] Magnesium may also reduce endothelial dysfunction,[118] decrease platelet aggregation,[119] and lower inflammation and oxidative stress,[120,121] all of which are pathophysiological processes involved in atherosclerosis and increased risk of CVD-related diseases.[122]

Selenium

Selenium is an important antioxidant micronutrient that partakes in redox reactions and thyroid metabolism.[40] Selenium operates as a component of selenoproteins, which have several important physiological roles in the body including cellular antioxidant functions[123] and cell growth.[124] Selenium has been implicated as a protective nutrient against the development of prostate and esophageal cancer,[125] and selenium deficiency has been associated with infertility, oxidative stress, decreased immunity, and cognitive impairment.[126]

It has been estimated that up to 1 billion people are selenium deficient and even more may have suboptimal levels of intake.[127] Wheat is an important dietary source of selenium and supplies almost half of the total selenium intake in the Australian population.[128] It is estimated that refined grain flour has approximately 27% less selenium than whole grain wheat flour, and thus consuming whole grain wheat foods would provide more selenium than refined grain food consumption.[127] However, significant variations in the soil concentrations of selenium worldwide mean that the selenium content of foods is highly variable.[129] For instance, concentrations of selenium in wheat range from 0.001 mg/kg in southwest of Western Australia to 30 mg/kg in South Dakota in the United States.[130]

Selenium, as part of the selenoprotein glutathione peroxidase complex, may protect against disease development through its free radical–scavenging properties, which protect DNA from oxidation and thereby reduce mutations that arise from cellular oxidative damage.[131,132] In addition to its antioxidant properties, selenium may also increase genomic stability by decreasing chromosome breakage and improving DNA repair mechanisms.[133] However, despite evidence that selenium is a protective dietary component, the health effects of selenium consumed as part of whole grain food are less clear. A study conducted by Wu and colleagues[126] investigated the effect of consuming selenium-enriched wheat products on biomarkers of cancer and cardiovascular risk, oxidative stress, and immune function. Despite a significant increase in selenium intake and consequent plasma selenium concentrations, there were no significant effects observed on any of the biomarkers studied; indicating that while selenium is bioavailable in an acute-feeding time frame, increased selenium intake between 105 and 315 μg in addition to habitual dietary intake is unlikely to benefit cancer or cardiovascular risk in the short term. Further studies are needed to examine whether selenium consumed as part of whole grain and wheat foods has an effect on biomarkers of disease risk in the medium to long term.

OTHER BIOACTIVE COMPOUNDS IN WHEAT

Polyphenols

Polyphenols are the most abundant group of phytochemical compounds in wheat and are also considered one of the most bioactive components of whole grains.[134] They are a diverse group of plant compounds that contain 1 or more hydroxyl groups and aromatic rings[135] and function as the plants endogenous defense system against pathogenic substances in the environment and UV light.[136] Major wheat polyphenols include PAs, alkylresorcinols, flavonoids, and lignans.[20,22,24,137]

Polyphenols are primarily recognized for their ability to combat oxidative stress[138] and by doing so potentially reduce the risk of diseases related to oxidative stress such as CVD,[139,140] cancer,[141] and neurodegenerative conditions.[30] However, a recent review determined that there is insufficient evidence to support the claim that polyphenols protect against CVD through antioxidant mechanisms.[142] Thus, future research is needed to investigate the role of antioxidants in disease prevention. In addition to proposed antioxidant properties, other biological activities may include anti-inflammatory actions,[143,144] promotion of optimum endothelial function, and reduced thrombosis.[145]

Phenolic Acids

Phenolic acids are the primary polyphenols found in wheat.[137] Like most polyphenols, they are concentrated in the bran fraction of the kernel and come in 3 forms: soluble free acids, soluble conjugates, and insoluble bound form.[22] Free phenolics may be digested and absorbed in the upper gastrointestinal tract; however, they constitute only a small proportion of the total phenolics found in wheat, approximately less than 0.5% to 1%.[137] Bound PAs account for approximately 77% of total phenolics in wheat.[137] They are cross-linked with arabinoxylan and hemicellulose polysaccharides, in plant cell walls,[18,146] making them relatively inaccessible for digestion in the upper gastrointestinal tract.[30] Bound PAs are released from the fiber matrix during fermentation by bacteria, in the colon.[9,134] As a consequence of their inaccessibility to absorption in the upper gastrointestinal tract, the majority of bound phenolics are proposed to exert their physiological effects within the colon and systemically after absorption.[9]

Ferulic Acids

Ferulic acid is the primary PA found in wheat and accounts for approximately 90% of the total polyphenol content.[147] Ferulic acid has been suggested as a potential biomarker of whole grain wheat antioxidant capacity and appears to be bioavailable.[148] Ferulic acid may have a range of health benefits including hypocholesterolemic and antiatherogenic properties.[136] However, other mechanisms may be involved, such as free radical scavenging,[138] stimulating a chemoprotective response by induction of phase 2 detoxification enzymes,[149] and inhibiting the expression of toxic enzymes.[141] Furthermore, antimutagenic[150] and anti-inflammatory effects in vitro have been documented.[144]

Alkylresorcinols

Alkylresorcinols are a group of polyphenolic compounds present in whole grain wheat and rye.[24] Alkylresorcinols may be suitable as a biomarker of whole grain wheat and rye intake,[151] as they are primarily found in whole grain rye and wheat and are bioavailable.[152,153] In vitro studies indicate that alkylresorcinols may have anticancer properties by a mechanism of inducing apoptosis in cells with DNA damage.[153] But unlike many polyphenols, their antioxidant activity has been reported to be 10 times weaker than that of vitamin E.[153,154]

Flavonoids

Flavonoids are polyphenolic compounds present in a range of plant foods.[155] Flavonoid consumption is inversely associated with cognitive decline, metabolic syndrome,[155] coronary heart disease,[140] and cancers,[155] in epidemiological studies. In the Zutphen Elderly Study,[140] for example, a significant inverse association was found between flavonoids and coronary heart disease. However, the contribution of wheat to these effects has not been investigated, and little is known of the bioavailability of wheat flavonoids or their relative contribution to health.[51] However, in vitro studies indicate that flavonoids may act as antioxidants through inhibiting LDL oxidation, chelation of redox-active metals, and free radical scavenging.[156] Flavonoids may inhibit the atherosclerotic process by reducing platelet aggregation,[157] inhibiting the expression of cell adhesion molecules[158] and moderating lipid profiles and blood pressure.[155] Mechanisms leading to reduced cancer risk may involve antiproliferative effects and apoptosis-inducing properties.[159] The combination of these mechanisms may in part account for the protective effects of flavonoids against chronic disease, and future investigation of wheat flavonoids is warranted to understand how wheat foods might contribute to these effects.

Lignans

Lignan is the name for a group of polyphenolic compounds that display mild phytoestrogenic activity.[20] Lignans are fermented by gut bacteria to produce enterolignans, which are subsequently absorbed and are then responsible for some of the metabolic activity associated with lignin consumption.[20] Food sources of lignan include flaxseed, cereal brans, whole grains, legumes, seaweed, fruits, and vegetables.[160] Whole grain cereals, including wheat, are a minor source of lignan and produce small quantities of mammalian lignans in vitro compared with flaxseed.[160] However, whole grains may contribute to a higher proportion of the total lignan intake than flaxseed because they are consumed in greater quantities.[161]

Inverse associations between enterolignans and several chronic diseases have been observed, including reduced risk of CVD and some cancers, including prostate, breast, endometrial, and thyroid.[20] Mechanisms by which lignans may offer protection include their strong antioxidant activity, including defense against lipid peroxidation[162] and inhibiting or delaying the growth of mammary cancer cells.[163] Anticancer effects may also extend to other sites of cancer. A study by Qu et al[25] found that wheat bran lignans were associated with antitumor activity in human colon cancer cell lines. This study suggests that wheat lignans may account for some of the protective effects of wheat fiber consumption against colon cancer.[25]

Sterols

Phytosterols are chemically similar to cholesterol.[164] They are present in most plant-based foods including fruits, vegetables, seeds, nuts, legumes, and cereals.[164] The sterol content of grains is low compared with oilseeds, but because of the high intake of grain foods compared with other plant sources of sterols, grains are considered an important source and may contribute up to 40% of the total daily intake.[165]

Epidemiological studies link plant sterol consumption to reduced risk of several types of cancer, including cancer of the lung, stomach, colon, prostate, and breast.[164,166,167] Phytosterols are well known for their cholesterol-lowering properties.[168] Meta-analyses show that sterols and stanols are able to reduce LDL cholesterol by ~8% to 10%, indicating a potential for use in the therapeutic management of blood cholesterol.[164]

A study by Ostlund et al[15] demonstrated the efficacy of wheat germ phytosterols to reduce cholesterol absorption, at levels naturally present in wheat germ. The study compared the efficacy of wheat germ muffins with or without 328 mg of phytosterols to inhibit cholesterol. Using heptadeuterated cholesterol tracer to measure cholesterol absorption from the meals, tracer enrichment of plasma cholesterol was 42.8% higher after consumption of phytosterol-free wheat germ, compared with the original wheat germ. Thus, cholesterol absorption was significantly lower after consumption of wheat germ–containing phytosterols. This study suggests that wheat germ phytosterols have an important role in reducing cholesterol absorption. Plant sterols and stanols have also been shown to reduce markers of inflammation and protect against lipid peroxidation, suggesting an additional role for sterols in improving the CVD risk profile.[152]

CONCLUSION

Whole grain wheat contains a wide variety of compounds with reputed health benefits. There is no one particular compound that accounts for all of the health benefits of consuming whole grain wheat, although some stand out as being of particular benefit in supporting optimum health and disease risk reduction. Some of the key wheat components with implications for health are DF including fermentable carbohydrates and polyphenols; however, alongside these 2 important categories of compounds, several other components may offer health benefits such as sterols, magnesium, selenium, and B vitamins.

The main potential health benefits conferred from consuming whole grain wheat components appear to be related to the regulation of bowel and cardiovascular health and the prevention of type 2 diabetes and some forms of cancer. These health benefits are partly related to the physiological mechanisms of consuming foods themselves and the compounds therein. Traditional theories to explain the health benefits of whole grain consumption focus on the modulation of blood lipids, reducing blood pressure, reducing obesity, and regulating bowel health through stimulating laxation. Modern theories linking whole grain consumption to disease reduction probe further to uncover some of the underlying mechanisms behind these relationships including the effects of colonic fermentation of carbohydrates influencing glucose homeostasis and bowel health and the diverse antioxidative and anti-inflammatory activities of polyphenols.

It is important to keep in mind that the reductive approach to understanding the complexities of human nutrition focuses on the impact of individual components, whereas the reality of food-host interactions is far more complex and likely to involve interactions with the food matrix, whole diets, and the human microflora. Looking at the composition, physiological effects of individual compounds and potential health benefits of compounds therein provide part of the unique picture of nutrition and health. In combination with evidence that takes into account whole diets and other influential variables, this perspective can provide rich information about the dietary contributors to human health. This fascinating area of science deserves future research, so as to unravel the complexities of human nutrition and to promote a greater understanding of the dietary forces that drive human health and disease.

This review has demonstrated that whole grain wheat is a valuable source of nutrients and compounds that may enrich the diet in a manner conducive to health and disease prevention. Given the availability of whole grain wheat foods on the market today, recommending the incorporation of whole grain wheat into the diet is a practical strategy to increase the intake of a variety of compounds, which may optimize health and reduce the risk of diet-related diseases.

REFERENCES

1. Anderson JW. Whole grains protect against atherosclerotic cardiovascular disease. *Proc Nutr Soc*. 2003;62(1):135–142.
2. Anderson JW, Hanna TJ, Peng X, Kryscio RJ. Whole grain foods and heart disease risk. *J Am Coll Nutr*. 2000;19(suppl 3): S291–S299.
3. Jacobs DR Jr, Gallaher DD. Whole grain intake and cardiovascular disease: a review. *Curr Atheroscler Rep*. 2004;6(6):415–423.
4. De Munter JSL, Hu FB, Spiegelman D, Franz M, van Dam RM. Whole grain, bran, and germ intake and risk of type 2 diabetes: a prospective cohort study and systematic review. *PLoS Med*. 2007;4(8):1385–1395.
5. Venn BJ, Mann JI. Cereal grains, legumes and diabetes. *Eur J Clin Nutr*. 2004;58(11):1443–1461.
6. Chan JM, Wang F, Holly AE. Whole grains and risk of pancreatic cancer in a large population-based case-control study in the San Francisco Bay Area, California. *Am J Epidemiol*. 2007;166(10): 1174–1185.
7. Chatenoud L, Tavani A, La Vecchia C, et al. Whole grain food intake and cancer risk. *Int J Cancer*. 1998;77(1):24–28.
8. Shewry PR. Wheat. *J Exp Bot*. 2009;60(6):1537–1553.
9. Adom KK, Liu RH. Antioxidant activity of grains. *J Agric Food Chem*. 2002;50(21):6182–6187.
10. Topping D. Relationship between whole grain intake and risk of coronary heart disease. Food Standards Australia and New Zealand. http://www.foodstandards.gov.au/_srcfiles/Wholegrain%20review.pdf. Published 2006. Accessed February 7, 2007.
11. Liu RH. Whole grain phytochemicals and health. *J Cereal Sci*. 2007;46:207–219.
12. Fardet A. New hypotheses for the health-protective mechanisms of whole grain cereals: what is beyond fibre? *Nutr Res Rev*. 2010; 23(1):65–134.
13. Lupton JR, Turner JD. Potential protective mechanisms of wheat bran fiber. *Am J Med*. 1999;106(suppl 1A):S24–S27.
14. Baublis AJ, Lu C, Clydesdale FM, Decker EA. Potential of wheat-based breakfast cereals as a source of dietary antioxidants. *J Am Coll Nutr*. 2000;19(suppl 3):S308–S311.
15. Ostlund RE Jr, Racette SB, Stenson WF, et al. Inhibition of cholesterol absorption by phytosterol-replete wheat germ compared with phytosterol-depleted wheat germ. *Am J Clin Nutr*. 2003; 77(6):1385–1389.
16. Jacobs DR, Steffen LM. Nutrients, foods, and dietary patterns as exposures in research: a framework for food synergy. *J Clin Nutr*. 2003;78(suppl):508S–513S.
17. Shewry PR. The Healthgrain Programme opens new opportunities for improving wheat for nutrition and health. *Nutr Bull*. 2009; 34:225–231.
18. Ward JL, Poutanen K, Gebruers K, et al. The Healthgrain Cereal Diversity Screen: concept, results, and prospects. *J Agric Food Chem*. 2008;56(21):9699–9709.
19. Adom KK, Sorrells ME, Liu RH. Phytochemical profiles and antioxidant activity of wheat varieties. *J Agric Food Chem*. 2003. 51(26):7825–7834.
20. Milder IEJ, Arts ICW, van de Putte B, Venema DP, Hollman PCH. Lignan contents of Dutch plant foods: a database including lariciresinol, pinoresinol, secoisolariciresinol and matairesinol. *Br J Nutr*. 2005;93:393–402.
21. Garcia-Estepa RM, Guerra-Hernandez E, Garcia-Villanova B. Phytic acid content in milled cereal products and breads. *Food Res Intl*. 1999;32:217–221.
22. Adom KK, Sorrells ME, Liu RH. Phytochemicals and antioxidant activity of milled fractions of different wheat varieties. *J Agric Food Chem*. 2005;53(6):2297–2306.
23. Nystrom L, Paasonen A, Lampi A, Piironen V. Total plant sterols, steryl ferulates and steryl glycosides in milling fractions of wheat and rye. *J Cereal Sci*. 2007;45:106–115.
24. Andersson AA, Kamal-Eldin A, Fraś A, Boros D, Aman P. Alkylresorcinols in wheat varieties in the Healthgrain Diversity Screen. *J Agric Food Chem*. 2008;56(21):9722–9725.
25. Qu H, Madl RL, Takemoto DJ, Baybutt RC, Wang W. Lignans are involved in the antitumor activity of wheat bran in colon cancer SW480 cells. *J Nutr*. 2005;135:598–602.
26. Normen L, Bryngelsson S, Johnsson M, et al. The phytosterol content of some cereal foods commonly consumed in Sweden and in the Netherlands. *J Food Compos Anal*. 2002;15:693–704.
27. Ross AB, Shepherd MJ, Schupphaus M, et al. Alkylresorcinols in cereals and cereal products. *J Agric Food Chem*. 2003;51: 4111–4118.
28. Nutrient Tables, 2010 (NUTTAB 2010). Commonwealth of Australia and Food Standards Australia New Zealand. 2010. http://www.foodstandards.gov.au/consumerinformation/nuttab2010/nuttab2010onlinesearchabledatabase/onlineversion.cfm. Accessed July 2, 2010.
29. Ross AB, Kochhar S. Rapid and sensitive analysis of alkylresorcinols from cereal grains and products using HPLC - Coularray-based electrochemical detection. *J Agric Food Chem*. 2009;57:5187–5193.
30. Manach C, Scalbert A, Morand C, et al. Polyphenols: food sources and bioavailability. *Am J Clin Nutr*. 2004;79(5):727–747.
31. Mpofu A, Sapirstein HD, Beta T. Genotype and environmental variation in phenolic content, phenolic acid composition, and antioxidant activity of hard spring wheat. *J Agric Food Chem*. 2006;54(4):1265–1270.
32. Shewry PR, Piironen V, Lampi A, et al. The Healthgrain Wheat Diversity Screen: effects of genotype and environment on phytochemicals and dietary fiber components. *J Agric Food Chem*. 2010;58(17):9291–9298.
33. Anson NM, Aura AM, Selinheimo E, et al. Bioprocessing of wheat bran in whole wheat bread increases the bioavailability of phenolic acids in men and exerts antiinflammatory effects ex vivo. *J Nutr*. 2011;141(1):137–143.
34. Moore J, Luther M, Cheng Z, Yu L. Effects of baking conditions, dough fermentation, and bran particle size on antioxidant properties of whole-wheat pizza crusts. *J Agric Food Chem*. 2009;57:832–839.
35. Fraser GE, Sabate J, Beeson WL, Strahan TM. A possible protective effect of nut consumption on risk of coronary heart disease—the Adventist Health Study. *Arch Intern Med*. 1992;152: 1416–1424.

36. Jacobs DR, Meyer KA, Kushi LH, Folsom AR. Is whole grain intake associated with reduced total and cause-specific death rates in older women? The Iowa Women's Health Study. *Am J Pub Health*. 1999;89(3):322–329.
37. Seal C, Brownlee IA. Whole grains and health, evidence from observational and intervention studies. *Cereal Chem*. 2010;87(2): 167–174.
38. Jacobs DR, Gross MD, Tapsell LC. Food Synergy: an operational concept for understanding nutrition. *Am J Clin Nutr*. 2009;89(5): 1543S–1548S.
39. Young GP, Hu Y, Le Leu RK, Nyskohus L. Dietary fibre and colorectal cancer: a model for environment-gene interactions. *Mol Nutr Food Res*. 2005;49(6):571–584.
40. National Health and Medical Research Council and New Zealand Ministry of Health. *Nutrient Reference Values for Australia and New Zealand Including Recommended Dietary Intakes*. Canberra: NHMRC; 2006.
41. Jenkins DJA, Kendall CWC, Vuksan V, et al. The effect of wheat bran particle size on laxation and colonic fermentation. *J Am Coll Nutr*. 1999;18(4):339–345.
42. Smith CR, Tucker KL. Health benefits of cereal fibre: a review of clinical trials. *Nutr Res Rev*. 2011;24:118–131.
43. Pang H, Li WH, Zhang HB, et al. Inheritance analysis of resistant starch content in kernels of wheat. *Yi Chuan*. 2010;32(2): 170–176.
44. Perera A, Meda V, Tyler RT. Resistant starch: a review of analytical protocols for determining resistant starch and of factors affecting the resistant starch content of foods. *Food Res Int*. 2010;43(8):1959–1974.
45. Slavin JL, Savarino V, Paredes-Diaz A, Fotopoulos G. A review of the role of soluble fiber in health with specific reference to wheat dextrin. *J Am Med Assoc*. 2009;37:1–7.
46. Cummings JH, Macfarlane GT, Englyst HN. Prebiotic digestion and fermentation. *Am J Clin Nutr*. 2001;73(suppl 1):415S–420S.
47. Freeland KR, Wilson C, Wolever TMS. Adaptation of colonic fermentation and glucagon-like prptide-1 secretion with increased wheat fibre intake for 1 year in hyperinsulinaemic human subjects. *Br J Nutr*. 2010;(103):82–90.
48. Jenkins DJA, Kendall CWC, Augustin LSA, et al. Effect of wheat bran on glycemic control and risk factors for cardiovascular disease in type 2 diabetes. *Diabetes Care*. 2002;25(9):1522–1528.
49. Sabovic M, Lavre S, Keber I. Supplementation of wheat fibre can improve risk profile in patients with dysmetabolic cardiovascular syndrome. *Eur J Cardiovasc Prev Rehabil*. 2004;11: 144–148.
50. Cara L, Armand M, Borel P, et al. Long-term wheat germ intake beneficially affects plasma lipids and lipoproteins in hypercholesterolemic human subjects. *J Nutr*. 1992;122(2):317–326.
51. Williams CL, Bollella MC, Strobino BA, Boccia L, Campanaro L. Plant stanol ester and bran fiber in childhood: effects on lipids, stool weight and stool frequency in preschool children. *J Am Coll Nutr*. 1999;18(6):572–581.
52. Lindegarde F, Larsson L. Effects of a concentrated bran fibre preparation on HDL-cholesterol in hypercholesterolaemic men. *Hum Nutr Clin Nutr*. 1984;38(1):39–45.
53. Jenkins DJA, Hill MS, Cummings JH. Effect of wheat fiber on blood lipids, fecal steroid excretion and serum iron. *Am J Clin Nutr*. 1975;28:1408–1411.
54. Giacco R, Clemente G, Cipriano D, et al. Effects of the regular consumption of wholemeal wheat foods on cardiovascular risk factors in healthy people. *Nutr Metab Cardiovasc Dis*. 2010; 20(3):186–194.
55. Neyrinck AM, Delzenne NM. Potential interest of gut microbial changes induced by non-digestible carbohydrates of wheat in the management of obesity related disorders. *Curr Opin Clin Nutr Metab Care*. 2010;13:722–728.
56. Costabile A, Klinder A, Fava F, et al. Whole grain wheat breakfast cereal has a prebiotic effect on the human gut microbiota: a double-blind, placebo-controlled, crossover study. *Br J Nutr*. 2008;99:110–120.
57. Slavin JL, Martini MC, Jacobs DR, Marquart L. Plausible mechanisms for the protectiveness of whole grains. *Am J Clin Nutr*. 1999;70(suppl):S459–S463.
58. Gao Z, Yin J, Zhang J, et al. Butyrate improves insulin sensitivity and increases energy expenditure in mice. *Diabetes*. 2009;58(7): 1509–1517.
59. Nilsson A, Granfeldt Y, Ostman E, Preston T, Bjork I. Effects of GI and content of indigestible carbohydrates of cereal-based evening meals on glucose tolerance at a subsequent standardised breakfast. *Eur J Clin Nutr*. 2006;60(2):1092–1099.
60. Burkitt D, Clements J, Eaton SB. Prevalence of diverticular disease, hiatus hernia and pelvic phleboliths in black and white Americans. *Lancet*. 1985;326(8460):880–881.
61. Aldoori W, Ryan-Harshman M. Preventing diverticular disease. Review of recent evidence on high-fibre diets. *Can Fam Phys*. 2002;48:1632–1637.
62. Alonso-Coello P, Mills E, Heels-Ansdell D, et al. Fiber for the treatment of hemorrhoids complications: a systematic review and meta-analysis. *Am J Gastroenterol*. 2006;101(1):181–188.
63. Anderson AS, Whichelow MJ. Constipation during pregnancy: dietary fibre intake and the effect of fibre supplementation. *Hum Nutr Appl Nutr*. 1985;39(3):202–207.
64. Schmelzer M. Effectiveness of wheat bran in preventing constipation of hospitalized orthopaedic surgery patients. *Orthop Nurs*. 1990;9(6):55–59.
65. Ouellet LL, Turner TR, Pond S, et al. Dietary fiber and laxation in postop orthopedic patients. *Clin Nurs Res*. 1996;5(4):428–440.
66. Stephen AM, Wiggins HS, Englyst HN, Cole TJ, Wayman BJ, Cummings JH. The effect of age, sex and level of intake of dietary fibre from wheat on large-bowel function in thirty healthy subjects. *Br J Nutr*. 1986;56(2):349–361.
67. Cann PA, Read NW, Holdsworth CD. What is the benefit of coarse wheat bran in patients with irritable bowel syndrome? *Gut*. 1984;25(2):168–173.
68. Payler DK, Pomare EW, Heaton KW, et al. The effect of wheat bran on intestinal transit. *Gut*. 1975;16(3):209–213.
69. Alberts DS, Einspahr J, Rees-McGee S, et al. Effects of dietary wheat bran fiber on rectal epithelial cell proliferation in patients with resection for colorectal cancers. *J Natl Cancer Inst*. 1990; 82(15):1280–1285.
70. Rooney PS, Hunt LM, Clarke PA, Gifford KA, Hardcastle JD, Armitage NC. Wheat fibre, lactulose and rectal mucosal proliferation in individuals with a family history of colorectal cancer. *Br J Surg*. 1994;81(12):1792–1794.
71. Anderson JW. Health implications of wheat fiber. *Am J Clin Nutr*. 1985;41(suppl 5):S1103–S1112.
72. Lewis SJ, Heaton KW. Increasing butyrate concentration in the distal colon by accelerating intestinal transit. *Gut*. 1997;41(2): 245–251.
73. Scharlau D, Borowicki A, Habermann N, et al. Mechanisms of primary cancer prevention by butyrate and other products formed during gut flora-mediated fermentation of dietary fibre. *Mutat Res*. 2009;682(1):39–53.
74. Bird AR, Brown IL, Topping DL. Starches, resistant starches, the gut microflora and human health. *Curr Issues Intest Microbiol*. 2000;1(1):25–37.
75. Topping DL, Balazs B, Anthony B, et al. Resistant starches as a vehicle for delivering health benefits to the human large bowel. *Microb Ecol Health Dis*. 2008;20(2):103–108.
76. Muir JG, Yeow EG, Keogh J, et al. Combining wheat bran with resistant starch has more beneficial effects on fecal indexes than does wheat bran alone. *Am J Clin Nutr*. 2004;79(6): 1020–1028.
77. Atkinson J, Harroun T, Wassall SR, et al. The location and behavior of alpha-tocopherol in membranes. *Mol Nutr Food Res*. 2010;54(5):641–651.

78. Lampi AM, Nurmi T, Ollilainen V, Piironen V. Tocopherols and tocotrienols in wheat genotypes in the Healthgrain Diversity Screen. *J Agric Food Chem*. 2008;56:9716–9721.
79. Traber M, Frei B, Beckman JS. Vitamin E revisited: do new data validate benefits for chronic disease prevention? *Curr Opin Lipidol*. 2008;19:30–38.
80. Milman U, Blum S, Shapira C, et al. Vitamin E supplementation reduces cardiovascular events in a subgroup of middle-aged individuals with both type 2 diabetes mellitus and the haptoglobin 2-2 genotype: a prospective double-blinded clinical trial. *Artherioscler Thromb Vasc Biol*. 2008;28(2):341–347.
81. Ortega RM, Requejo AM, López-Sobaler AM, et al. Cognitive function in elderly people is influenced by vitamin E status. *J Nutr*. 2002;132(7):2065–2068.
82. Morris MC, Evans DA, Bienias JL, et al. Vitamin E and cognitive decline in older persons. *Arch Neurol*. 2002;59(7):1125–1132.
83. Klein EA, Thompson IM, Tangen CM et al. Vitamin E and the risk of prostate cancer. *JAMA*. 2011;306(14):1549–1556
84. Liu S, Manson JE, Stampfer MJ, et al. Whole grain consumption and risk of ischemic stroke in women: a prospective study. *J Am Med Assoc*. 2000;284(12):1534–1540.
85. McLennan W, Podger A. *National Nutrition Survey: Foods Eaten, Australia, 1995*. ABS Cat No. 4804.0. Canberra: Australian Bureau of Statistics; 1999.
86. Shewry PR, Schaik FV, Ravel C, et al. Genotype and environment effects on the contents of vitamins B_1, B_2, B_3, and B_6 in wheat grain. *J Agric Food Chem*. 2011;59:10564–10571.
87. Huskisson E, Maggini S, Ruf M. The role of vitamins and minerals in energy metabolism and well-being. *J Int Med Res*. 2007;35(3):277–289.
88. Jacob RA. Folate, DNA methylation, and gene expression: factors of nature and nurture. *Am J Clin Nutr*. 2000;72(4):903–904.
89. Duthie SJ. Folic acid deficiency and cancer: mechanisms of DNA instability. *Br Med Bull*. 1999;55(3):578–592.
90. Roddie C, Davis B. Iron, B_{12} and folate. *Medicine*. 2009;37(3): 125–128.
91. Ciaccio M, Bellia C. Hyperhomocysteinemia and cardiovascular risk: effect of vitamin supplementation in risk reduction. *Curr Clin Pharmacol*. 2010;5(1):30–36.
92. Blencowe H, Cousens S, Modell B, et al. Folic acid to reduce neonatal mortality from neural tube disorders. *Int J Epidemiol*. 2010;39:110–121.
93. Du W, Li WY, Lu R, Fang JY, et al. Folate and fiber in the prevention of colorectal cancer: between shadows and the light. *World J Gastroenterol*. 2010;16(8):921–926.
94. Ericson U, Sonestedt E, Ivarsson MI, et al. Folate intake, methylenetetrahydrofolate reductase polymorphisms, and breast cancer risk in women from the MalmÃ diet and cancer cohort. *Cancer Epidemiol Biomarkers Prev*. 2009;18(4):1101–1110.
95. Tanaka Y, Sasaki N, Ohmiya A. Biosynthesis of plant pigments: anthocyanins, betalains and carotenoids. *Plant J*. 2008;54(4): 733–749.
96. Ma L, Lin XM. Effects of lutein and zeaxanthin on aspects of eye health. *J Sci Food Agric*. 2010;90(1):2–12.
97. Graham RD, Rosser JM. Carotenoids in staple foods: their potential to improve human nutrition. *Food Nutr Bull*. 2000;21(4): 404–409.
98. Nishino H, Murakoshi M, Tokuda H, Satomi Y. Cancer prevention by carotenoids. *Arch Biochem Biophys*. 2009;483(2):165–168.
99. Kohlmeier L, Hastings SB. Epidemiologic evidence of a role of carotenoids in cardiovascular disease prevention. *Am J Clin Nutr*. 1995;62(suppl):1370S–1376S.
100. Zhao L, Sweet BV. Lutein and zeaxanthin for macular degeneration. *Am J Health Syst Pharm*. 2008;65(13):1232–1238.
101. Krinsky NI, Landrum JT, Bone RA. Biologic mechanisms of the protective role of lutein and zeaxanthin in the eye. *Ann Rev Nutr*. 2003;23:171–201.
102. Brown L, Rimm EB, Seddon JM, et al. A prospective study of carotenoid intake and risk of cataract extraction in US men. *Am J Clin Nutr*. 1999;70(4):517–524.
103. Bahrami H, Melia M, Dagnelie G. Lutein supplementation in retinitis pigmentosa: PC-based vision assessment in a randomized double-masked placebo-controlled clinical trial. *BMC Ophthalmol*. 2006;6:23.
104. Olson JA. Carotenoids and human health. *Arch Latinoam Nutr*. 1999;49(1):7–11.
105. Ferrando R. Vitamin A and immunity. *Bull Acad Natl Med*. 1994; 178(7):1383–1388.
106. Pool-Zobel BL, Bub A, Müller H, et al. Consumption of vegetables reduces genetic damage in humans: first results of a human intervention trial with carotenoid-rich foods. *Carcinogenesis*. 1997;18(9):1847–1850.
107. Druesne-Pecollo N, Latino-Martel P, Norat T, et al. beta-Carotene supplementation and cancer risk: a systematic review and meta-analysis of randomized controlled trials. *Int J Cancer*. 2010;127(1): 172–184.
108. Chaudhary D, Sharma R, Bansal D. Implications of magnesium deficiency in type 2 diabetes: a review. *Biol Trace Elem Res*. 2010; 134(2):19–129.
109. Lin P, Aickin M, Champagne C, et al. Food group sources of nutrients in the dietary patterns of DASH-Sodium trial. *J Am Diet Assoc*. 2003;103(4):488–496.
110. Hussain A, Larsson H, Kuktaite R, Johansson E. Mineral composition of organically grown wheat genotypes: contribution to daily minerals intake. *Int J Environ Res Public Health*. 2010;7:3442–3456.
111. McCarty MF. Magnesium may mediate the favorable impact of whole grains on insulin sensitivity by acting as a mild calcium antagonist. *Med Hypotheses*. 2005;64(3):619–627.
112. Pereira MA, Jacobs DR Jr, Pins JJ, et al. Effect of whole grains on insulin sensitivity in overweight hyperinsulinemic adults. *Am J Clin Nutr*. 2002;75(5):848–855.
113. Fung TT, Hu FB, Pereira MA, et al. Whole grain intake and the risk of type 2 diabetes: a prospective study in men. *Am J Clin Nutr*. 2002;76(3):535–540.
114. Colditz GA, Manson JE, Stampfer MJ, Rosner B, Willett WC, Speizer FE. Diet and risk of clinical diabetes in women. *Am J Clin Nutr*. 1992;55(5):1018–1023.
115. Houston MC, Harper KJ. Potassium, magnesium, and calcium: their role in both the cause and treatment of hypertension. *J Clin Hypertens (Greenwich)*. 2008;10(7 suppl 2):S3–S11.
116. Mathers TW, Beckstrand RL. Oral magnesium supplementation in adults with coronary heart disease or coronary heart disease risk. *J Am Acad Nurse Pract*. 2009;21(12):651–657.
117. Champagne CM. Magnesium in hypertension, cardiovascular disease, metabolic syndrome, and other conditions: a review. *Nutr Clin Prac*. 2008;23(2):142–151.
118. Chacko SA, Song Y, Nathan L, et al. Relations of dietary magnesium intake to biomarkers of inflammation and endothelial dysfunction in an ethnically diverse cohort of postmenopausal women. *Diabetes Care*. 2010;33(2):304–310.
119. Gawaz M. Antithrombotic effectiveness of magnesium. *Fortschr Med*. 1996;114(26):329–332.
120. Hasebe N. Oxidative stress and magnesium. *Clin Calcium*. 2005; 15(2):194–202.
121. Bo S, Pisu E. Role of dietary magnesium in cardiovascular disease prevention, insulin sensitivity and diabetes. *Curr Opin Lipidol*. 2008;19(1):50–56.
122. Gade W, Schmit J, Collins M, Gade J. Beyond obesity: the diagnosis and pathophysiology of metabolic syndrome. *Clin Lab Sci*. 2010;23(1):51–61.
123. Arbogast S, Ferreiro A. Selenoproteins and protection against oxidative stress: selenoprotein N as a novel player at the crossroads of redox signaling and calcium homeostasis. *Antioxid Redox Signal*. 2010;12(7):893–904.
124. Beckett GJ, Arthur JR. Selenium and endocrine systems. *J Endocrinol*. 2005;184(3):455–465.

125. Clark LC, Dalkin B, Krongrad A, et al. Decreased incidence of prostate cancer with selenium supplementation: results of a double-blind cancer prevention trial. *Br J Urol*. 1998;81(5):730–734.
126. Wu J, Salisbury C, Graham R, et al. Increased consumption of wheat biofortified with selenium does not modify biomarkers of cancer risk, oxidative stress, or immune function in healthy Australian males. *Environ Mol Mutagen*. 2009;50(6):489–501.
127. Lyons GH, Genc Y, Stangoulis JCR, Palmer LT, Graham RD. Selenium distribution in wheat grain, and the effect of postharvest processing on wheat selenium content. *Biol Trace Elem Res*. 2005;103:155–168.
128. Lyons GH, Judson GJ, Ortiz-Monasterio I, Genc Y, Stangoulis JCR, Graham RD. Selenium in Australia: selenium status and biofortification of wheat for better health. *J Trace Elem Med Biol*. 2005; 19:75–82.
129. Combs GF. Selenium in global food systems. *Br J Nutr*. 2001; 85:517–547.
130. Lyons G, Stangoulis J, Graham R. High-selenium wheat: biofortification for better health. *Nutr Res Rev*. 2003;16:45–60.
131. El-Bayoumy K. The protective role of selenium on genetic damage and on cancer. *Mutat Res*. 2001;475(1–2):123–139.
132. Duthie SJ, Ma A, Ross MA, Collins AR. Antioxidant supplementation decreases oxidative DNA damage in human lymphocytes. *Cancer Res*. 1996;56(6):1291–1295.
133. Laffon B, Valdiglesias V, Pásaro E, Méndez J. The organic selenium compound selenomethionine modulates bleomycin-induced DNA damage and repair in human leukocytes. *Biol Trace Elem Res*. 2010;133(1):12–19.
134. Selma MV, Espín JC, Tomás-Barberán FA. Interaction between phenolics and gut microbiota: role in human health. *J Agric Food Chem*. 2009;57(15):6485–6501.
135. Hasna El G. Polyphenols: food sources, properties and applications; a review. *Int J Food Sci Technol*. 2009;44(12):2512–2518.
136. Graf E. Antioxidant potential of ferulic acid. *Free Radic Biol Med*. 1992;13(4):435–448.
137. Li L, Shewry PR, Ward JL. Phenolic acids in wheat varieties in the Healthgrain Diversity Screen. *J Agric Food Chem*. 2008;56(21): 9732–9739.
138. Anouar E, Kosinová P, Kozlowski D, Mokrini R, Duroux JL, Trouillas P. New aspects of the antioxidant properties of phenolic acids: a combined theoretical and experimental approach. *Phys Chem*. 2009;11(35):7659–7668.
139. Aviram M, Kaplan M, Rosenblat M, Fuhrman B. Dietary antioxidants and paraoxonases against LDL oxidation and atherosclerosis development. *Handb Exp Pharmacol*. 2005;(170):263–300.
140. Hertog MG, Feskens EJ, Hollman PC, Katan MB, Kromhout D. Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen Elderly Study. *Lancet*. 1993;342(8878):1007.
141. Barone E, Calabrese V, Mancuso C. Ferulic acid and its therapeutic potential as a hormetin for age-related diseases. *Biogerontology*. 2009;10(2):97–108.
142. Hollman PC, Cassidy A, Comte B, et al. The biological relevance of direct antioxidant effects of polyphenols for cardiovascular health in humans is not established. *J Nutr*. 2011; 141(5):989S–1009S.
143. Cheng CY, Ho TY, Lee EJ, Su SY, Tang NY, Hsieh CL. Ferulic acid reduces cerebral infarct through its antioxidative and anti-inflammatory effects following transient focal cerebral ischemia in rats. *Am J Chin Med*. 2008;36(6):1105–1119.
144. Ozaki Y. Antiinflammatory effect of tetramethylpyrazine and ferulic acid. *Chem Pharm Bull (Tokyo)*. 1992;40(4):954–956.
145. Duffy SJ, Vita JA. Effects of phenolics on vascular endothelial function. *Curr Opin Lipidiol*. 2003;14(1):21–27.
146. Shiyi O, Kin-Chor K. Ferulic acid: pharmaceutical functions, preparation and applications in foods. *J Sci Food Agric*. 2004;84(11): 1261–1269.
147. Gharras HE. Polyphenols: food sources, properties and applications—a review. *Int J Food Sci Technol*. 2009;44(12): 2512–2518.
148. Bourne LC, Rice-Evans C. Bioavailability of ferulic acid. *Biochem Biophys Res Commun*. 1998;253(2):222–227.
149. Kawabata K, Yamamoto T, Hara A. Modifying effects of ferulic acid on azoxymethane-induced colon carcinogenesis in F344 rats. *Cancer Lett*. 2000;157(1):15–21.
150. Birosova L, Mikulasova M, Vaverkova S. Antimutagenic effect of phenolic acids. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*. 2005;149(2):489–491.
151. Landberg R, Kamal-Eldin A, Andersson A, Vessby B, Aman P. Alkylresorcinols as biomarkers of whole grain wheat and rye intake: plasma concentration and intake estimated from dietary records. *Am J Clin Nutr*. 2008;87(4):832–838.
152. Linko AM, Adlercreutz H. Whole grain rye and wheat alkylresorcinols are incorporated into human erythrocyte membranes. *Br J Nutr*. 2005;93(1):11–13.
153. Ross AB, Aman P, Kamal-Eldin A. Identification of cereal alkylresorcinol metabolites in human urine-potential biomarkers of wholegrain wheat and rye intake. *J Chromatogr B Anal Technol Biomed Life Sci*. 2004;809(1):125–130.
154. Ross AB, Kamal-Eldin A, Aman P. Dietary alkylresorcinols: absorption, bioactivities, and possible use as biomarkers of whole grain wheat- and rye-rich foods. *Nutr Rev*. 2004;62(3):81–95.
155. Prasain JK, Carlson SH, Wyss JM. Flavonoids and age-related disease: risk, benefits and critical windows. *Maturitas*. 2010;66(2): 163–171.
156. Heim KE, Tagliaferro AR, Bobilya DJ. Flavonoid antioxidants: chemistry, metabolism and structure-activity relationships. *J Nutr Biochem*. 2002;13(10):572–584.
157. Ostertag LM, O'Kennedy N, Kroon PA, Duthie GG, de Roos B. Impact of dietary polyphenols on human platelet function—a critical review of controlled dietary intervention studies. *Mol Nutr Food Res*. 2010;54(1):60–81.
158. Kris-Etherton PM, Lefevre M, Beecher GR, Gross MD, Keen CL, Etherton TD. Bioactive compounds in nutrition and health research methodologies for establishing biological function: the antioxidant and anti-inflammatory effects of flavonoids on atherosclerosis. *Ann Rev Nutr*. 2004;24:511–538.
159. Lopez-Lazaro M. Flavonoids as anticancer agents: structure-activity relationship study. *Curr Med Chem Anticancer Agents*. 2002; 2(6):691–714.
160. Thompson LU, Robb P, Serraino M, Cheung F. Mammalian lignan production from various foods. *Nutr Cancer*. 1991;16(1):43–52.
161. Kilkkinen A, Valsta LM, Virtamo J, Stumpf K, Adlercreutz H, Pietinen P. Intake of lignans is associated with serum enterolactone concentration in Finnish men and women. *J Nutr*. 2003; 133:1830–1833.
162. Adolphe JL, Whiting SJ, Juurlink BH, Thorpe LU, Alcorn J. Health effects with consumption of the flax lignan secoisolariciresinol diglucoside. *Br J Nutr*. 2010;103(7):929–938.
163. Saarinen NM, Warri A, Airio M, Smeds A, Makela S. Role of dietary lignans in the reduction of breast cancer risk. *Mol Nutr Food Res*. 2007;51:857–866.
164. Rudowska I. Plant sterols and stanols for healthy ageing. *Maturitas*. 2010;66:158–162.
165. Nystrom L, Paasonen A, Lampi A, Piironen V. Total plant sterols, steryl ferulates and steryl glycosides in milling fractions of wheat and rye. *J Cereal Sci*. 2007;45:106–115.
166. Trautwein EA, Demonty I. Phytosterols: natural compounds with established and emerging health benefits. *OCL Oleagineux Corps Gras Lipides*. 2007;14(5):259–266.
167. Woyengo TA, Ramprasath VR, Jones PJH. Anticancer effects of phytosterols. *Eur J Clin Nutr*. 2009;63(7):813–820.
168. Nurmi T, Nyström L, Edelmann M, Lampi AM, Piironen V. Phytosterols in wheat genotypes in the Healthgrain Diversity Screen. *J Agric Food Chem*. 2008;56(21):9710–9715.