Food & Function

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Cite this: DOI: 10.1039/c1fo10165j

www.rsc.org/foodfunction

REVIEW

Whole grain cereals: functional components and health benefits

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Received 18th August 2011, Accepted 4th November 2011
DOI: 10.1039/c1fo10165j

Cereal-based food products have been the basis of the human diet since ancient times. Dietary guidelines all over the world are recommending the inclusion of whole grains because of the increasing evidence that whole grains and whole-grain-based products have the ability to enhance health beyond the simple provision of energy and nutrients. In this review we will examine the main chemical components present in whole grains that may have health enhancing properties (dietary fiber, inulin, beta-glucan, resistant starch, carotenoids, phenolics, tocotrienols, and tocopherols) and the role that whole grains may play in disease prevention (cardiovascular diseases and strokes, hypertension, metabolic syndrome, type 2 diabetes mellitus, obesity, as well as different forms of cancer). The knowledge derived from the functional properties of the different chemical components present in whole grains will aid in the formulation and development of new food products with health enhancing characteristics.

Currently, the scientific knowledge regarding nutrition, diet, and the effect of specific components on human health has reached unprecedented levels. Although the information we need to select an appropriate diet that includes all the important nutritional factors is available, we are witness to a time of increased global obesity with a significant increase of cardiovascular (coronary heart disease, hypertension, and strokes) and metabolic diseases (type 2 diabetes, metabolic syndrome, and insulin resistance). The consensus among healthcare professionals is that we need to

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select high-fiber diets which are rich in grains, fruits, and vegetables. Also, we need to regulate the type of fat to be consumed (less saturated fat, more polyunsaturated ones) and increase energy expenditure through moderate cardiovascular exercise.[1]

Cereal-based food products have been the basis of the human diet for a long time. Cereals contain all the macronutrients (proteins, fats, and carbohydrates) we need for support and maintenance. They are an excellent source of minerals, vitamins, and other micronutrients required for adequate health. However, most cereals, particularly in the western hemisphere, are consumed after milling. Milling involves the removal of the outer layers of the grain (bran and germ) and the preservation of the starch-rich white endosperm. But in so doing, milling takes out the key components from cereals, since those outer layers of the grain are rich in vitamins, minerals, fiber, phytochemicals, and many other nutrients. This removal of the key components from cereal grains may be preventing us from becoming aware of the enormous health-enhancing properties of cereals.

There is an increased amount of evidence showing that consumption of whole grains (WG) and whole-grain-based products is associated with a reduction of the risk of developing many diseases, including cardiovascular diseases,[2–4] hypertension,[5,6] strokes,[7,8] metabolic syndrome and type 2 diabetes,[9–11] and different types of cancer.[12,13] Although cereals, and particularly the carbohydrates they contain, have been implicated as part of the problem in the current obesity epidemic, studies show that WG consumption can aid in weight management.[14–17]

It is becoming evident that WGs have the ability to enhance health beyond the simple provision of major nutrients and energy. The objective of this work is to review the main functional components of WGs and their health benefits. We will start with a review of the main chemical components that may exert functional effects and then progress towards examining the effects that those functional components have on human health.

1. What are whole grains?

The starting point to review the functional components of WG cereals and their health related benefits is to provide as precise a definition as possible about WGs. Perhaps the most concise definition of WGs is that given by the American Association of Cereal Chemists International (AACCI). In 1999, the AACCI issued a formal definition of WGs:[18] "whole grains shall consist of the intact, ground, cracked, or flaked caryopsis (kernel or seed), whose principal anatomical components—the starchy endosperm, germ, and bran—are present in the same relative proportion as they exist in the intact caryopsis." However, in 2006, the AACCI WGs Task Force broadened the definition of WGs to include pseudocereals[19] (Table 1). Pseudocereals were included because they have an overall macronutrient composition similar to that of cereals and because they are used in the same traditional ways as cereals. Also, some traditionally and minimally processed forms of WGs—such as lightly pearled barley or wheat, bulghur, and mixtamalized corn—are considered WGs.[19] The AACCI is moving towards setting a new definition of WGs that may acknowledge the use of minimal processing to enable good manufacturing practices and enhance food safety of WGs.[20]

2. Carbohydrate functional components

2.1. Dietary fiber

The carbohydrates present in WGs can broadly be divided into two groups, based on the ability of the human digestive system to digest them. Starch is the only complex carbohydrate in WGs that can be digested (due to the presence of α-amylase in the human digestive system). The small intestine enzymes are unable to digest any of the other complex carbohydrates present in WGs. Non digestibility is at the basis of the definition of dietary fiber:[21] "dietary fiber is the edible parts of plants or analogous carbohydrates that are resistant to digestion and absorption in the human small intestine with complete or partial fermentation in the large intestine." Non digestible complex polysaccharides are formed by oligosaccharides (OS) and non-starch polysaccharides (NSP). Whole grains NSPs have been further classified into two major groups based on their solubility in water. Thus, soluble and insoluble NSP, or "soluble fiber" and "insoluble fiber" as they are usually called are recognizable fractions of dietary WG polysaccharides that have shown to be related to physiological effects on humans.

The definition of dietary fiber by the AACCI[21] includes the chemical components that form this carbohydrate fraction of WGs: "dietary fiber includes polysaccharides, oligosaccharides, lignin, and associated plants substances". In addition, the definition of dietary fiber highlights the most documented physiological effects of dietary fiber:[21] "dietary fibers promote beneficial physiological effects including laxation, and/or blood cholesterol attenuation, and/or blood glucose attenuation." It should be kept in mind that at the time the definition was elaborated only the most well-known and documented health benefits were included in it.

2.2. Inulin

Inulin is a mixture of fructose chains (2–60 units) linked by β-(2–1) glycosidic linkages (Fig. 1) with a terminal glucose molecule.[22] Because of the β-configuration of the anomeric C2 in their fructose monomers, inulin resists hydrolysis by intestinal digestive enzymes. Thus, they are non-digestible and are part of the dietary fiber. Several edible plants (chicory, leek, onions, garlic, bananas, and cereals) have a natural high content of inulin. Among cereals, wheat, barley, and rye have high contents of inulin oligosaccharides.[23] Wheat is the primary source of inulin (69%) in the American diet.[24] Inulin is a prebiotic, it stimulates the growth of healthy intestinal bacteria (probiotics).[25]

2.3. β-Glucan

β-Glucan, also known as (1,3;1,4)-β-glucan, is a general term used to describe a group of complex carbohydrates made of linear polymers of glucose units joined together by β-(1–4) and β-(1–3) glycosidic bonds. The proportion of these β-(1–4) and β-(1–3) linkages is 70% and 30%, respectively. Together with cellulose, hemicelluloses, and other carbohydrates, β-glucan is a common component of cell walls in cereal grains.[26] The presence of the β-(1–3) bonds within the molecule makes β-glucan more flexible, soluble, and viscous, as opposed to a rigid and insoluble polymer containing only β-(1–4) bonds (cellulose).

Table 1 Cereals and pseudocereals[18,19]

True cereals	Botanic name	Pseudocereals	Botanic name
Wheat	*Triticum* spp.	Amaranth	*Amarantus caudatus*
Corn	*Zea mays*	Quinoa	*Chenopodium quinoa* Willd.
Rice	*Oryza* spp.	Buckwheat	*Fagopyrum* spp.
Barley	*Hordeum* spp.		
Oats	*Avena* spp.		
Millets	*Brachiarya* spp., *Pennisetum* spp., *Panicum* spp., *Paspulum* spp., *Eleusine* spp., *Echinochloa* spp.		
Sorghum	*Sorgum* spp.		
Triticale	*Triticale*		
Teff	*Eragostris* spp.		
Canary seed	*Phalaris arundinacea*		
Jobs tears	*Coix lachrymal-jobi*		
Fonio, Black fonio, Asian millet	*Digitaria* spp.		
Wild rice	*Zizania aquatica*		
Rye	*Secale cereale*		

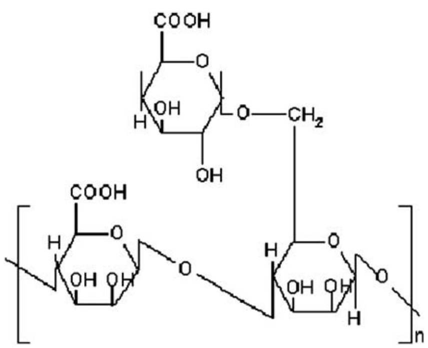


Fig. 1 Inulin structure.

Microfibrils of cellulose constitute the reinforcing rods of cell walls, while the non cellulosic polysaccharides (which include β-glucan) form a gel-like matrix structure in cell walls which provides the flexibility needed by plant tissues.[27] Results from research on oat β-glucan has shown a lowering blood cholesterol effect.[28] In fact, the Federal Drug Administration approved in 1997 the health claims that consumption of 3 g day^{-1} of β-glucan soluble fibers reduce blood cholesterol levels.[29]

2.4. Resistant starch

Starch is a polymer of glucose units joined together by α-(1–4) bonds. However, some (3–6%) are α-(1–6). There two distinct structural components in starch: amylose and amylopectin. Amylose is essentially linear (although some branching may occur) containing 10 000–100 000 glucose residues. Amylopectin molecules are larger than amylose containing 200 000 to 1 000 000 glucose units. The amylopectin molecule is branched by means of the occasional occurrence of α-(1–6) glycosidic bonds.[30] Starch is degraded by α-amylases present in saliva and pancreatic juice.[31] However, not all starches are easily digested. Some of them seem to be "resistant" to amylolysis. More specifically, resistant starch (RS) has been defined as the sum of starch and starch degradation products not absorbed in the small intestine of healthy individuals.[32] There are four types of RS based on the factor that makes it resistant: RS1 (physically inaccessible trapped starch found in seeds, legumes and unprocessed cereal grains), RS2 (natural raw and ungelatinized starch granules resistant to digestion), RS3 (retrograded starch formed when starch present is food is heated and cooled), and RS4 (chemically modified starches).[33,34] RS passes through the small intestine and reaches the large intestine where it serves as a substrate for fermentation by the colonic microflora. The production of short-chain fatty acids in this fermentation process is associated with the health benefits of resistant starch.[35]

3. Non-carbohydrate functional components

3.1. Carotenoids

Carotenoids refer to a group of pigments synthesized by plants and microorganisms but not animals.[36] Fruits and vegetables are the major sources of these compounds in humans.[37] Carotenoids are responsible for red, yellow, and orange colors in fruits, vegetables and WGs, and have recently received much attention due to their antioxidant properties.[36,38] More than 600 carotenoids are present in nature. However, only 40 are present in the

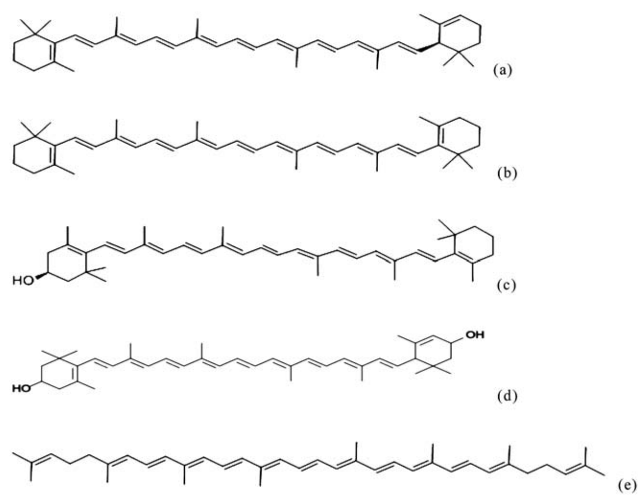


Fig. 2 Structure of carotenoids: (a) α-carotene, (b) β-carotene, (c) cryptoxanthin, (d) lutein, and (e) lycopene.

human diet.[38] Nearly 90% of the carotenoids in the human diets are β-carotene, α-carotene, lycopene, cryptoxanthin, and lutein (Fig. 2).[36]

Structurally, carotenoids have a long conjugated chain of double bonds, in which the isoprene units repeat. One or both ends of the molecule may or may not be cyclised or may have oxygen-related functional groups. Lycopene (Fig. 2e) represents an acyclised carotenoid, while β-carotene represents a cyclised one. β-Cryptoxanthin and lutein possess hydroxyl (–OH) groups at one or both ends.[39]

Common carotenoids found in WGs include α- and β-carotene, β-cryptoxanthin, zeaxanthin, and lutein.[40,41] Although vegetables and fruits are the principal sources of carotenoids in human diets, WGs are being increasingly recognized as an important source of these phytochemicals. Many biological activities have been ascribed to carotenoids in the prevention of chronic diseases, including the prevention of cardiovascular disease and different types of cancer.[42–45]

3.2. Phenolic acids

Phenolics are compounds characterized by the presence of one or more aromatic rings with one or more hydroxyl groups. Phenols, phenolic acids and flavonoids (Fig. 3) are all phenolics. Chemically, phenolic acids are derivatives of benzoic and cinnamic acids (Fig. 4). The difference among these derivatives is the type and number of functional groups substituted on the aromatic ring. Common phenolic acids found in whole cereal grains include ferulic acid, vanillin acid, caffeic acid, syringic acid, and *p*-coumaric acids.[46] The most common phenolic acid compound in whole grains is ferulic acid,[47] which is present abundantly in the pericarp, aleurone, and embryo but only minimally in the starchy endosperm of the cereal grain.[48] Ferulic acid can be found free, conjugated (soluble), or bound (insoluble) in whole cereal grains (corn, rice, wheat, oats, rye).[49]

Health benefits of phenolic acids are generally associated with their antioxidant activity. The conjugated double bond of the aromatic ring is responsible for the phenolic acids antioxidant capacity.[50] Hydroxycinnamic acid derivatives (ferulic acid and caffeic acid) have excellent radical scavenging ability.[51] These derivatives have also shown antioxidant capabilities in other oxidation models, such as liposome and LDL (low density lipoprotein) systems.[52,53]

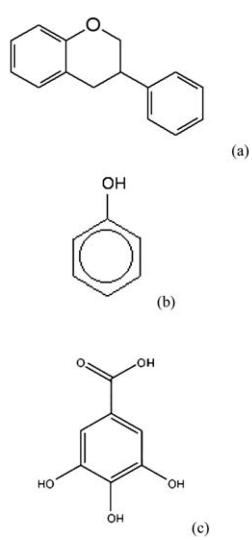


Fig. 3 Structure of common phenolic compounds: (a) flavonoids (b) phenols, and (c) phenolic acids.

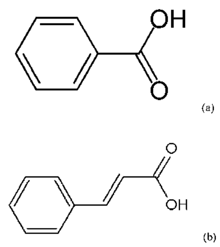
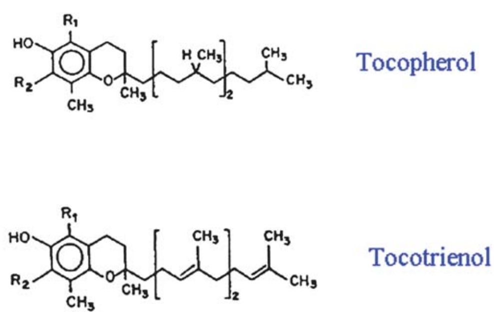


Fig. 4 Structure of (a) benzoic acid (b) cinammic acid.

3.3. Vitamin E

Vitamin E comprises a group of eight lipophilic compounds with similar structures. The basic chemical backbone of natural vitamin E compounds is a polar chromanol head (6-hydroxylchroman group) with a long isoprenoid side chain. Two distinctive groups of vitamin E compounds can be found in nature: tocopherols and tocotrienols. Tocopherols contain a side phytyl chain while tocotrienols contain a geranylgeranyl chain.[54] Among each group, α-, β-, δ-, and γ-types of structures can be found based on the position at which the chroman group is methylated (Fig. 5). A free hydroxyl group is present in both trienols and tocopherols. This free OH group is responsible for the antioxidant activity of vitamin E.[38] The ability of α-tocopherol to scavenge free radicals is the greatest among tocopherols, followed by γ-, β-, and δ-tocopherols.[55] The health benefits of vitamin E is associated with its antioxidant activity. However, there are non-antioxidant functional benefits of vitamin E. Recent studies suggest the potential of tocopherols as a gene regulator.[56]



	R1	R2
Alfa	CH_3	CH_3
Beta	CH_3	H
Gamma	H	CH_3
Delta	H	H

Fig. 5 Basic structures of tocopherols and tocotrienols.

4. Whole grain cereals and health

4.1. Hypertension

Different epidemiological, cohort, and intervention studies[57–66] have shown that a high consumption of whole-grain cereals is associated with a reduced risk of hypertension.

In a small (18 people) randomized, controlled, pilot study[57] that lasted six weeks, researchers looked at the effect of oat consumption on mild and borderline hypertensive patients. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) effects, as well as other biochemical parameters (blood lipids, fasting glucose, and insulin levels), were measured. People were randomly assigned to two groups: the cereal treatment group (CT), who ingested 5.52 g day^{-1} β-glucan from oats, and the low cereal control group (LCC), who consumed less than 1 g day^{-1} of total fiber. Blood pressure was measured weekly over the 6-week period. Overall, the CT group had a reduction in SBP of 7.5 mm Hg (average) which was statistically significant ($P < 0.01$) while DBP was reduced to 5.5 mm Hg. The control group did not show any change in SBP or DBP values. Other small studies,[58,59,60] have shown inconclusive results.

Dietary modifications that helped reduce blood pressure were explored in what has been known as the Dietary Approach to Stop Hypertension (DASH) trial.[57,58] Among the dietary modifications of the DASH study, increasing consumption of whole grains was one of them.[61,62] However, the blood pressure reduction observed may have been an overall effect of many dietary modifications (increased exercise, sodium reduction, *etc.*).

A prospective multi-center cohort study[63] involving 3588 men and women, free of cardiovascular diseases (CVD) at the baseline (1989–1990), examined the effect of fiber consumption (from vegetables, fruits, and whole-grain cereals) on the development of CVD in elderly patients (65 and older). Although the main outcome of the study was the evaluation of combined CVD, hypertension was measured (hypertension is a known risk factor for CVD). Systolic blood pressure was reduced by only 3 mm Hg in this elderly population study when the consumption of cereal fiber was increased from <1.7 g day^{-1} to <6.3 g day^{-1} (this amounts to two additional slices of whole-grain bread per day).

In a population-based cross sectional study,[64] carried out in Iran and involving 827 participants the relationship between hypertension risk and whole grain intake was evaluated. After adjusting for different factors, a statistically significant decreasing trend was observed in the hypertension risk factor when whole grain intake was increased. The hypertension risk factor went from 1.0 (reference, lowest amount of whole grains consumed, equivalent to less than 6 g day^{-1}) to 0.84 for the high whole grain intake group (229 g day^{-1}).While the hypertension risk factor increased dramatically (from 1.0 to 1.69) when the intake of refined grains was incremented.

The Women's Health Study (WHS)[6] involved 39 876 female professional women who were free of CVDs at the baseline (1992–1995). After excluding 10 317 women with self reported hypertension at the baseline, it was found that women who reported eating at least 4 servings of whole-grain cereals per day had a 11% reduction in the hypertension risk when compared to those women who ate less than 0.5 servings per day (after adjusting for lifestyle, clinical, and dietary factors). Increasing ingestion of refined grains did not affect the hypertension risk according to this study.

4.2. Cardiovascular disease and strokes

Cardiovascular disease (CVD) is responsible for 1 out of 3 deaths worldwide and is the leading cause of death in the industrialized world.[65] The World Health Organization (WHO) is warning about the rise of CVD in developing countries.[66] Epidemiological and clinical evidence has been gathered suggesting a reduced risk of developing CVD with increased intake of WGs.[67] More than three-hundred subjects were followed for 10–20 years in their dietary habits and heart diseases (HD) risk.[68] It was concluded that HD risk was reduced due to a high intake of cereal fiber (pectin and other vegetable fiber sources did not have an effect on HD risk). A meta-analysis, about the cholesterol-lowering effects (cholesterol is a marker for CVD) of dietary fiber, established small but significant effects of high-fiber diets on cholesterol levels.[69]

In 1992, Fraser *et al.*[70] showed that individuals who consumed wheat bread (whole-wheat bread) experienced a 55% reduction in the risk of myocardial infarction as compared to those who ate white bread (made of refined white wheat flour). Five prospective studies that evaluated WG consumption and CVD risk showed that higher intake of WGs accounted for a 25% lower risk of cardiovascular events.[71]

The beneficial effects of WGs on CVD have been established by large prospective studies such as the Iowa Women's Health Study (IWHS),[72] the Nurses Health Study (NHS),[72] the Norwegian County Study (NCS),[73] the Physician's Health Study (PHS),[74] and the Health Professionals Follow-up Study (HPFS).[75] For example, in the NHS trial[72] 68 000 women (aged 37–64) were followed for 10 years. Among other things, a link between WGs and CVD risk was examined. After adjusting for age, CVD risk factors, dietary factors, and other factors, it was found that only cereal fiber was strongly associated with a reduced risk of developing coronary heart disease (CHD). A 5 g day^{-1} increase in cereal fiber reduced the total multivariate risk of developing CHD from 0.88 to 0.63. In the IWHS involving more than 34 000 women, the mortality level from CHD was lower for the high cereal fiber intake group.[72]

For the elderly (a particularly high CVD risk population) the positive effects of WGs have been shown.[76] After an 8-year follow-up participants in the highest quintile of cereal fiber intake had 21% lower risk of CVD. Fruits and vegetables did not exert the same benefit. Post-menopausal women who consumed only 1 serving of WG per day experienced better internal coronary artery diameter.[77] More recently, a study[78] showed that arterial stiffness was reduced significantly in the intact whole grain treatment group. This group ingested 48 g of intact WGs daily. Another group of participants who consumed either 48 g of milled WGs or 48 g of refined grain (grains were fiber-rich fractions have been removed) experienced no changes in arterial stiffness.

The type of WG ingested may have a definite effect of cardiovascular disease. Haldar *et al.*[79] found that rye was more effective in reducing blood cholesterol (a CVD risk factor) than wheat (both groups ate 48 g of WG per day for four weeks). This study suggests that other factors or components may account for CVD risk reduction besides fiber.

Due to the high association that exists between CVD and strokes, it is easy to understand the positive correlation between WG ingestion and strokes (see for example the study we referred to before according to which a 55% reduction in the risk of myocardial infarction was associated to WG consumption).[70] Large epidemiological studies[7,8,80] have also shown that WGs consumption reduces the risk of strokes. In the NHS trial 36% decrease in total stroke risk as observed in the higher cereal fiber intake groups. Hemorragic stroke risk was reduced by 50%.

4.3. Type 2 diabetes mellitus

Epidemiological studies have repeatedly shown that the risk for diabetes mellitus type II (T2DM) decreases with the increase in consumption of whole grains.[32,81] An inverse relationship has also been found between the consumption of cereal fiber and T2DM.

Large long-term studies,[82,83] involving 90 000 women and 45 000 men, have shown that groups with the highest intake of cereal fiber had 30% less risk of developing T2DM than the group with the lowest intake. Additionally, the IWHS (35 000 participants) showed that women who consumed refined cereals had a 57% increased risk of T2DM when compared with those who consumed larger amounts of whole grains.[73] The Health Professionals Follow-up Study (HPFS), a research study that followed 42 898 men, found an associated 37% lower risk of T2DM with consumption of approximately 3 servings of whole grain per day.[84] A cohort study,[85] reported an inverse relationship between whole grain and cereal fiber intake and risk of T2DM. Other studies[86,87] have similar results. However, in a recent review[88] the authors concluded that although large prospective studies are showing a reduced risk of developing T2DM in people who consume more WGs foods (27–30%) or cereal fiber (38–37%), evidence from prospective cohort trials is weak and cannot validate a definite conclusion of the preventive effect of WGs on the development of T2DM.

Some feeding studies[89,90] have been carried out to investigate the relationship between WGs consumption and diabetes. One study[89] fed participants with different cereal products: breads made with rye seeds or pumpernickel flour containing concentrated oat β-glucan, dark durum wheat pasta and wheat bread made with white wheat flour. The study showed that the shape and structure of food products may be important in the glucose response to them. Another study[90] examined whether intake of whole grains and dietary fiber was associated with indicators of systemic inflammation among[91] women with diabetes. They suggest that consumption of WGs with low glycemic index may reduce systemic inflammation among women with type 2 diabetes.

4.4. Weight management

Seventy percent of all American adults are either overweight or obese.[91,92] Rates of overweight and obese people are increasing in both industrialized and developing countries. Epidemiologic studies have shown that there is an inverse relationship between whole grain consumption and the change of certain obesity markers such as body mass index (BMI), waist circumference (WC), and/or abdominal adiposity in both women and men.[93–97] Small studies based on food frequency recall procedures have also established the inverse relationship between WG intake and BMI and WC.[10,14,98] However, some studies have failed to show any significant relationship between WGs and obesity.[99,100] Perhaps confounding factors (fiber content) and the effect of other lifestyle choices (people who eat more WGs are more likely to make other healthy choices, such as exercise more, and eat more low fat food) may be responsible for not knowing exactly the effect of WGs on weight management.

4.5. Cancer

The association of WG ingestion and cancer has been evaluated in the past and continues to be an issue of debate among the scientific community. There is scientific evidence that backs the idea that ingesting WGs reduces the risk of cancer. In a meta-analysis study,[101] it was found that 95% of the studies included in the analysis (43 out of 45, after adjusting for flawed design) mentioned the protective effect of WGs intake against the following types of cancer: colorectal cancer and polyps, gastric cancers, other digestive tract cancers, hormone-related cancers, pancreatic cancers, and "other" types of cancer.

Case-control studies in Italy[102] found that higher whole grain consumption (such as whole-grain bread and pasta) was associated with cancer risk reduction. Large epidemiological studies, such as the EPICN (European Prospective Investigation into Cancer and Nutrition),[103] with an $n = 519\,978$ have also shown cancer risk reduction. In this study a 25% risk reduction of large bowel cancer was observed in participants located in the group which consumed the most cereal fiber. The Pooling Project,[104] with an n of 725 628, showed a 16% risk reduction in the United States. Also, the National Institutes of Health-ARRP Diet and Health Study[105] ($n = 294\,998$ men and 197 623 women) found a 21% reduction in the risk.

The reduction in risk associated with WGs was stronger for rectal cancer and less strong for colon cancer, although previous epidemiological studies[106] had shown an inverse relationship between WG consumption and colorectal cancer. The Swedish Mammography Cohort Study ($n = 61\,433$)[106] reported that women who ate more than 4.5 servings per day of WGs had lower risk of developing colon cancer, but not rectum cancer (as compared to those who ate less than 1.5 servings per day). More recently[107] it was found that WG consumption relates inversely to colorectal risk but the effect of WGs was small.

The relationship between WGs and other types of cancer (breast cancer, pancreatic cancer, oral and pharyngeal cancer, *etc*) is less studied[108–110] and results are often conflicting.

5. Proposed biological mechanisms for whole grain protective effects

The preceding sections have shown that WGs are rich in a great variety of chemical compounds that may have protective effects against several chronic illnesses such as cardiovascular disease, hypertension, diabetes, different types of cancer, and obesity. Fig. 6 summarizes functional components with known health effects.

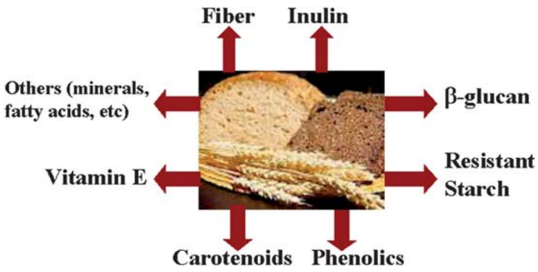


Fig. 6 Phytonutrients of whole grains.

In this section we will examine some of the proposed mechanisms that may explain the protective effect of WGs. Although these mechanisms are proposed based on studies in which one component is isolated and tested (the "magic bullet approach")[111] readers should be aware that the protective effects of WGs consumption may go beyond what would be estimated by considering the addition of the effects of each individual component[112] suggesting that synergistic effects and interactions between these components may be as important (or perhaps more important) than the individual effects.

5.1. Hypertension

Whole grains are rich in fiber and fiber has shown to improve the lipid profile in obese men and women[60] and to lower systolic and diastolic hypertension.[113] In addition, many other components present in cereals (magnesium, potassium, and certain proteins) have shown to be helpful in lowering blood pressure.[114] Vascular reactivity response may be improved by whole grains ingestion contributing to a better blood pressure down-regulation.[115]

Gene expression of known inflammatory markers (such as interleukin-IL-10) may be attenuated by WG ingestion[116] while the expression of anti-inflammatory markers (such as adiponectin) may be induced by whole grains.[117] These and many other mechanisms acting in tandem may explain the known beneficial effects of WGs on hypertension.

5.2. CVD and strokes

Since hypertension is a known risk factor for CVD and strokes, it is plausible to say that those mechanisms will be possible mechanisms in the protection of the heart and in the prevention of CVD and strokes. Additionally, dietary fiber, *per se*, may have direct effects on serum cholesterol[118] and being cholesterol another risk factor for CVD it is highly possible to state that fiber may have beneficial effects on heart related diseases. Some of these mechanisms include: the fermentation of β-glucans in the gut,[118] the fermentation of certain WG,s carbohydrates in the colon with the subsequent production of short-chain fatty acids that may inhibit the synthesis of cholesterol in the liver,[119] and the reduction of serum tryglicerides (another known risk factors for CVD and strokes).[120]

The high content of antioxidants present in WGs may also explain the beneficial effects on the cardiovascular system. Phenolics in grains may inhibit platelet aggregation and LDL cholesterol oxidation,[121] two known risk factors in CVD. Vitamin E (tocotrienols and tocopherols), another potent group of antioxidants present in WGs, protects cell membranes from oxidative damage.[122]

5.3. Type 2 diabetes mellitus

There are several proposed mechanisms about the effect of WGs, components on diabetes. One of them is related to the ability of WGs to decrease insulin resistance[123,124] and improve insulin sensitivity.[125] The exact mechanism is not defined yet but attention has been given to the fact that WGs have low values of the glycemic index (GI).[126,127] Lower serum glucose levels and decreased insulin production have been observed after consumption of low GI products in both obese and non obese people.[128]

Two other mechanisms that may help explain the protective effects on diabetes mellitus patients are: improvement in glucose tolerance[129,130] and the high concentration of magnesium in WGs.[131]

5.4. Cancer

Whole grains have a high content of fermentable carbohydrates (dietary fiber, resistant starch, and oligosaccharides). It is a known fact that dietary fiber increases fecal bulk and decreases transit time[132] reducing, thus, the chance of mutagens to interact with gut epithelial cells. WG oligosaccharides (such as inulin) act as prebiotics.[23] Oligosaccharides in human studies[133,134] have been shown to alter the gut microflora increasing bifidobacteria and decreasing dangerous microorganisms such as *E. coli* and clostridia.

Fermentation of dietary fiber produces short-chain fatty acids such as butyrate that has shown to be antineoplastic.[135] Moreover, butyrate is able to cause aberrant cells to apoptose.[136] Short-chain fatty acids also decrease the colonic pH, which is associated[137] with lower carcinogenic potential.[138]

Since WGs have a high content of antioxidant compounds it has been proposed that these may have direct protective effects on colonic cell from reactive oxygen species and other damaging radicals.[139] Phytic acid, vitamin E and phenolics may all inhibit the formation of carcinogens from precursor compounds. Phytic acid is able to chelate various metals inhibit iron-redox damaging reactions.[140] Phenolics may induce detoxification systems.[122]

5.5. Weight management

It is difficult to point out a specific mechanism by which WGs may benefit weight control or weight reduction. The issue of body weight control is very complex and beyond the scope of this review. Additionally, consumption of WGs is highly associated with the adoption of other healthy habits (such as increase of consumption of fruits and vegetables, increase in physical activity, *etc.*) that may act concomitantly with the beneficial effects of WGs.

Despite these issues a number of mechanisms have been proposed as to why WGs are beneficial in weight management. Invariably, these mechanisms have something to do with dietary fiber and the effect of WGs on satiety.

It has been proposed that diets rich in WGs offer greater food volume and lower energy density which may reduce hunger and increase satiety.[141] Adequate levels of dietary fiber may increase the secretion of gut hormones that in turn may increase satiety.[141,142] β-Glucan dietary fiber and resistant starch have shown to decrease the glycemic response.[143] Additionally, reduced levels of known markers of obesity (leptin, insulin, and C-peptide) are associated with increased levels of ingestion of WGs.[144]

6. Final remarks

Scientific evidence shows that regular intake of WGs reduces the risks associated with many diseases, including cardiovascular diseases and strokes, hypertension, metabolic syndrome and diabetes, as well as different forms of cancer. Because of the great variety of functional components present in WGs (dietary fiber, inulin, glucans, resistant starch, phenolics, carotenoids, vitamin E, *etc.*) there is a need to identify which of these components may have the most protective effect for specific diseases so appropriate food products can be formulated to include these potentially protective chemical compounds. There is a great variety of plausible mechanisms by which WGs may have beneficial effects on certain diseases. These mechanisms are postulated on the basis of single functional components effects and rarely examine the possible synergistic and interaction effects that these components may have.

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