Critical Reviews in Food Science and Nutrition

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/bfsn20

Whole grain cereals: the potential roles of functional components in human health

Huiqin Guo, Haili Wu, Amin Sajid & Zhuoyu Li

CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
https://doi.org/10.1080/10408398.2021.1928596

Taylor & Francis
Taylor & Francis Group

REVIEW

Whole grain cereals: the potential roles of functional components in human health

Huiqin Guo[a], Haili Wu[b], Amin Sajid[a], and Zhuoyu Li[a,b]

[a]Institute of Biotechnology, The Key Laboratory of Chemical Biology and Molecular Engineering of Ministry of Education, Shanxi University, Taiyuan, PR China; ; [b]College of Life Science, Shanxi University, Taiyuan, PR China

ABSTRACT
Whole grain cereals have been the basis of human diet since ancient times. Due to rich in a variety of unique bioactive ingredients, they play an important role in human health. This review highlights the contents and distribution of primary functional components and their health effects in commonly consumed whole grain cereals, especially dietary fiber, protein, polyphenols, and alkaloids. In general, cereals exert positive effects in the following ways: 1) Restoring intestinal flora diversity and increasing intestinal short-chain fatty acids. 2) Regulating plasma glucose and lipid metabolism, thereby the improvement of obesity, cardiovascular and cerebrovascular diseases, diabetes, and other chronic metabolic diseases. 3) Exhibiting antioxidant activity by scavenging free radicals. 4) Preventing gastrointestinal cancer *via* the regulation of classical signaling pathways. In summary, this review provides a scientific basis for the formulation of whole-grain cereals-related dietary guidelines, and guides people to form scientific dietary habits, so as to promote the development and utilization of whole-grain cereals.

KEYWORDS
Cereals; nutrients; function components; bioactivities; chronic disease prophylaxis

Introduction

Cereals are the main crop and the most common staple food for populations around the globe (Luithui, Baghya, and Meera 2019). The planting area for cereals accounts for more than 73% of the total world harvested area. At present, the main economic grains are wheat, rice, corn, barley, sorghum, millet, and oats (Nations and Latham 1997). Over the long haul, cereals are known for their rich in nutrients and pharmacological properties and are the primary source of dietary nutrition that forms the basis of our daily diet. Cereals provide 70–80% carbohydrate, 7.5–15% protein, less fat, about 1–4%, minerals approximately 1.5–3% which are mainly phosphorus and calcium, mostly in the form of phytate and minimal vitamins, which are beneficial to human health (Gong et al. 2018; McKevith 2004; Nicole et al. 2014). In contrast, with the continuous improvement in men's living standards, the intake of animal source foods has been gradually increasing than that of cereals, which makes the diet unbalanced and leads to a wide range of pathological conditions, recently (Eckel, Grundy, and Zimmet 2005; Givens 2005; Richter et al. 2015).

Grains occupy an important position in the diet as they meet the needs of most vital nutrients, such as proteins, minerals, vitamins, and fiber, however, their proportion is varying in different grains (Table 1) (Charalampopoulos et al. 2002; Fao 1995; Shahidi and Chandrasekara 2013). Barley, for example, is one of the most abundant sources of carbohydrates (77.2/100 g edible portion), and its fiber content is as high as 15.6/100 g edible portion, compared to only 1.0 or 2.0/100 g edible portion of rice, wheat, sorghum, and corn (Knudsen 2014; Mckee and Latner 2000). Oats on the other hand, are rich in the protein (16.89 g), fat (5.93 g), and thiamin (0.76 mg) contents as well as energy (389 kcal) is higher than other cereals. Although the essential amino acids of grains, such as threonine, lysine, and tryptophan are limited, studies have shown that other amino acid composition of oats is comprehensive, rich in the eight essential amino acids required by human body, ranking first among cereals and being known as the champion of cereal protein (Wang et al; Wei et al. 2003). In addition, the calcium content (350 mg/100 g edible portion) in finger millet is over ten times higher than other similar grains (Fao 1995; Shahidi and Chandrasekara 2013). Iron contents are up to 18.6 mg/100 g edible portion in barnyard millet, followed by pearl millet 11.0 mg/100 g edible portion, considerably higher than Kodo millet (1.7 mg/100 g edible portion), and rice (1.8 mg/100 g edible portion).

It has been documented that grains, crude grains, or by-products are rich in phytochemicals including phenolic compounds, phytosterols, and β-glucans (Charalampopoulos et al. 2002; Chethan and Malleshi 2007b; Shi et al. 2015a). Increasing evidence from epidemiological and clinical studies have demonstrated that regular consumption of grains and grain foods not just simply provide energy and nutrients, but can effectively prevent a series of chronic diseases, including cardiovascular disease (CVD), type 2

CONTACT Zhuoyu Li lzy@sxu.edu.cn Institute of Biotechnology, The Key Laboratory of Chemical Biology and Molecular Engineering of Ministry of Education, Shanxi University, Taiyuan 030006, PR China.

Table 1. The primary nutritional contents of commonly consumed cereals.

Crops	Carbohydrate (g)	Protein (g)	Fat (g)	Fiber (g)	Energy (kcal)	Ca (mg)	Fe (mg)	P (mg)	K (mg)	Mg (mg)	Thiamin (mg)	Riboflavin (mg)	Niacin (mg)
Rice	76	7.9	2.7	1.0	362	33	1.8	221	400	140	0.41	0.04	4.3
Wheat	71	11.6	2.0	2.0	348	30	3.5	372	370	113	0.41	0.10	5.1
Barley	77.2	9.9	1.2	15.6	352	29	2.5	–	–	–	0.19	0.11	4.6
Oats	66.27	16.89	5.93	10.6	389	54	4.7	–	–	–	0.76	0.13	0.96
Corn	72.2	8.9	3.9	2.0	336	22	2.1	268	284	147	0.37	0.12	2.2
Sorghum	70.7	10.4	3.1	2.0	329	25	3.9	287	350	–	0.38	0.15	4.3
Pearl millet	67.0	11.8	4.8	2.3	363	42	11.0	–	–	–	0.38	0.21	2.8
Finger millet	72.6	7.7	1.5	3.6	336	350	3.9	–	–	–	0.42	0.19	1.1
Foxtail millet	63.2	11.2	4.0	6.7	351	31	2.8	–	–	–	0.59	0.11	3.2
Common millet	63.8	12.5	3.5	5.2	364	8	2.9	–	–	–	0.51	0.28	4.5
Little millet	60.9	9.7	5.2	7.6	60.9	17	9.3	–	–	–	0.41	0.09	3.2
Kodo millet	66.6	9.8	3.6	5.2	66.6	35	1.7	–	–	–	0.15	0.09	2.0
Barnyard millet	55.0	11.0	3.9	13.6	55	22	18.6	–	–	–	0.33	0.10	4.2

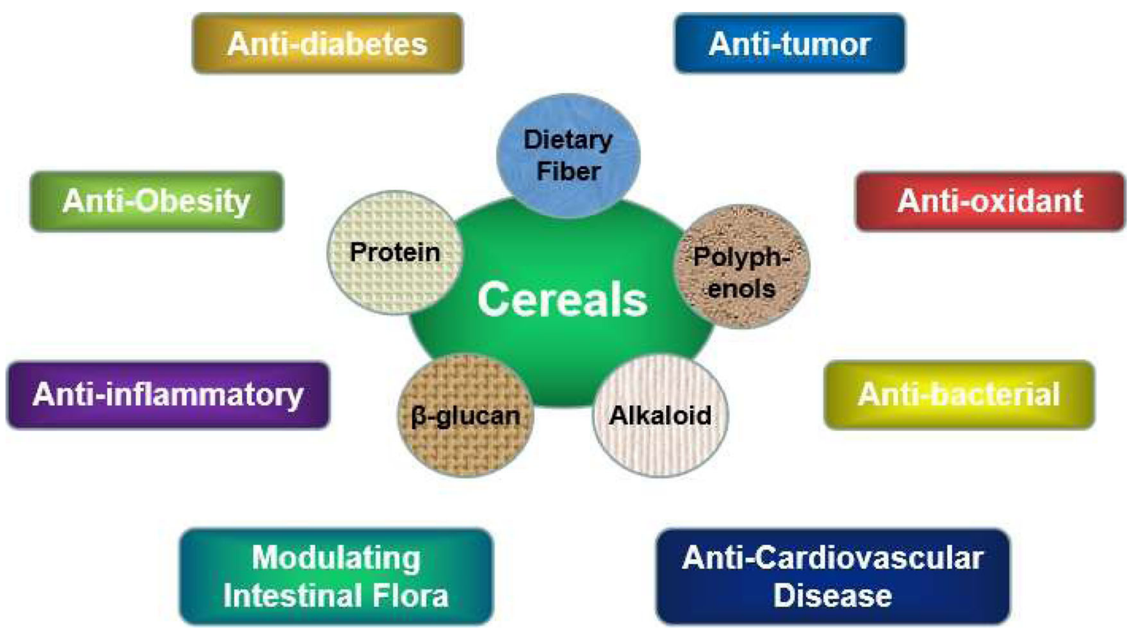

Figure 1. The bioactive components of cereals and the relationship to human health.

diabetes, gastrointestinal cancer, and obesity (Aune et al. 2016; Lattimer and Haub 2010). Taking into account the potential of grains against various diseases, the aim of this systematic review is to highlight the main bioactive components of cereals and their relationship to human health such as some chronic disease prophylaxis (Figure 1).

Main bioactive components of cereals

Dietary fiber

As early as 1953, Hipsley, a British epidemiologist, has first introduces the term "dietary fiber," which is plant fiber and cannot be absorbed by the human body (Fuller et al., 2016Slavi). In 2001, the Institute of Medicine food and Nutrition Committee defined the dietary fiber as a complex group of indigestible carbohydrates and lignin inherent in plants (Medicine 2001). About a decade ago, the Codex Alimentarius Commission has described the dietary fiber as a carbohydrate polymer with three or more monomers, which are neither digested nor absorbed in the human small intestine (Howlett et al. 2010). Dietary fibers on the basis of their solubility in water at a particular pH are divided into two categories: soluble fiber and insoluble fiber. Soluble fiber mainly refers to the storage substances and secretions in plant cells as well as some microbial polysaccharides, synthetic polysaccharides, such as gum, dextran, fungal polysaccharides, and some hemicellulose (Soliman 2019). Primarily, the soluble fibers could not be digested by human digestive enzymes, yet they are soluble in warm water and can be partially or fully fermented by colonic bacteria into short-chain fatty acids in the large intestine (Korczak et al. 2017; Soliman 2019). Thus, the soluble dietary fibers change the gut microbiota environment, promote beneficial physiological effects, such as laxation and blood cholesterol and/or glucose attenuation (Story, 1985; Sun et al. 2019). On the other hand, insoluble fibers are commonly found in whole grains, wheat bran and seeds, cellulose, hemicellulose, lignin, and vegetable waxes (Slavin 2013; Soliman 2019). They can neither be digested by human digestive enzymes (Gibson et al. 2004) nor dissolved in hot water (Wong 2007), and just pass in intact through the digestive tract. They reduce the time of running in the stomach and intestines, increases the amount of feces, thus effectively relieves constipation (Slavin

Table 2. Daily dietary fiber intake of different genders at different ages.

Male	Age	Daily intake (g/d)	Female	Age	Daily intake (g/d)
	≤ 3	19		≤ 3	19
	4–8	25		4–8	25
	9–13	31		9–18	26
	14–18	38		–	–
	19–50	38		19–50	25
	≥ 51	31		≥ 51	21

2013; Soliman 2019). Despite the numerous human health benefits of dietary fiber, daily fiber intake varies widely among different gender and age, which reminds us to eat reasonably (Table 2) (Soliman 2019).

β-Glucan

β-Glucan is a complex non-starchy polysaccharide composed of D-glucose molecules linked together by either *β*-(1–3), *β*-(1–4) or *β*-(1–6) glycosidic bonds and is part of dietary fibers (Ciecierska et al. 2019), which is a crucial structural compound present in the cell walls of microorganisms, including yeast and algae, and certain cereals, such as oats and barley (Akramiene et al. 2007). Glucans are generally divided into two categories: insoluble and water-soluble. Insoluble dextran fibers consist of *β*-(1–3/1–4) d-linked glucose units (Nakashima et al. 2018), while soluble glucan fibers consist of *β*-(1–3/1–6) d-linked glucose units (Mirończuk-Chodakowska et al. 2017; Rakowska et al. 2017). Oat has been reported to contain more soluble fibers compared to other grains, and the content of glucan in oats is several times higher (about 3–7%) than that of wheat glucan (about 1%) (Singh, De, and Belkheir 2013). However, the content varies greatly with the varieties of oats and its growth conditions (Manthey, Hareland, and Huseby 1999; Singh, De, and Belkheir 2013; Wood, Weisz, and Fede). Numerous experimental investigations have shown that the *β*-glucan content in oat accounts for 1.8–5.5% of the total dry weight (Ajithkumar, Andersson, and Åman 2005; Dvonová et al. 2010; Lattimer and Haub 2010; Li, Cui, and Kakuda 2006; Saastamoinen et al. 2008; Wood 2010), while some oat varieties contain as much as 7% glucan (Manthey, Hareland, and Huseby 1999; Kiarie, Romero, and Ravindran 2014). The *β*-glucan of oat is primarily located in the cell wall of amyloid endosperm and increases the viscosity of food pellets. Studies have shown that the changes in the viscosity during digestion are important, resulting in delayed gastric emptying, increased intestinal viscosity, and slow down the absorption of nutrients. As a result, much more stool is produced, and spread more quickly through the gut, which reduces the exposure time of the intestinal lining tissues to various irritants and carcinogens present in the wastes (Henrion et al. 2019; Singh, De, and Belkheir 2013). These evidences have clarified the human health benefits of glucans present in oats.

Arabinoxylan

Arabinoxylan, a non-starch polysaccharide, is a major component of dietary fiber in whole grains and is often found in wheat, barley, rye, and millet (Mendis, Leclerc, and Simsek 2016; Neyrinck et al. 2011). In millet, arabinoxylan is an important ingredient of dietary fiber. It is reported that arabinoxylan is positively associated with health, including the improvement of colon cancer, atherosclerosis, diabetes, and the stimulation of beneficial intestinal flora (Saleh et al. 2013). Sarma et al. found that it could significantly improve glucose tolerance, lipid levels, insulin, LPS levels, and body weight by feeding millet arabinoxylan to mice on a high-fat diet (Sarma et al. 2018). Giving 15 g of arabinoxylan supplementation for 6 weeks to individuals with impaired glucose tolerance, Garcia et al. detected that it obviously reduced postprandial serum glucose levels and insulin (Garcia et al. 2007). Studies have also shown that wheat arabinoxylan has been thought to exert hypocholesterolemic, anti-inflammatory, anti-obesity, and prebiotic effects in mice (Neyrinck et al. 2011).

Inulin

Inulin is a fructan, an indigestible soluble fiber, found in foods like wheat, onions, and bananas (Lattimer and Haub 2010). The inulin content of whole-grain wheat flour is about 0.6–1/100 g (Jones 2007), which is frequently used as a functional food ingredient due to its nutritional properties. Studies have demonstrated that inulin can notably reduce plasma triglycerides, total cholesterol, and low density lipoprotein cholesterol (Beylot 2005; Davidson and Maki 1999; Jackson et al. 1999; Letexier, Diraison, and Beylot 2003; Russo et al. 2008; Williams and Jackson 2002). Surprisingly, inulin has been shown to have a prebiotic effect, which can increase the markers of colonic fermentation and affect appetite (Fernandes, Vogt, and Wolever 2011; Tarini and Wolever 2010). Besides, as a kind of insoluble fiber, wheat fiber, is particularly present in wheat kernels, the content of which is about 12/100 g of wheat (Biesiekierski et al. 2011). Weickert et al. discovered that administer overweight people more insoluble fiber from fortified bread could enhance their glucose utilization (Weickert et al. 2006), suggesting that wheat fiber would reinforce peripheral insulin sensitivity.

Protein

Cereal crops are the nutritionally important source of protein in the human diet. According to the recommendations of "The Pagoda of Balanced Diet for Chinese Residents," cereals can meet more than 50% of the body's daily protein intake. For example, wheat is rich in gliadin (40–50%) and glutenin (30–45%), rice protein is mainly composed of glutenin (75–90%), and buckwheat is relatively high in albumin (20.99–30.30%) (Wei et al. 2003). Wang et al. determined the contents of four major proteins including albumin, globulin, gliadin, and glutenin in oat, and found that their contents were 6.8%, 52.4%, 13.6%, and 8.3%, respectively, while the contents of other proteins were about 5.7%. The protein levels of five different grains were then tested and found to be at the average of 14.09%. Among them, the average protein content of oat was 18.25%, followed by barley 15.30%, wheat and barley 14.98%, buckwheat 13.93%, and rice 7.29% .

Wheat is the most important grain and one of the main reasons for wheat's popularity as a food ingredient is the presence of protein. Studies have shown that the protein content of wheat is 11.70%, and the purity is up to 83.24%. Moreover, the majority of proteins are found in seed's endosperm and known as storage proteins. Cereal storage proteins are generally classified based on whether they are soluble in water (albumin; 60.27%), dilute saline (globulin; 3.68%), and dilute acids/bases (glutenin; 3.05%, gliadin; 2.91%). In addition, other proteins account for 30.09%. The isolated protein contains abundant amino acids and a complete variety. The essential amino acids account for 29.06% of the total amino acids, and the glutamic acid content is as high as 39.82%. In addition, the solubility is the lowest when the protein isoelectric point is 5.0 and pH = 6.0. The high oil retention of wheat protein is 5.98 g/g, which can improve the absorption and retention of fat in foods and reduce the loss of fat during processing.

Protein in rice is recognized as the high-quality protein (Lima, Guraya, and Champagne 2002), and are classified based on their functions and solubility. On the one hand, they can be divided into storage proteins, which come from endosperm and are the most abundant, and structural proteins that maintain the normal metabolism of seed cells. On the other hand, they can be divided based on their solubility in various solvent into globulin (2–10%), albumin (2–5%), gliadin (1–5%), and gluten (75–90%) as discussed above. Gluten, second only to starch, is the main component in endosperm and is an important storage protein in rice that is easily digested and absorbed by human body. In addition, it is the most abundant as accounts for about 80% of the total protein of seeds (He, Wang, and Ding 2013). Growing number of evidence from epidemiological studies have shown that rice protein has effectively lowered the cholesterol level and body fat in humans (Hao et al. 2015; Lima, Guraya, and Champagne 2002).

Sorghum grain has protein content varying from 6 to 18%, with an average of 11% (Lasztity 1996). Similarly, Geng et al. studied 827 varieties of Shanxi sorghum and found that most varieties have protein content of 10–12% and lysine content of 1.5–3.0% (Geng and Jia 1992). Sorghum storage protein accounts for 70–90% of total protein. In addition, sorghum is rich in essential amino acids, such as lysine, tryptophan, arginine, methionine, and aspartamide (Omoba and Isah, 2018).

Polyphenols

In addition to being rich in other nutrients, extensive research has demonstrated that cereals are good source of variety of phytochemicals, such as flavonoids, phytic acid, coumarins, terpenes, and phenolic compounds (Harborne and Williams 1992; Rhodes and Price 1997). Phenolic compounds, the secondary metabolites of plants, are characterized by the presence of one or more aromatic rings with one or more hydroxyl groups (Borneo and León 2011). Chemically, they are the derivatives of benzoic acids and cinnamic acids, mainly concentrated in the cortex and aleurone layer of grains and are exist in two forms of either free state and/or combined state (Hahn, Faubion, and Roone; Hahn, Rooney, and Ear; Kim et al. 2006; Krygier, Sosulski, and Hogge 1982; Mattila, Pihlava, and Hellström 2005; Rao and Muralikrishna 2002; Robbins 2003). Numerous independent studies have demonstrated that the husks of wheat, barley, oats, rice, and sorghum are rich in phenolic compounds (Daniel et al. 2015; Dykes 2007; Shao, Zhang, and Bao 2011; Žilić 2016). However, the content and composition of phenolic compounds vary with the type of grain (Tables 3 and 4) (Andreasen et al. 2000; Hahn, Faubion, and Roone; Holtekjølen, Kinitz, and Knutsen 2006; Kim et al. 2006; Krygier, Sosulski, and Hogge 1982; Mattila, Pihlava, and Hellström 2005; Subba Rao and Muralikrishna 2002; Tian et al. 2005; Waniska, Poe, and Bandyopadhyay 1989; Zhou et al. 2004). More recently, a comparative analytical study has determined the content of total phenolic compounds in grains including buckwheat, barley, wheat, and rice, and concluded that the total content of phenolics and flavonoids in buckwheat were significantly higher (15 phenolic compounds) than those of the other three cereal extracts (3 – 5 phenolic compounds each).

Besides, millet is another good source of phenolic compounds concentrated in their seed coat, and the content is about 6% (Chethan and Malleshi 2007a). Phenolic acids in millet were reported as 903 times more than that of flavonoids, where the bound phenolics were 46 times as compared to free phenolics, indicating that bound phenolic acids are more abundant in millet (Shahidi and Chandrasekara 2013). Similarly, in our previous study, we have obtained bound and free polyphenols from millet and the inner and outer shells of bran, respectively. The polyphenols are mainly enriched in gluten bran, and the content of bound polyphenols in the gluten shell is relatively high (Shi et al. 2015a). The twelve bound polyphenols identified by UPLC-Triple-TOF liquid chromatography-mass spectrometry includes vanillic acid 4-O-β-d-glucopyranoside, glucuronic acid, ferulic acid 4-O-β-d-glucopyranoside, 4-hydroxybenzoic acid, vanillic acid, syringic acid, p-coumaric acid, vitexin, ferulic acid, isoferulic acid, dimer ferulic acid derivatives, and dimer cinnamic acid derivatives, among which p-coumaric acid, and ferulic acid are the two components with the highest content (Shi et al. 2015a). In general, polyphenolic compounds are active substances with various physiological functions, including antioxidant, anti-tumor, immunomodulation, anti-hyperglycemia, hypertension, antibacterial, anti-radiation, and anti-aging, discussed in detail in the second part of the review.

Table 3. Phenolic acids reported in different cereals.

Cereals	Phenolic acids
Millet	Gallic, Protocatechuic, p-Hydroxybenzoic, Gentisis, Vanillic, Syringic, Eerulic, Caffeic, p-Coumaric, and Cinnamic
Rice	Gallic, Protocatechuic, p-Hydroxybenzoic, Vanillic, Syringic, Eerulic, Caffeic, and p-Coumaric
Sorghum	Gallic, Protocatechuic, p-Hydroxybenzoic, Gentisis, Salicylic, Vanillic, Syringic, Eerulic, Caffeic, p-Coumaric, and Cinnamic
Barley	Protocatechuic, p-Hydroxybenzoic, Salicylic, Vanillic, Syringic, Eerulic, o-Coumaric, m-Coumaric, and p-Coumaric
Maize	Protocatechuic, p-Hydroxybenzoic, Vanillic, Syringic, Eerulic, Caffeic, and p-Coumaric
Oat	Protocatechuic, p-Hydroxybenzoic, Vanillic, Syringic, Eerulic, Caffeic, and p-Coumaric
Rye	Protocatechuic, p-Hydroxybenzoic, Vanillic, Syringic, Eerulic, Caffeic, and p-Coumaric
Wheat	Protocatechuic, p-Hydroxybenzoic, Salicylic, Vanillic, Syringic, Eerulic, Caffeic, and Cinnamic

Table 4. Different contents of phenolic acids in cereals.

Cereals	Content in whole grains (μg/g)	Amount in brans (μg/g)
Barley	450 – 1346	–
Maize	601	–
Millet	612 – 3907	–
Oat	47	651
Rice	197 – 376	–
Rye	1362 – 1366	4190
Sorghum	385 – 746	–
Wheat	1342	4527

Alkaloid

Alkaloids are basic organic compounds with complex ring structures, and are mainly concentrated in dicotyledonous plants, the roots and fruits of Ranunculaceae, Rutaceae, and Leguminosae, while its distribution is rare in animal tissues. Chemically, they exist in the forms of free bases, salts, amides (colchicine), N-oxide (matrine), and nitrogen-containing complex aldehydes (Liu et al. 2019a). Because of their complex ring structure and nitrogen content, alkaloids have significant biological activities, and are one of the important and effective ingredients in Chinese herbal medicine as well as in Western medicine. The most common alkaloids including but not limited to indole alkaloid, avenanthramides (AVNs), tocols, organic acids, flavonoids, saponins, and sterols are abundantly present in the human food chain and are an intrinsic part of the regular Western diet (Singh, De, and Belkheir 2013).

Recently, researchers have discovered that compared with other cereals, oats, a versatile grain that involves a unique set of natural phenols, contain approximately 40 different oat alkaloids. AVNs for example, are formed by connecting a series of anthranilic acid and its derivatives and a sequence of cinnamic acid and its derivatives through amide bonds (Turrini et al. 2019). Specifically, it is synthesized by the condensation reaction of substituted anthranilates and substituted cinnamoyl-CoA thioesters, which is catalyzed by hydroxycinnamoyl-CoA, hydroxyanthranilic acid, and N-hydroxycinnamon acyltransferase. AVN A, B, and C among other alkaloids are the three main AVNs with relatively high content. They are formed by hydroxyanthraquinone acid and p-coumarin, ferulic acid, or caffeic acid. The avenatin concentration is relatively high in whole grains, reaching up to approximately 200 mg/kg (Peterson 2001), that in oat grains is 2 – 53 mg/kg. In addition, oat husks also contain more than 25 different AVNs . Consistent with previous literature, our research group has extracted the three primary AVNs including AVN A, B, and C using HPLC-MS, and determined that the total content of AVNs in oat bran is approximately 37.9 mg per 100 g of oat bran (3.79%) (Fu et al. 2019a, 2019b).

Health benefits of bioactive components in cereals

Mounting evidence revealed that the consumers are now more conscious about their diet and health, and a confining relationship between them has been disclosed in recent decades (Gentile and Weir, 2018; Horn 2006a, 2006b). Numerous plant-derived bioactive components have been shown to possess positive effects on human health and disease prevention. In this part of the review, we highlight the human health benefits of cereal-derived functional components.

Modulating intestinal flora

Microecological and nutritional studies have shown that the structural disorder of the intestinal flora is the direct cause of many chronic diseases including obesity, diabetes, hypertension, coronary heart disease, other cardiovascular and cerebrovascular diseases, and colorectal cancer (Ma et al. 2019; Tang and Hazen 2017; Keiko 2016). Existing data show that probiotics, such as bifidobacterium, lactobacillus, and certain enterococci provide nutrients for intestinal cells and promote the absorption of nutrients, creating a healthy intestinal environment (Hu, Wang, and Jiang 2017). Moreover, long-term fixed eating habits may negatively affect the intestinal microorganisms, and even lead to the creation of new strains in the host. Additionally, the gut microbiome synthesizes many beneficial metabolites, especially the short-chain fatty acids including acetic acid, propionic acid, and butyric acid (Cummings et al. 1987; Koh et al. 2016; Morrison and Preston, 2016; Tan et al. 2017; Thorburn, Macia, and Mackay 2014), which contribute to the human health. For example, butyric acid, an important substrate for the maintenance of colonic epithelium, enhances intestinal barrier function by increasing the expression of Claudin-1 and Zonula occluden-1, and the redistribution of occludin (Manco, Putignani, and Bottazzo 2010). Existing literature reported that *Akkermansia muciniphila* has been identified as key propionic acid-producing mucin degrading organisms (Reichardt et al. 2014). And microorganisms, such as *Faecalibacterium prausnitzii*, *Eubacterium hallii*, and *R. bromii*, are beneficial to butyrate production (Ze et al. 2012).

Adding dietary fiber can restore beneficial microbes, reduce the toxic microbial metabolites and increase the production of short-chain fatty acids (Sanchez et al. 2009). Extensive research efforts have demonstrated that cereals are rich in the fermentable carbohydrates that usually cannot be decomposed by the human digestive enzymes; however, the intestinal microbial community selectively decomposes and ferments them into short-chain fatty acids. These short-chain fatty acids are absorbed and utilized by the intestinal wall of the host, as well as used by the beneficial bacteria, such as bifidobacteria and lactobacilli in the intestine, thus improving the intestinal microbial environment, lowering the intestinal pH, and enhancing the body's immunity. In addition, undigested carbohydrates increase the water content of the feces and accelerate peristalsis of the intestine. Given this, researchers proposed that appropriate increase in cereal intake can leads to the abundance of probiotics and enhanced intestinal function, thereby having multiple positive effects on various diseases (Samantha et al. 2020). For example, barley and oats, rich in dietary fibers, promote the growth of probiotics and optimize the intestinal microecology (Dvonová et al. 2010; Peterson, Wesenberg, and Burrup 1995). Oat foods, barley husks and rye bran, wheat germ, whole wheat flakes, and wheat bran have been reported to selectively increase the growth and number of the probiotic bifidobacterium or lactobacillus in vivo and in vitro (Adele et al. 2002; Hamaker and Tuncil 2014; Suchecka et al. 2017; Zhao and Cheung 2013), thereby exerting anti-tumor potential and enhancing the formation of short-chain fatty acids, such as acetate and butyrate (Kiarie, Romero, and Ravindran 2014). Connolly et al. used in vitro fermentation to study the probiotic effect of whole grains and found that whole grains significantly increased the amount of bifidobacterium and lactobacillus (Connolly, Lovegrove, and Tuohy 2012). Another in vitro study showed that oatmeal also promotes the growth of bifidobacterium and lactobacillus, and greatly promotes the production of propionic acid and butyric acid (Zhao and Cheung 2013). Rye bran, oat bran, and whole wheat bran have also been shown to significantly increased the short-chain fatty acid levels in the colon of rats.

Soluble β-glucan in grains is used as fermented dietary fiber and through the in vivo intervention and in vitro fermentation experiments, it has been documented that β-glucan exerts positive effects on intestinal flora. Oat foods, for example, rich in β-glucan significantly promotes the proliferation of bifidobacterium and lactobacillus, inhibits *E. coli* and bacteroides, reduces the pH of the intestine, and increases the content of cecal short-chain fatty acids that prevents the inflammatory bowel disease (Ajithkumar, Andersson, and Åman 2005). In addition, high molecular weight β-glucan has positively changed the composition and function of intestinal flora that significantly reduced the cardiovascular and cerebrovascular risk markers in the patients with mild hypercholesterolemia (Wang et al. 2016).

Our previous study evaluated the regulatory effect of bound polyphenol of the inner shell (BPIS) from foxtail millet bran on intestinal flora in AOM/DSS-induced colorectal cancer C57BL/6 mice models, and indicated that BPIS had effectively restored the diversity of intestinal microflora, improved the structure of the bacterial community, including remolding the growth of phylum, such as firmicutes, bacteroidetes, and protected the intestinal barrier function in mice. Briefly, this research data suggest that increasing the ratio of cereal intake in the diet structures increases the diversity of probiotics in intestinal flora and is highly beneficial in disease prevention and to overall human health (Yang et al. 2020).

Anti-obesity

A body of epidemiological research shows that obesity has become a huge healthcare problem, worldwide, and is a risk factor for several chronic diseases such as type 2 diabetes, CVD, and cancer (Gadde et al. 2018). Approximately, 2.8 million people die each year from being overweight or obese. Because the prevalence of obesity has reached to pandemic proportion, this metabolic disease is estimated to become the biggest cause of mortality in the near future, which is closely related to our daily life habits, especially the diet has undergone a great change. Dietary fibers and whole grains intake have been showed to be associated with reduced risks of obesity, overweight, and high waist-to-hip ratio (Lattimer and Haub 2010). The ingestion of dietary fiber increases the volume and cause satiation easily, thus reducing the food intake (Lattimer and Haub 2010; Tucker and Thomas 2009). Soluble dietary fiber has a strong ability to absorb water to increase the volume and weight by $10-15$ times, which results in the increased satiety and reduced absorption of fat in food, so that the body weight can be effectively controlled. Certain fibers can also slow down the gastric emptying and reduces the rate of glucose absorption in the small intestine, thus increasing the intestinal satiety. In short, it has been suggested that high intake of fibrous food can control obesity and associated anomalies by preventing excessive food intake and fat accumulation in the body.

Anti-cardiovascular disease

CVD is a common disease with high morbidity and mortality, which is a serious threat to human health around the globe (Li, Ikram, and Wong 2016). China's cardiovascular health and diseases report (Whelton and Lisandro, 2019) has revealed that its morbidity rate is in a continuous rising stage (290 million), and its mortality rate is over top than that of cancer and other diseases (Liu 2019a). The published data in the past 30 years $(1982-2012)$ have shown that the main food intake of Chinese residents has changed largely, especially their intake of whole-grain foods has profoundly decreased. Numerous epidemiological studies have shown that dietary fiber intake is associated with a reduced risk of CVD, primarily through a sustained reduction in LDL levels (Soliman 2019; Higginson and Pepler; Fisher et al. 1964). Whole grains, compared with refined grains, contain more dietary fibers, protein, vitamins, and inorganic salts, and their energy density is relatively low. Increasing the whole grains intake can reduce the risk factors of coronary heart disease and stroke by adjusting the blood lipids and controlling the blood pressure, thus reducing the risk of CVD.

Cereal β-glucan increases the intestinal viscosity, combines with bile acids, absorbs excess cholesterol and triglycerides, thereby reducing the hepatic and intestinal circulation of cholesterol, and facilitating its excretion. Studies have shown that oat β-glucan significantly reduces the levels of serum total triglycerides and serum cholesterol in mice caused by consuming high-fat diet (Chen 2008; Sima, Vannucci, and Vetvicka 2018). Roach and Topping reported that feeding rat simultaneously with oat bran and fish oil reduced the blood cholesterol level (Roach et al. 1992; Topping et al. 1990). Similarly, feeding Syrian hamsters with barley and insoluble fiber also reduced cholesterol level (Wilson et al. 2004). One recent study demonstrated that β-glucan upregulates the expression of cholesterol 7α-hydroxylase gene, results in the rapid conversion of cholesterol into cholic acid and reduced cholesterol level in obese-mice (Aoki et al. 2015). A randomized controlled trial of 30 patients with high cholesterol comparing with the dietary intake of β-glucan was followed for 5 weeks. The patients in the β-glucan intake group had increased bile acid synthesis and significantly lowered the cholesterol level (Wang et al. 2017). In addition, plant sterol ester oat β-glucan promotes the expansion of Verrucomicrobia population, which positively affects the circulating lipids and downregulates the degree of aortic wall plaque in atherosclerotic mice (Hager et al. 2011). Similarly, our laboratory demonstrated that FMBP, a peroxidase protein derived from foxtail millet bran, has increased HDL-C by inhibiting the expression of CD36 and STAT3, thereby alleviated atherosclerosis induced by the high-fat diet in ApoE$^{-/-}$ mice model (Liu et al. 2020).

Anti-diabetes

The global prevalence of diabetes, with the continued development of social economy and men's lifestyle, is rising with high pace. Diabetes is one of the most common metabolic anomalies and the second most serious chronic non-communicable disease after the cardiovascular and cerebrovascular diseases (Goff et al. 2007). According to the International Diabetes Federation (IDF) report (2019), about 463 million adults aged 20–79 were suffering from diabetes worldwide and approximately 4.2 million people died of diabetes or its complications (Saeedi et al. 2019). Surprisingly, China tops the list having larger number of diabetic patients (Chen et al. 2020). Nevertheless, the IDF covers that global spending on diabetes healthcare in 2019 had reached $760 billion, and the number of diabetic patients in low- and middle-income families is increasing, which has become a heavy burden for society (Saeedi et al. 2019). The prevention and control of diabetes and its complications has become the most severe challenge facing mankind all over the world.

Lifestyle interventions such as reducing body weight, increasing regular physical activity, and healthy diet represent the cornerstone of diabetes prevention and management. Epidemiological studies on dietary fiber and diabetes have shown that the increased incidence of diabetes is closely related to low intake of dietary fiber. Foods rich in cellulose including oats, corn, and brown rice have been suggested to control cholesterol level. Li et al. studied the effect of konjac, oatmeal, and corn fiber on carbohydrate metabolism in healthy subjects and demonstrated that the test meal supplemented with dietary fiber reduced the blood glucose and delayed the peak time. Blood glucose was reduced in patient with gestational diabetes without insulin injection by consuming rice, oats, and other grains with high dietary fiber (Tan, Yeo, and Liauw 1996). Similarly, another study by Schulze et al. on large number of young and middle-aged women (91,249) demonstrated that cereal fiber intake was significantly negatively correlated with the incidence of diabetes (Schulze et al. 2004). Consistent with previous literature, a meta-analysis on the perspective cohort studies demonstrated that higher consumption of whole-grain foods including whole-grain breakfast cereal, oatmeal, brown rice, and wheat germ was significantly correlated with lower risk of diabetes (Yang et al., 2020). Moreover, increasing dietary fiber intake can reduce the dietary glycemic index, thus reducing the dietary sugar effect (Fuller et al., 2016). The inhibition of postprandial blood glucose rise by dietary fiber can be achieved by increasing the viscosity of intestinal fluid, hindering the diffusion, and restraining the synthesis of glucose, and reduce its effective concentration in intestinal fluid and finally extending the degradation time of starch by α-amylase and reduce the release rate of glucose in intestinal fluid. In short, based on the current research data, the regular consumption of appropriate amounts of cereal dietary fiber is highly recommended for the effective prevention and management of diabetes.

In addition, β-glucan in cereals advantageously regulates the blood glucose level. Soluble polysaccharides increase the viscosity of chyme, thereby delaying the ability of nutrients to be absorbed from the intestinal tract. The cross-linked network structure of cereal β-glucan molecules hinders the contact between food and digestive enzymes. The formation of mucus in the gastrointestinal tract prolongs gastric emptying, slows down the contraction rate of the small intestine, and reduces insulin release, thereby reducing glucose absorption rate and the risk of type 2 diabetes (Qi and Ellis 2014). β-glucan in oat is reported to accelerate the speed of food movement in the small intestine by stimulating the peristalsis of smooth muscle, shorten the residence time of food in the intestine, reduce the absorption and utilization of sugar, and generate a high viscosity environment in the intestine, and reduce the contact between small intestine and food, thus regulating the blood glucose level (Qi and Ellis 2014; Lieselotte et al. 2012). Moreover, healthy subjects who consumed glucose beverages containing samples of extracted and purified β-glucan in different doses and molecular weights showed an inverse linear relationship between the peak blood glucose level and the increase of insulin and $\log_{(\text{viscosity})}$ (Wood et al. 1994). The hypoglycemic effect of β-glucan depends on its ability to form a viscous solution, its molecular weight, and the concentration. For example, compared with barley β-glucan, β-glucan in oats (with high molecular weight and viscosity) significantly affects the reduction of blood glucose and insulinemia (Biörklund et al. 2005). Another possible mechanism for β-glucan to reduce blood glucose levels is mediated by the activation of PI3K/Akt signaling pathways (Chen, Gu, and Zhao 2011). β-glucan has been corroborated to increase PI3K/Akt through several receptors such as decatin-1, complement receptor 3, lactose ceramide, scavenger, and toll-like receptors (Brown 2006; Hiller et al. 2000; Lee et al. 2008; Li, Cui, and Kakuda 2006; Olsson and Sundler 2007; Trinidad et al. 2006; Underhill et al. 2005). However, the specific underlying mechanism(s) of active ingredients in cereals in the treatment of diabetes are not well studied and needs further elucidation.

Antioxidant

Phenolic compounds are secondary metabolites widely found in plants (Shi et al. 2015a). The physiological activity of polyphenols is closely related to their strong free radical scavenging and antioxidant properties (Shi et al. 2015a; Chandrasekara and Shahidi 2011c). Phenols not only provide protons through phenolic hydroxyl groups to directly scavenge free radicals, but also interact with enzymes that generate free radicals to complex excess metal ions that induce oxidation, thereby indirectly removing free radicals (Shi et al. 2015a; Chandrasekara and Shahidi 2011b, 2011c). Being rich in phenols, cereal is the adequate example of antioxidants. Continuously emerging research data revealed that dietary and age-related diseases, including metabolic syndrome, CVDs, type 2 diabetes, and cancer, which are related to the increased oxidative stress, can be effectively prevented through regular intake of grains (Daou and Zhang 2012; Gupta, Abu-Ghannam, and Gallaghar 2010; Kunitomo 2007; Shah et al. 2015).

Phenolic compounds in black rice can scavenge peroxy radicals, 1,1-diphenyl-2-trinitrophenylhydrazine (DPPH) radicals, and hydroxyl radicals, thereby effectively controlling the oxidation of low-density protein cholesterol. Millet grain phenols can significantly inhibit the oxidation of human low-density lipoprotein (LDL) cholesterol catalyzed by copper (Chandrasekara and Shahidi 2010). Moreover, ultraviolet rays are known to directly or indirectly damage lipid membranes through ROS. The millet grain phenolic compounds inhibit the formation of conjugated dienes and hydroperoxides in phosphatidylcholine (PC) liposome membranes oxidized under UVA light (Chandrasekara and Shahidi 2011a, 2011b, 2011c). Frequently exposed to ultraviolet light, free radicals participating in the photosynthesis of photocarcinogens, thus increases the incidence of skin cancer. What is more, the bran is discarded as the hull of millet, but the antioxidant capacity of phenolic acid in its extract is obviously higher than that of whole grains and millet (Shi et al. 2015a; Chandrasekara and Shahidi 2011a, 2011 b, 2011c).

Studies have shown that different extract methods affect the antioxidant capacity. Kunyanga et al. used three methods: water extraction, ethanol extraction, and methanol extraction to obtain millet and bran extracts. By comparing their antioxidant properties, the antioxidant ability of methanol extracts, ethanol extracts, and water extracts was found to gradually decrease (Kunyanga et al. 2012). Lu et al. compared the DPPH free radical scavenging ability of barley extracts with five different extraction solvents of 100% methanol, 80% methanol, 80% ethanol, 80% acetone, and water. The results showed that 80% acetone extract has the highest DPPH free radical scavenging rate. Comparing the oxidation resistance of four different millet total phenols, the results demonstrated that the higher the total phenol content, the stronger the ability to scavenge DPPH free radicals, indicating that there may be differences in the DPPH free radical scavenging activity.

Anti-tumor activity

The significance of whole-grain cereals in chronic disease prevention is of strong interest. The World Cancer Research Fund (WCRF) states that dietary habits have an important role in the prevention and causation of cancer (Petimar et al. 2019). A variety of phytochemicals in cereals have been reported to exert antitumor effects through different mechanisms. For example, the extract of buckwheat, barley, rice, and wheat exhibited obvious inhibitory effect on Caco-2 cell proliferation, where the buckwheat showed the strongest effect and the inhibition rate of buckwheat on Caco-2 cell proliferation reached 55.62%. Moreover, followed by the digestion in gastrointestinal tract, the insoluble phenolic compounds bound in grains reach into the colon in intact form and protect the colon after fermentation and release of microorganisms, thereby preventing the occurrence of colon cancer (Kim et al. 2009; Kroon et al. 1997). The bound phenols in cereal bran are mostly linked to cellulose, which releases phenolic acid such as ferulic acid through microbial degradation in the large intestine to exert biological activity against colon cancer. Subsequently, we and others have demonstrated the underlying mechanisms of cereal polyphenols mediated inhibition of cancer progression. Given that, cereal polyphenols inhibit the proliferation of colon cancer cells by regulating AK2/STAT3 and PI3K/Akt/mTOR signaling pathways (Darvin et al. 2015; Liao et al. 2006; Qian et al. 2004; Shan et al. 2014b), as well as millet polyphenols specifically inhibited the HT-29 cell proliferation by ameliorating DNA replication (Chandrasekara and Shahidi 2011a). Concurrently, we demonstrated that polyphenols and BPIS extract (containing 12 main components including p-coumaric acid and ferulic acid, which were the two most abundant monomers) from millet bran showed significant antitumor activity in vivo and in vitro (Lu et al. 2018; Shi et al. 2015a; Shi et al. 2019a). BPIS significantly elevated the ROS production in tumor cells, which induced the cancer cell apoptosis and inhibited the proliferation of various tumor cells (Shi et al. 2015a). In addition, BPIS also significantly reversed the drug resistance activity of human colon cancer multi-drug resistant cell lines by upregulating the expression of miR-149 (Lu et al. 2018) (Figure 2). BPIS is likely to disrupt lipid metabolism in cells by blocking lipid transport and metabolism through the PI3K/AKT and FoxO signals,

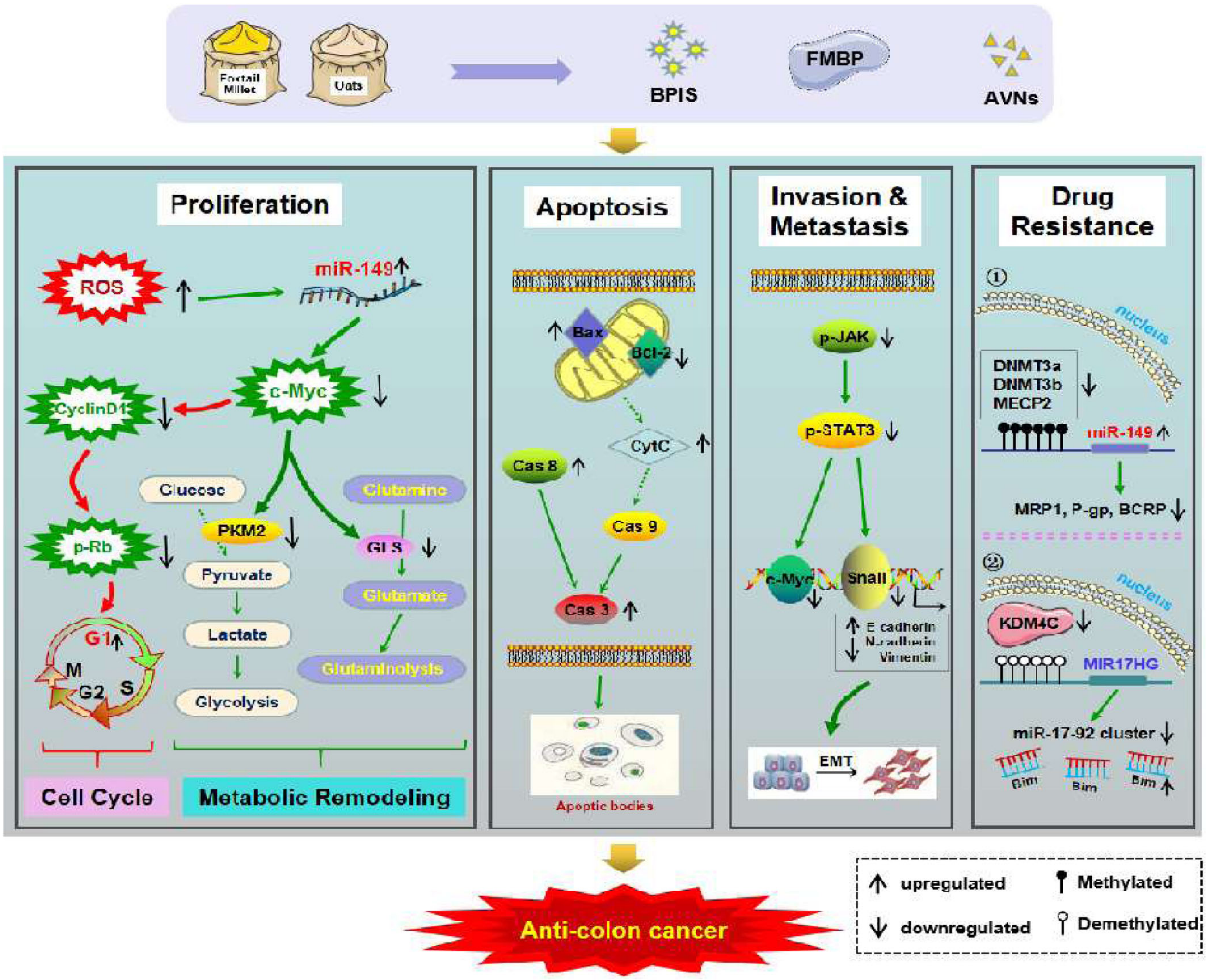

Figure 2. The anti-colon cancer effect of active ingredients from cereals.

thereby triggering autophagy, and excessive autophagy leads to normal cell functions damage and further cell death. Our laboratory also extracted and purified a novel active ingredient, peroxidase protein (FMBP) from millet bran, which suppressed the growth of colon cancer cells through inducing G1 phase arrest and causes the loss of mitochondrial transmembrane potential, thus leading to caspase-dependent apoptosis in colon cancer cells (Shan et al. 2014a, 2014b, 2015) (Figure 2).

We further indicated that AVNs effectively inhibited the growth of colon cancer in vivo and in vitro. Mechanistically, AVNs intervention significantly changed the mitochondrial morphology, and mitochondrial aerobic respiratory pathway was blocked and electron transport chain (ETC) complex is destroyed, which trigger the elevated ROS generation. In addition, the opening of membrane permeability transition pore (MPTP), loss of mitochondrial membrane potential (MMP), release of cytochrome c, and activation of caspase 3 promote the endogenous apoptosis. Furthermore, AVNs treatment can lead to ubiquitination and degradation of DDX3, an RNA helical enzyme that regulates mitochondrial translation, which in turn hinders the synthesis of key subunits of ETC complex encoded by mitochondria, leaving cells in a state of oxidative stress and eventually inducing apoptosis (Fu et al. 2019a, 2019b). Similarly, avenal alkaloid extracts and synthetic AVN A can inhibit the growth of colon cancer cells, breast cancer cells, and prostate cancer cells, and have the most significant inhibitory effect on colon cancer proliferative cells (Guo et al. 2010). Wang et al. experiments showed that AVN C and its main metabolism product M6 (dihydroavenan thramide-C) are biologically active compounds that induce apoptosis of human colon cancer cells (Wang et al. 2015). Researchers also proposed that AVNs inhibit cyclooxygenase (COX-2) activity and the production of prostaglandin E (PGE) by lipopolysaccharide-stimulated mouse peritoneal macrophages, thereby inhibiting the proliferation of colon cancer cells It is known that cyclooxygenase is highly expressed in 80–85% of human adenocarcinoma, colon cancer, and mouse adenocarcinoma. PGE2 signaling mediated by cyclooxygenase has a causal relationship with the occurrence of epithelial cancers in the gastrointestinal tract, which is considered a good target for colon cancer. Guo et al. found that AVNs can also reduce the risk of colon cancer by inhibiting the production of PGE2 in peritoneal macrophages and the expression of COX-2 in colon cancer cells (Guo et al. 2010).

In addition, AVN A inhibited the formation of β-catenin-TCFS complex, preventing the transcription of Wnt target genes related to the development of various types of cancer, and preventing carcinogenesis (Wang et al. 2012). In human breast cancer cell MCF-7, dihydroxyaven alkaloid D inhibits the expression of mitogen-activated protein kinase MMP-9 induced by protein kinase C agonist TPA *via* inhibiting MAPK/NF-κB and MAPK/AP-1 pathway, which has potential application value in the inhibition of breast cancer metastasis (Lee et al. 2011).

Anti-inflammatory and anti-bacterial

Inflammation is the robust body's response to infection, injury, and disease, which is required for the host to clear pestilent stimuli and repair the subsequent tissue damage (Song et al. 2019). Macrophages, tissue-residing immune cells, initiate inflammatory response by producing inducible nitric oxide synthase, cyclooxygenase-2, and numerous pro-inflammatory cytokines such as tumor necrosis factor (TNF)-α, interleukin (IL)-6, and (IL)-12 (Bogdan 2015; Medzhitov 2008). However, uncontrolled and inappropriate macrophage response may hamper the healing process of the host, leading to chronic inflammation that can eventually start damaging healthy tissues. Cereal and cereal-derived active ingredients are documented to exert anti-inflammatory activity. Yao et al. isolated and identified 11 monomeric saponins from quinoa grains and evaluated their effects on nitric oxide, TNF-α, and IL-6 expression. The quinoa saponin inhibited the release of inflammatory mediators and downstream pathways to reduce chronic inflammation (Yao, Shi, and Ren 2014). In line with, the millet polyphenols also significantly inhibited the secretion of pro-inflammatory factors TNF-α and IL-6 in Raw264.7 cells (Hosoda et al. 2012). Our recently published data demonstrated that BPIS inhibits the production of multiple inflammatory factors in HT-29 cells through the miR-149/Akt/NF-κB signal axis, thereby exerting an anti-inflammatory effect (Shi et al. 2017a). On the other hand, p-coumaric acid and ferulic acid in polyphenol extracts of cereals have shown antimicrobial activity (Antony, Moses, and Chandra 1998; Chethan and Malleshi 2007b; Viswanath, Urooj, and Malleshi 2009). Mechanistically, they inhibit the proliferation of bacterial cells by reducing the oxidation of microbial enzymes and microbial membranes (Shahidi and Chandrasekara 2013). The epidermal extract of millet seed coat showed high antibacterial and antifungal activity, especially caffeic acid, p-coumaric acid, ferulic acid, and protocatechuic acid (Dragland et al. 2003; Moure et al. 2001).

Summary

This narrative review primarily focuses on the main active ingredients of commonly consumed cereals and their relationship with human health regarding the regulation of intestinal flora, reducing obesity, minimizing the risk of CVD, and diabetes, as well as their anti-oxidation, anti-tumor, anti-inflammatory, and antibacterial activity. Scientific evidence shows that regular intake of whole-grain cereals can minimize the risk of such types of chronic diseases and improve the human health to a great extent. However, there are relatively few studies on the effects of grain processing on human health and the intake of active ingredients, and further studies are needed to determine. Therefore, the utmost important factor that needs to be considered is the intake of active ingredients, and how to properly match the diet will benefit the health? For healthy life, it is recommended to consume cereals and cereal products in every meal in accordance with the dietary guidelines. Second, how the changes in the active ingredients during processing would affect preference for the product, such as taste and senses? It is believed that combining these factors may increase, the attention toward whole grains, and the sustainable growth rate of human diseases may gradually decrease, which further provides the broad prospects for the development of novel and sound products, full of strength and vigor as well as freedom from sign of diseases.

Disclosure statement

The authors declare no conflict of interest.

Funding

This research was funded by the National Natural Science Foundation of China (No. 31800290, 32072220, 31770382, 82072718), the Key Projects of Shanxi Applied Basic Research Program (No. 201801D111001), Science and Technology Innovation Project of Colleges and Universities in Shanxi Province (No. 2019L0027), Project of the Central Government Guiding Local Science and Technology (No. YDZX20201400001436).

References

Adele, C., Q. Wang, D. Ka'ohimanu, R. Alison, and T. Andre. 2002. Intestinal apolipoprotein B secretion is inhibited by the flavonoid quercetin: Potentialrole of microsomal triglyceride transfer protein and diacylglycerol acyltransferase. *Lipids* 37 (7):647–52. doi: 10.1007/s11745-002-0945-8..

Ajithkumar, A., R. Andersson, and P. Åman. 2005. Content and molecular weight of extractable b-glucan in American and Swedish oat samples. *Journal of Agricultural and Food Chemistry* 53 (4):1205–9. doi: 10.1021/jf040322c.

Akramiene, D., A. Kondrotas, J. Didziapetriene, and E. Kevelaitis. 2007. Effects of beta-glucans on the immune system. *Medicina (Kaunas, Lithuania)* 43 (8):597–606. doi: 10.3390/medicina43080076.

Andreasen, M. F., L. P. Christensen, A. S. Meyer, and S. H. Åse. 2000. Content of phenolic acids and ferulic acid dehydrodimers in 17 rye (Secale cereale L.) varieties. *Journal of Agricultural and Food Chemistry* 48 (7):2837–42. doi: 10.1021/jf991266w.

Antony, U., L. G. Moses, and T. S. Chandra. 1998. Inhibition of Salmonella typhimurium and Escherichia coli by fermentedflour of finger millet (Eleusine coracana). *World Journal of Microbiology and Biotechnology* 14 (6):883–6. doi: 10.1023/A:1008871412183.

Aoki, S., A. Iwai, K. Kawata, D. Muramatsu, H. Uchiyama, M. Okabe, M. Ikesue, N. Maeda, and T. Uede. 2015. Oral administration of the Aureobasidium pullulans-derived β-glucan effectively prevents the development of high fat diet-induced fatty liver in mice. *Scientific Reports* 5:10457. doi: 10.1038/srep10457.

Aune, D., NNa Keum, E. Giovannucci, L. T. Fadnes, P. Boffetta, D. C. Greenwood, S. Tonstad, L. J. Vatten, E. Riboli, and T. Norat. 2016. Whole grain consumption and risk of cardiovascular disease, cancer, and all cause and cause specific mortality: Systematic review and dose-response meta-analysis of prospective studies. *BMJ* 353:i2716. doi: 10.1136/bmj.i2716..

Beylot, M. 2005. Effects of inulin-type fructans on lipid metabolism in man and in animal models. *British Journal of Nutrition* 93 (S1): S163–S168. doi: 10.1079/BJN20041339.

Biesiekierski, J. R., O. Rosella, R. Rose, K. Liels, J. S. Barrett, S. J. Shepherd, P. R. Gibson, and J. G. Muir. 2011. Quantification of fructans, galacto-oligosacharides and other short-chain carbohydrates in processed grains and cereals. *Journal of Human Nutrition and Dietetics: The Official Journal of the British Dietetic Association* 24 (2):154–76. doi: 10.1111/j.1365-277X.2010.01139.x.

Biörklund, M., R. A. Van, R. P. Mensink, and G. Onning. 2005. Changes in serum lipids and postprandial glucose and insulin concentrations after consumption of beverages with beta-glucans from oats or barley: A randomised dose-controlled trial. *European Journal of Clinical Nutrition* 59 (11):1272–81. doi: 10.1038/sj.ejcn.1602240.

Bogdan, C. 2015. Nitric oxide synthase in innate and adaptive immunity: An update. *Trends in Immunology* 36 (3):161–78. doi: 10.1016/j.it.2015.01.003..

Borneo, R., and A. E. León. 2012. Whole grain cereals: Functional components and health benefits. *Food & Function* 3 (2):110–9. doi: 10.1039/c1fo10165j..

Brown, G. D. 2006. Dectin-1: A signalling non-TLR pattern-recognition receptor. Nature Reviews Immunology 6:33–43. doi: 10.1038/nri1745..

Chandrasekara, A., and F. Shahidi. 2010. Content of insoluble bound phenolics in millets and their contribution to antioxidant capacity. Journal of Agricultural and Food Chemistry 58:6706–14. doi: 10.1021/jf100868b..

Chandrasekara, A., and F. Shahidi. 2011a. Antiproliferative potential and DNA scission inhibitory activity of phenolics from whole millet grains. Journal of Functional Foods 3 (3):159–70. doi: 10.1016/j.jff.2011.03.008.

Chandrasekara, A., and F. Shahidi. 2011b. Bioactivities and antiradical properties of millet grains and hulls. Journal of Agricultural and Food Chemistry 59:9563–71. doi: 10.1021/jf201849d..

Chandrasekara, A., and F. Shahidi. 2011c. Determination of antioxidant activity in free and hydrolyzed fractions of millet grains and characterization of their phenolic profiles by HPLC-DAD-ESI-MSn. Journal of Functional Foods 3 (3):144–58. doi: 10.1016/j.jff.2011.03.007.

Charalampopoulos, D., R. Wang, S. S. Pandiella, and C. Webb. 2002. Application of cereals and cereal components in functional foods: A review. International Journal of Food Microbiology 79:131–41. doi: 10.1016/S0168-1605(02)00187-3.

Chen, C., J. L. Song, X. L. Xu, L. M. Zhou, Y. H. Wang, and H. Chen. 2020. Analysis of influencing factors of economic burden and medical service utilization of diabetic patients in China. *PLoS One* 15 (10):e0239844. doi: 10.1371/journal.pone.0239844.

Chen, J. 2008. Beta-glucans in the treatment of diabetes and associated cardiovascular risks. *Vascular Health and Risk Management* 4: 1265–72. doi: 10.2147/vhrm.s3803..

Chen, J., W. Gu, and K. Zhao. 2011. The role of PI3K/Akt pathway in β-glucan-induced dendritic cell maturation. International Immunopharmacology 11 (4):529. doi: 10.1016/j.intimp.2011.01.027.

Chethan, S., and N. G. Malleshi. 2007a. Finger millet polyphenols: Optimization of extraction and the effect of pH on their stability. *Food Chemistry* 105 (2):862–70. doi: 10.1016/j.foodchem.2007.02.012.

Chethan, S., and N. G. Malleshi. 2007b. Finger millet polyphenols: Characterization and their nutraceutical potential. *American Journal of Food Technology* 2 (7):582–92. doi: 10.3923/ajft.2007.582.592.

Ciecierska, A., M. E. Drywień, J. Hamulka, and T. Sadkowski. 2019. Nutraceutical functions of beta-glucans in human nutrition. *Roczniki Państwowego Zakadu Higieny* 70:315–24. doi: 10.32394/rpzh.2019.0082.

Connolly, M. L., J. A. Lovegrove, and K. M. Tuohy. 2012. In vitro fermentation characteristics of whole grain wheat flakes and the effect of toasting on prebiotic potential. Journal of Medicinal Food 15 (1): 33–43. doi: 10.1089/jmf.2011.0006.

Cummings, J. H., E. W. Pomare, W. J. Branch, C. P. Naylor, and G. T. Macfarlane. 1987. Short chain fatty acids in human large intestine, portal, hepatic and venous blood. *Gut* 28:1221–7. doi: 10.1136/gut.28.10.1221..

Carvalho, D. O., A. F. Curto, and L. F. Guido. 2015. Determination of phenolic content in different barley varieties and corresponding malts by liquid chromatography-diode array detection-electrospray ionization tandem mass spectrometry. *Antioxid* 4:563–76. doi: 10.3390/antiox4030563..

Daou, C., and H. Zhang. 2012. Oat beta-glucan: Its role in health promotion and prevention of diseases. *Comprehensive Reviews in Food Science and Food Safety* 11 (4):355–65. doi: 10.1111/j.1541-4337.2012.00189.x.

Darvin, P., Y. H. Joung, S. P. Nipin, D. Y. Kang, H. J. Byun, D. Y. Hwang, K. H. Cho, K. D. Park, H. K. Lee, and Y. M. Yang. 2015. Sorghum polyphenol suppresses the growth as well as metastasis of colon cancer xenografts through co-targeting JAK2/STAT3 and PI3K/Akt/mTOR pathways. Journal of Functional Foods 15:193–206. doi: 10.1016/j.jff.2015.03.020.

Davidson, M. H., and K. C. Maki. 1999. Effects of dietary inulin on serum lipids. *The Journal of Nutrition* 129 (7):1474S–7S. doi: 10.1093/jn/129.7.1474S.

Dragland, S., H. Senoo, K. Wake, K. Holte, and R. Blomhoff. 2003. Several culinary and medicinal herbs are important sources of dietary antioxidants. Journal of Nutrition 133:1286–90. doi: 10.1093/jn/133.5.1286..

Dvonová, D., M. Havrlentová, A. Hlinková, and P. Hozlár. 2010. Effect of fertilization and variety on the b-glucan content in the grain of oats. *Journal of Food Science and Technology* 17:108–116. doi: 10.15193/zntj/2010/70/108-116.

Dykes. 2007. Phenolic compounds in cereal grains and their health benefits. *Cereal Food World* 52:105–111. doi: 10.1094/CFW-52-3-0105.

Eckel, R. H., S. M. Grundy, and P. Z. Zimmet. 2005. The metabolic syndrome. The Lancet 365 (9468):1415–28. doi: 10.1016/S0140-6736(05)66378-7.

Fao, R. 1995. Sorghum and millets in human nutrition. *FAO Food and Nutrition Series (FAO).* Rome, Lazio, Italy: FAO.

Fernandes, J., J. Vogt, and T. M. Wolever. 2011. Inulin increases short-term markers for colonic fermentation similarly in healthy and hyperinsulinaemic humans. *European Journal of Clinical Nutrition* 65 (12):1279–86. doi: 10.1038/ejcn.2011.116.

Fisher, H., P. Griminger, H. S. Weiss, and W. G. Siller. 1964. Avian atherosclerosis: Retardation by pectin. *Science* 146:1063–4. doi: 10.1126/science.146.3647.1063-a..

Fu, R., P. Yang, A. Sajid, and Z. Y. Li. 2019a. Avenanthramide A induces cellular senescence via miR-129-3p/Pirh2/p53 signaling pathway to suppress colon cancer growth. Journal of Agricultural and Food Chemistry 67:4808–16. doi: 10.1021/acs.jafc.9b00833..

Fu, R., P. Yang, Z. Li, W. Liu, A. Sajid, and Z. Y. Li. 2019b. Avenanthramide A triggers potent ROS mediated anti-tumor effects in colorectal cancer by directly targeting DDX3. *Cell Death and Disease.* 10:593. doi: 10.1038/s41419-019-1825-5.

Fuller, S., E. Beck, H. Salman, and L. Tapsell. 2016. New Horizons for the Study of Dietary Fiber and Health: A Review. *Plant Foods for Human Nutrition (Dordrecht, Netherlands)* 71 (1):1–12. doi:10.1007/s11130-016-0529-6.

Gadde, K. M., C. K. Martin, H. R. Berthoud, and S. B. Heymsfield. 2018. Obesity: Pathophysiology and management. Journal of the American College of Cardiology 71:69–84. doi: 10.1016/j.jacc.2017.11.011..

Garcia, A. L., B. Otto, S. C. Reich, M. O. Weickert, J. Steiniger, A. Machowetz, N. N. Rudovich, N. Katz, M. Möhlig, N. M. Speth, et al. 2007. Arabinoxylan consumption decreases postprandial serum glucose, serum insulin and plasma total ghrelin response in subjects with impaired glucose tolerance. *European Journal of Clinical Nutrition* 61 (3):334–41. doi: 10.1038/sj.ejcn.1602525.

Geng, Z. P., and L. J. Jia. 1992. Study on protein, lysine and tannin content of sorghum varieties from Shanxi Province. *Crop Variety Resources* 04:26–7.

Gentile, C. L., and T. L. Weir. 2018. The gut microbiota at the intersection of diet and human health. *Science (New York, N.Y.)* 362 (6416): 776–80. doi:10.1126/science.aau5812.

Gibson, G. R., H. M. Probert, J. V. Loo, R. A. Rastall, and M. B. Roberfroid. 2004. Dietary modulation of the human colonic microbiota: Updating the concept of prebiotics. Nutrition Research Reviews 17:259–75. doi: 10.1079/NRR200479.

Givens, D. I. 2005. The role of animal nutrition in improving the nutritive value of animal-derived foods in relation to chronic disease. Proceedings of the Nutrition Society 64:395–402. doi: 10.1079/pns2005448..

Goff, D. C., H. C. Gerstein, H. N. Ginsberg, W. C. Cushman, K. L. Margolis, R. P. Byington, J. B. Buse, S. Genuth, J. L. Probstfield, and D. G. Simons-Morton. 2007. Prevention of cardiovascular disease in persons with type 2 diabetes mellitus: Current knowledge and rationale for the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. The American Journal of Cardiology 99 (12): S4–S20. doi: 10.1016/j.amjcard.2007.03.002.

Gong, L. X., W. Y. Cao, H. L. Chi, J. Wang, H. J. Zhang, J. Liu, and B. G. Sun. 2018. Whole cereal grains and potential health effects: Involvement of the gut microbiota. *Food Research International.* 103: 84–102. doi: 10.1016/j.foodres.2017.10.025..

Guo, W. M., L. Nie, D. Y. Wu, M. L. Wise, F. W. Collins, S. N. Meydani, and M. Meydani. 2010. Avenanthramides inhibit proliferation of human colon cancer cell lines in vitro. *Nutrition and Cancer* 62:1007–16. doi: 10.1080/01635581.2010.492090.

Gupta, M., N. Abu-Ghannam, and E. Gallaghar. 2010. Barley for brewing: Characteristic changes during malting, brewing and applications of its by-products. *Comprehensive Reviews in Food Science and Food Safety* 9 (3):318–28. doi: 10.1111/j.1541-4337.2010.00112.x.

Hager, A. S., L. A. M. Ryan, C. Schwab, M. G. Ganzle, J. V. O. Doherty, and E. K. Arendt. 2011. Influence of the soluble fibres inulin and oat β-glucan on quality of dough and bread. *European Food Research and Technology* 232 (3):405–413. doi: 10.1007/s00217-010-1409-1.

Hamaker, B. R., and Y. E. Tuncil. 2014. Aperspective on the complexity of dietary fiber structures and their potential effect on the gut microbiota. Journal of Molecular Biology 426 (23):3838–50. doi: 10.1016/j.jmb.2014.07.028.

Hao, J., H. Zhu, Z. Q. Zhang, S. L. Yang, and H. Li. 2015. Identification of anthocyanins in black rice (Oryza sativa L.) by UPLC/Q-TOF-MS and their in vitro and in vivo antioxidant activities. Journal of Cereal Science 64:92–9. doi: 10.1016/j.jcs.2015.05.003.

Harborne, J. B., and C. A. Williams. 2000. Advances in flavonoid research since 1992. *Phytochemistry* 55 (6):481–504. doi:10.1016/S0031-9422(00)00235-1.

He, Y., S. Z. Wang, and Y. Ding. 2013. Identification of novel glutelin subunits and a comparison of glutelin composition between japonica and indica rice (Oryza sativa L.). Journal of Cereal Science 57 (3): 362–71. doi: 10.1016/j.jcs.2012.12.009.

Henrion, M., C. Francey, K. A. Lê, and L. Lamothe. 2019. Cereal B-glucans: The impact of processing and how it affects physiological responses. *Nutrients* 11 (8):1729. doi: 10.3390/nu11081729.

Higginson, J., and W. J. Pepler. 1954. Fat intake, serum cholesterol concentration, and atherosclerosis in the South African Bantu. II. Atherosclerosis and coronary artery disease. *Journal of Clinical Investigation* 33:1366–71. doi: 10.1172/JCI103013..

Hiller, G., M. Sternby, R. Sundler, and J. Wijkander. 2000. Phosphatidylinositol 3-kinase in zymosan- and bacteria-induced signalling to mobilisation of arachidonic acid in macrophages. Biochimica et Biophysica Acta 1485:163–72. doi: 10.1016/S1388-1981(00)00037-8.

Holtekjølen, A. K., C. Kinitz, and S. H. Knutsen. 2006. Flavanol and bound phenolic acid contents in different barley varieties. Journal of Agricultural and Food Chemistry 54:2253–60. doi: 10.1021/jf052394p.

Horn, L. V. 2006a. Promoting the value of early nutritional intervention. *Journal of the American Dietetic Association* 106(5):649–9. doi: 10.1016/j.jada.2006.03.017.

Horn, L. V. 2006b. Nutrition month: An overview. *Journal of the American Dietetic Association* 106(3):339–9.doi: 10.1016/j.jada.2006.01.022.

Hosoda, A., Y. Okai, E. Kasahara, E. Kasahara, M. Inoue, M. Snhimizu, Y. Usui, A. Sekiyama, and K. Higashi-Okai. 2012. Potent immunomodulating effects of bran extracts of traditional Japanese millets on nitric oxide and cytokine production of macrophages (RAW264.7) induced by lipopolysaccharide. *Journal of UOEH* 34:258–96. doi: 10.7888/juoeh.34.285.

Howlett, J. J., V. A. Betteridge, M. Champ, S. A. S. Craig, A. Meheust, and J. M. Jones. 2010. The definition of dietary fiber-discussions at the ninth vahouny fiber symposium: Building scientific agreement. *Food & Nutrition Research* 54:5750–5. doi: 10.3402/fnr.v54i0.5750.

Hu, S. L., L. Wang, and Z. Y. Jiang. 2017. Dietary additive probiotics modulation of the intestinal microbiota. *Protein & Peptide Letters* 24:382–87. doi: 10.2174/0929866524666170223143615..

Jackson, K. G., G. R. Taylor, A. M. Clohessy, and C. M. Williams. 1999. The effect of the daily intake of inulin on fasting lipid, insulin and glucose concentrations in middle-aged men and women. *British Journal of Nutrition* 82 (1):23–30. doi: 10.1017/S0007114599001087.

Jones, J. M. 2007. Mining whole grains for functional components. *Food Science & Technology Bulletin: Functional Foods* 4 (7):67–86. doi: 10.1616/1476-2137.15050.

Keiko, K. 2016. The intestinal microbiota and its role in human health and disease. *The Journal of Medical Investigation* 63:27–37. doi: 10.2152/jmi.63.27.

Kiarie, E., L. F. Romero, and V. Ravindran. 2014. Growth performance, nutrient utilization, and digesta characteristics in broiler chickens fed corn or wheat diets without or with supplemental xylanase. Poultry Science 93 (5):1186–96. doi: 10.3382/ps.2013-03715.

Kim, K. H., R. Tsao, R. Yang, and S. W. Cui. 2006. Phenolic acid profiles and antioxidant activities of wheat bran extracts and the effect of hydrolysis conditions. *Food Chemistry* 95 (3):466–73. doi: 10.1016/j.foodchem.2005.01.032.

Kim, M. J., S. Y. Hong, S. K. Kim, C. Cheong, H. J. Park, H. K. Chun, K. H. Jang, B. D. Yoon, C. H. Kim, and S. A. Kang. 2009. β-Glucan enhanced apoptosis in human colon cancer cells SNU-C4. *Nutrition Research and Practice* 3 (3):180–4. doi: 10.4162/nrp.2009.3.3.180.

Knudsen, K. E. B. 2014. Fiber and nonstarch polysaccharide content and variation in common crops used in broiler diets. *Poultry Science* 93:2380–93. doi: 10.3382/ps.2014-03902.

Koh, A., F. D. Vadder, P. Kovatcheva-Datchary, and F. Bäckhed. 2016. From dietary fiber to host physiology: Short-chain fatty acids as key bacterial metabolites. *Cell* 165:1332–45. doi: 10.1016/j.cell.2016.05.041..

Korczak, R., A. Kamil, L. Fleige, S. M. Donovan, and J. L. Slavin. 2017. Dietary fiber and digestive health in children. *Nutrition Reviews* 75: 241. doi: 10.1093/nutrit/nuw068.

Kroon, P. A., C. B. Faulds, P. Ryden, J. A. Robertson, and G. Williamson. 1997. Release of covalently bound ferulic acid from fiber in the human colon. *Journal of Agricultural and Food Chemistry* 45 (3):661–7. doi: 10.1021/jf9604403.

Krygier, K., F. Sosulski, and L. Hogge. 1982. Free, esterified, and insoluble-bound phenolic acids. 1. Extraction and purification procedure. *Journal of Agricultural and Food Chemistry* 30 (2):330–4. doi: 10.1021/jf00110a028.

Kunitomo, M. 2007. Oxidative stress and atherosclerosis. *Yakugaku Zasshi* 127:1997–2014. doi: 10.1248/yakushi.127.1997..

Kunyanga, C. N., J. K. Imungi, M. W. Okoth, H. K. Biesalski, and V. Vadivel. 2012. Total phenolic content, antioxidant and antidiabetic properties of methanolic extract of raw and traditionally processed Kenyan indigenous food ingredients. *LWT - Food Science and Technology* 45 (2):269–76. doi: 10.1016/j.lwt.2011.08.006.

Lasztity, R. 1996. *The chemistry of cereal protein.* Boca Raton, FL: CRC Press.

Lattimer, J. M., and M. D. Haub. 2010. Effects of dietary fiber and its components on metabolic health. *Nutrients* 2 (12):1266–89. doi: 10.3390/nu2121266.

Lee, J. Y., J. Y. Kim, Y. G. Lee, M. H. Rhee, and J. Y. Cho. 2008. Molecular mechanism of macrophage activation by exopolysaccharides from liquid culture of Lentinus edodes. Journal of Microbiology and Biotechnology 18(2):355–364. PMID: 18309284.

Lee, Y. R., E. M. Noh, H. J. Oh, H. Hur, J. M. Kim, J. H. Han, J. K. Hwang, B. H. Park, J. W. Park, and H. J. Youn. 2011. Dihydroavenanthramide D inhibits human breast cancer cell invasion through suppression of MMP-9 expression. *Biochemical and Biophysical Research Communications* 405:552–557. doi: 10.1016/j.bbrc.2011.01.065..

Letexier, D., F. Diraison, and M. Beylot. 2003. Addition of inulin to a moderately high-carbohydrate diet reduces hepatic lipogenesis and plasma triacylglycerol concentrations in humans. *The American Journal of Clinical Nutrition* 77 (3):559–564. doi: 10.1093/ajcn/77.3.559.

Li, L. J., M. K. Ikram, and T. Y. Wong. 2016. Retinal vascular imaging in early life: Insights into processes and risk of cardiovascular disease. Journal of Physiology 594:2175–203. doi: 10.1113/JP270947.

Li, W., S. W. Cui, and Y. Kakuda. 2006. Extraction, fractionation, structural and physical characterization of wheat β-D-glucans. Carbohydrate Polymers 63 (3):408–16. doi: 10.1016/j.carbpol.2005.09.025.

Liao, J. H., S. M. Planchon, J. C. Wolfman, and A. Wolfman. 2006. Growth factor-dependent AKT activation and cell migration requires the function of c-K(B)-Ras versus other cellular ras isoforms. Journal of Biological Chemistry 281:29730–8. doi: 10.1074/jbc.M600668200.

Lieselotte, C., U. Matilda, J. P. Anna, Å. Björn, and Ö. Gunilla. 2012. Role of dietary beta-glucans in the prevention of the metabolic syndrome. *Nutrition Reviews* 70:444–58. doi: 10.1111/j.1753-4887.2012.00494.x..

Lima, I., H. Guraya, and E. Champagne. 2002. The functional effectiveness of reprocessed rice bran as an ingredient in bakery products. *Nahrung/Food* 46 (2):112–7. doi: 10.1002/1521-3803(20020301)46:2<112::AID-FOOD112>3.0.CO;2-N.

Liu, C., S. Yang, K. Wang, X. M. Bao, Y. M. Liu, S. Y. Zhou, H. W. Liu, Y. L. Qiu, T. Wang, and H. Y. Yu. 2019a. Alkaloids from traditional Chinese medicine against hepatocellular carcinoma. Biomedicine & Pharmacotherapy 120:109543. doi: 10.1016/j.biopha.2019.109543.

Liu, F. M., S. H. Shan, H. Q. Li, and Z. Y. Li. 2020. Treatment of peroxidase derived from foxtail millet bran attenuates atherosclerosis by inhibition of cd36 and stat3 in vitro and in vivo. Journal of Agricultural and Food Chemistry 68:1276–85. doi: 10.1021/acs.jafc.9b06963.

Lu, Y., S. H. Shan, H. Q. Li, J. Y. Shi, X. L. Zhang, and Z. Y. Li. 2018. Reversal effects of bound polyphenol from foxtail millet bran on multidrug resistance in human HCT-8/Fu colorectal cancer cell. *Journal of Agricultural and Food Chemistry* 66 (20):5190–5199. doi: 10.1021/acs.jafc.8b01659.

Luithui, Y., N. R. Baghya, and M. S. Meera. 2019. Cereal by-products as an important functional ingredient: Effect of processing. *Journal of Food Science and Technology* 56:1–11. doi: 10.1007/s13197-018-3461-y..

Ma, Q. T., Y. Q. Li, P. F. Li, M. Wang, J. K. Wang, Z. Y. Tang, T. Wang, L. L. Luo, C. G. Wang, and T. Wang. 2019. Research progress in the relationship between type 2 diabetes mellitus and intestinal flora. Biomedicine & Pharmacotherapy 117:109138. doi: 10.1016/j.biopha.2019.109138..

Manco, M.,. L. Putignani, and G. F. Bottazzo. 2010. Gut microbiota, lipopolysaccharides, and innate immunity in the pathogenesis of obesity and cardiovascular risk. *Endocrine Reviews* 31:817–44. doi: 10.1210/er.2009-0030..

Manthey, F. A., G. A. Hareland, and D. J. Huseby. 1999. Soluble and insoluble dietary fiber content and composition in oat. *Cereal Chemistry* 76 (3):417–20. doi: 10.1094/CCHEM.1999.76.3.417.

Mattila, P., J. M. Pihlava, and J. Hellström. 2005. Contents of phenolic acids, alkyl- and alkenylresorcinols, and avenanthramides in commercial grain products. Journal of Agricultural and Food Chemistry 53:8290–8295. doi: 10.1021/jf051437z.

McKevith, B. 2004. Nutritional aspects of cereals. *Nutrition* Bulletin 29:112–42. doi: 10.1111/j.1467-3010.2004.00418.x.

Mckee, L. H., and T. A. Latner. 2000. Underutilized sources of dietary fiber: A review. *Plant Food Hum Nutr* 55:285–304. doi: 10.1023/A:1008144310986.

Medicine, I. O. 2001. *Dietary reference intakes: Proposed definition of dietary fiber*. Washington DC: National Academies Press.

Medzhitov, R. 2008. Origin and physiological roles of inflammation. *Nature* 454:428–35. doi: 10.1038/nature07201..

Mendis, M.,. E. Leclerc, and S. Simsek. 2016. Arabinoxylans, gut microbiota and immunity. Carbohydrate Polymers 139:159–66. doi: 10.1016/j.carbpol.2015.11.068.

Mirończuk-Chodakowska, I., A. M. Witkowska, M. E. Zujko, and K. M. Terlikowska. 2017. Quantitative evaluation of 1,3,1,6 β-D-glucan contents in wild-growing species of edible Polish mushrooms. *Roczniki Państwowego Zakładu Higieny* 68(3):281–90. PMID: 28895671.

Morrison, D. J., and T. Preston. 2016. Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism. *Gut Microbes* 7 (3):189–200. doi:10.1080/19490976.2015.1134082.

Moure, A., J. M. Cruz, D. Franco, J. M. Domı́nguez, J. Sineiro, H. Domı́nguez, M. José Núñez, and J. C. Parajó, 2001. Natural antioxidants from residual sources. *Food Chemistry* 72 (2):145–71. doi: 10.1016/S0308-8146(00)00223-5.

Nakashima, A., K. Yamada, O. Iwata, R. Sugimoto, K. Atsuji, T. Ogawa, N. Ishibashi-Ohgo, and K. Suzuki. 2018. β-Glucan in foods and its physiological functions. *Journal of Nutritional Science and Vitaminology (Tokyo)* 64:8–17. doi: 10.3177/jnsv.64.8.

Nations, F. A. O. O., and M. C. Latham. 1997. Human nutrition in the developing world. *Population and Development Review* 24:177. doi: 10.2307/2808139.

Neyrinck, A. M., S. Possemiers, C. Druart, T. V. D. Wiele, F. D. Backer, P. D. Cani, Y. Larondelle, and N. M. Delzenne. 2011. Prebiotic effects of wheat arabinoxylan related to the increase in bifidobacteria, Roseburia and Bacteroides/Prevotella in diet-induced obese mice. *PLoS One* 6 (6):e20944. doi: 10.1371/journal.pone.0020944.

Nicole, R., S. H. Duncan, P. Young, A. Belenguer, L. C. McWilliam, K. P. Scott, H. J. Flint, and P. Louis. 2014. Phylogenetic distribution of three pathways for propionate production within the human gut microbiota. *ISME Journal* 8:1323–35. doi: 10.1038/ismej.2014.14.

Olsson, S., and R. Sundler. 2007. The macrophage beta-glucan receptor mediates arachidonate release induced by zymosan: Essential role for Src family kinases. *Molecular Immunology* 44:1509–15. doi: 10.1016/j.molimm.2006.09.004.

Omoba, O. S., and L. R. Isah. 2018. Influence of Sourdough Fermentation on Amino Acids Composition, Phenolic Profile, and Antioxidant Properties of Sorghum Biscuits. *Preventive Nutrition and Food Science* 23 (3):220–7. doi:10.3746/pnf.2018.23.3.220.

Peterson, D. M. 2001. Oat antioxidants. Journal of Cereal Science 33 (2):115–29. doi: 10.1006/jcrs.2000.0349.

Peterson, D. M., D. M. Wesenberg, and D. E. Burrup. 1995. b-Glucan content and its relationship to agronomic characteristics in elite oat germplasm. *Crop Science* 35 (4):965–70. doi: 10.2135/cropsci1995.0011183X003500040005x.

Petimar, J., S. A. Smith-Warner, B. Rosner, A. T. Chan, E. L. Giovannucci, and F. K. Tabung. 2019. Adherence to the world cancer research fund/American institute for cancer research 2018 recommendations for cancer prevention and risk of colorectal cancer. *Cancer Epidemiology, Biomarkers & Prevention* 28:1469–79. doi: 10.1158/1055-9965.EPI-19-0165..

Qi, W., and P. R. Ellis. 2014. Oat β-glucan: Physico-chemical characteristics in relation to its blood-glucose and cholesterol-lowering properties. British Journal of Nutrition 112:S4–S13. doi: 10.1017/S0007114514002256.

Qian, Y., L. Corum, Q. Meng, J. Blenis, J. Z. Zheng, X. L. Shi, D. C. Flynn, and B. H. Jiang. 2004. PI3K induced actin filament remodeling through Akt and p70S6K1: Implication of essential role in cell migration. *American Journal of Physiology-Cell Physiology* 286: C153–63. doi: 10.1152/ajpcell.00142.2003..

Rakowska, R., A. Sadowska, E. Dybkowska, and F. Świderski. 2017. Spent yeast as natural source of functional food additives. *Roczniki Państwowego Zakładu Higieny* 68(2):115–21. PMID: 28646828.

Rao, S. M. V. S. S. T., and G. Muralikrishna. 2002. Evaluation of the antioxidant properties of free and bound phenolic acids from native and malted finger millet (Ragi, Eleusine coracana Indaf-15). Journal of Agricultural and Food Chemistry 50:889–92. doi: 10.1021/jf011210d.

Reichardt, N., S. H. Duncan, P. Young, A. Belenguer, C. M. Leitch, K. P. Scott, H. J. Flint, and P. Louis. 2014. Phylogenetic distribution of three pathways for propionate production within the human gut microbiota. *ISME Journal* 8:1323–35. doi: 10.1038/ismej.2014.14.

Rhodes, M. J. C., and K. R. Price. 1997. Identification and analysis of plant phenolic antioxidants. *European Journal of Cancer Prevention* 6:518–21. doi: 10.1097/00008469-199712000-00005.

Richter, C. K., A. Skulas-Ray, C. M. Champagne, and P. M. Kris-Etherton. 2015. Plant protein and animal proteins: Do they differentially affect cardiovascular disease risk? Advances in Nutrition 6: 712–28. doi: 10.3945/an.115.009654..

Roach, P. D., K. Dowling, S. Balasubramaniam, R. J. Illman, A. M. Kambouris, P. J. Nestel, and D. L. Topping. 1992. Fish oil and oat bran in combination effectively lower plasma cholesterol in the rat. *Atherosclerosis* 96:219–26. doi: 10.1016/0021-9150(92)90068-R.

Robbins, R. J. 2003. Phenolic acids in foods: An overview of analytical methodology. Journal of Agricultural and Food Chemistry 51: 2866–87. doi: 10.1021/jf026182t..

Russo, F., G. Chimienti, G. Riezzo, G. Pepe, G. Petrosillo, M. Chiloiro, and E. Marconi. 2008. Inulin-enriched pasta affects lipid profile and Lp (a) concentrations in Italian young healthy male volunteers. *European Journal of Nutrition* 47:453–9. doi: 10.1007/s00394-008-0748-1..

Saastamoinen, M., V. Hietaniemi, J. M. Pihlava, M. Urola, M. Kontturi, H. Tuuri, M. Niskanen, and A. Kangas. 2008. b-Glucan contents of groats of different oat cultivars in official variety, in organic cultivation, and in nitrogen fertilization trials in Finland. *Agricultural and Food Science* 13 (1–2):68–79. doi: 10.2137/1239099041838076.

Saeedi, P., I. Petersohn, P. Salpea, B. Malanda, S. Karuranga, N. Unwin, S. Colagiuri, L. Guariguata, A. A. Motala, K. Ogurtsova, IDF Diabetes Atlas Committee, et al. 2019. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the international diabetes federation diabetes atlas, 9 th edition. *Diabetes Research and Clinical Practice* 157:107843. doi: 10.1016/j.diabres.2019.107843..

Saleh, A. S., Q. Zhang, J. Chen, and Q. Shen. 2013. Millet grains: Nutritional quality, processing, and potential health benefits. Comprehensive Reviews in Food Science and Food Safety 12 (3): 281–95. doi: 10.1111/1541-4337.12012.

Samantha, K. G., R. Megan, B. Balazs, and W. Kevin. 2020. Dietary fibre in gastrointestinal health and disease. Nature Reviews Gastroenterology & Hepatology 18:101–16. doi: 10.1038/s41575-020-00375-4.

Sanchez, J. I., M. Marzorati, C. Grootaert, M. Baran, V. V. Craeyveld, C. M. Courtin, W. F. Broekaert, J. A. Delcour, W. Verstraete, and T. V. Wiele. 2009. Arabinoxylan-oligosaccharides (AXOS) affect the protein/carbohydrate fermentation balance and microbial population dynamics of the Simulator of Human Intestinal Microbial Ecosystem. Microbial Biotechnology 2:101–13. doi: 10.1111/j.1751-7915.2008.00064.x.

Sarma, S. M., D. P. Singh, P. Singh, P. Khare, P. Mangal, S. Singh, V. Bijalwan, J. Kaur, S. Mantri, R. K. Boparai, et al. 2018. Finger millet arabinoxylan protects mice from high-fat diet induced lipid derangements, inflammation, endotoxemia and gut bacterial dysbiosis. International Journal of Biological Macromolecules 106:994–1003. doi: 10.1016/j.ijbiomac.2017.08.100..

Schulze, M. B., S. Liu, B. E. Rimm, J. E. Manson, and F. B. Hu. 2004. Glycemic index, glycemic load, and dietary fiber intake and incidence of type 2 diabetes in younger and middle-aged women 1-3. American Journal of Clinical Nutrition 80:348–56. doi: 10.1093/ajcn/80.2.348..

Shah, A., M. Ahmad, B. A. Ashwar, A. Gani, F. A. Masoodi, I. A. Wani, S. M. Wani, and A. Gani. 2015. Effect of γ-irradiation on structure and nutraceutical potential of β-D-glucan from barley (Hordeum vulgare). International Journal of Biological Macromolecules 72:1168–75. doi: 10.1016/j.ijbiomac.2014.08.056..

Shahidi, F., and A. Chandrasekara. 2013. Millet grain phenolics and their role in disease risk reduction and health promotion: A review. Journal of Functional Foods 5 (2):570–81. doi: 10.1016/j.jff.2013.02.004.

Shan, S. H., Z. W. Li, I. P. Newton, C. Zhao, Z. Y. Li, and M. L. Guo. 2014a. A novel protein extraxted from foxtail millet bran displays anti-carcinogenic effects in human colon cancer cells. Toxicology Letters 227:129–38. doi: 10.1016/j.toxlet.2014.03.008..

Shan, S. H., Z. W. Li, S. J. Guo, Z. Y. Li, T. L. Shi, and J. Y. Shi. 2014b. A millet bran-derived peroxidase inhibits cell migration by antagonizing STAT3-mediated epithelial-mesenchymal transition in human colon cancer. Journal of Functional Foods 10:444–55. doi: 10.1016/j.jff.2014.07.005.

Shan, S. H., J. Y. Shi, Z. Li, H. X. Gao, T. L. Shi, Z. W. Li, and Z. Y. Li. 2015. Targeted anti-colon cancer activities of a millet bran-derived peroxidase were mediated by elevated ROS generation. *Food & Function* 6:2331–8. doi: 10.1039/C5FO00260E.

Shao, Y. F., G. Zhang, and J. S. Bao. 2011. Total phenolic content and antioxidant capacity of rice grains with extremely small size. *African Journal of Agricultural Research* 6:2289–93. doi: 10.5897/AJAR11.124.

Shi, J. Y., S. H. Shan, G. F. Zhou, H. Q. Li, G. S. Song, Z. Y. Li, and D. F. Yang. 2019a. Bound polyphenol from foxtail millet bran exhibits an antiproliferative activity in HT-29 cells by reprogramming miR-149-mediated aerobic glycolysis. Journal of Functional Foods 56:246–54. doi: 10.1016/j.jff.2019.03.021.

Shi, J. Y., S. H. Shan, H. Q. Li, G. S. Song, and Z. Y. Li. 2017a. Anti-inflammatory effects of millet bran derived-bound polyphenols in LPS-induced HT-29 cell via ROS/miR-149/Akt/NF-κB signaling pathway. *Oncotarget* 8:74582–94. doi: 10.18632/oncotarget.20216..

Shi, J. Y., S. H. Shan, Z. W. Li, H. Q. Li, X. F. Li, and Z. Y. Li. 2015a. Bound polyphenol from foxtail millet bran induces apoptosis in HCT-116 cell through ROS generation. Journal of Functional Foods 17:958–68. doi: 10.1016/j.jff.2015.06.049.

Sima, P., L. Vannucci, and V. Vetvicka. 2018. β-glucans and cholesterol (review). International Journal of Molecular Medicine 41:1799–808. doi: 10.3892/ijmm.2018.3411.

Singh, R., S. De, and A. Belkheir. 2013. Avena sativa (Oat), a potential neutraceutical and therapeutic agent: An overview. Critical Reviews in Food Science and Nutrition 53:126–44. doi: 10.1080/10408398.2010.526725..

Slavin, J. 2013. Fiber and prebiotics: Mechanisms and health benefits. *Nutrients* 5 (4):1417–35. doi: 10.3390/nu5041417.

Soliman, G. A. 2019. Dietary fiber, atherosclerosis, and cardiovascular disease. *Nutrients* 11 (5):1155. doi: 10.3390/nu11051155.

Song, Y. J., H. Y. Jeong, J. K. Lee, Y. S. Choi, D. Kim, D. Jang, C. Park, S. Maeng, and H. Kang. 2019. Enzyme treatment alters the anti-inflammatory activity of the water extract of wheat germ in vitro and in vivo. *Nutrients* 11 (10):2490. doi: 10.3390/nu11102490.

Story, J. A. 1985. Dietary fiber and lipid metabolism. *Proceedings of the Society for Experimental Biology and Medicine. Society for Experimental Biology and Medicine (New York, N.Y.)* 180 (3):447–52. doi:10.3181/00379727-180-42201.

Subba Rao, M. V. S. S. T., and G. Muralikrishna. 2002. Evaluation of the antioxidant properties of free and bound phenolic acids from native and malted finger millet (Ragi, Eleusine coracana Indaf-15). Journal of Agricultural and Food Chemistry 50:889–92. doi: 10.1021/jf011210d.

Suchecka, D., J. Gromadzka-Ostrowska, E. Żyła, J. P. Harasym, and M. Oczkowski. 2017. Selected physiological activities and health promoting properties of cereal betaglucans. A review. *Journal of Animal and Feed Sciences* 26:183–91. doi: 10.22358/jafs/70066/2017..

Sun, N. X., L. T. Tong, T. T. Liang, L. L. Wang, L. Y. Liu, X. R. Zhou, and S. M. Zhou. 2019. Effect of oat and Tartary buckwheat-based food on cholesterol-lowering and gut microbiota in hypercholesterolemic hamsters. *Journal of Oleo Science* 68 (3):251–9. doi: 10.5650/jos.ess18221.

Tan, J. K., C. McKenzie, E. Mariño, L. Macia, and C. R. Mackay. 2017. Metabolite-sensing G protein-coupled receptors-facilitators of diet-related immune regulation. *Annual Review of Immunology* 35 (1): 371–402. doi: 10.1146/annurev-immunol-051116-052235.

Tan, Y. Y., S. H. Yeo, and P. C. Y. Liauw. 1996. Is postnatal oral glucose tolerance testing necessary in all women with gestational diabetes. *Singapore Medical Journal* 37(4):384–8. PMID: 8993138.

Tang, W. H. W., and S. L. Hazen. 2017. Gut microbiome and its role in cardiovascular diseases. *Current Opinion in Cardiology* 32:761–6. doi: 10.1097/HCO.0000000000000445..

Tarini, J., and T. M. Wolever. 2010. The fermentable fibre inulin increases postprandial serum short-chain fatty acids and reduces free-fatty acids and ghrelin in healthy subjects. *Applied Physiology, Nutrition, and Metabolism* 35 (1):9–16. doi: 10.1139/H09-119.

Thorburn, A. N., L. Macia, and C. R. Mackay. 2014. Diet, metabolites, and "western-lifestyle" inflflammatory diseases. *Immunity* 40:833–42. doi: 10.1016/j.immuni.2014.05.014..

Tian, S., K. Nakamura, T. Cui, and H. Kayahara. 2005. High-performance liquid chromatographic determination of phenolic compounds in rice. Journal of Chromatography 1063:121–8. doi: 10.1016/j.chroma.2004.11.075..

Topping, D. L., R. J. Illman, P. D. Roach, R. P. Trimble, A. Kambouris, and P. J. Nestel. 1990. Modulation of the hypolipidemic effect of fish oils by dietary fiber in rats: Studies with rice and wheat bran. Journal of Nutrition 120:325–30. doi: 10.1093/jn/120.4.325..

Trinidad, A. G., M. L. de la Puerta, N. Fernández, Y. Bayón, M. S. Crespo, and A. Alonso. 2006. Coupling of C3bi to IgG inhibits the tyrosine phosphorylation signaling cascade downstream Syk and reduces cytokine induction in monocytes. *Journal of Leukocyte Biology* 79:1073–82. doi: 10.1189/jlb.1205701..

Tucker, L. A., and K. S. Thomas. 2009. Increasing total fiber intake reduces risk of weight and fat gains in women. Journal of Nutrition 139:576–81. doi: 10.3945/jn.108.096685..

Turrini, E., F. Maffei, A. Milelli, C. Calcabrini, and C. Fimognari. 2019. Overview of the anticancer profile of avenanthramides from oat. *International Journal of Molecular Sciences* 20 (18):4536. doi: 10.3390/ijms20184536.

Underhill, D. M., E. Rossnagle, C. A. Lowell, and R. M. Simmons. 2005. Dectin-1 activates Syk tyrosine kinase in a dynamic subset of macrophages for reactive oxygen production. *Blood* 106:2543–50. doi: 10.1182/blood-2005-03-1239..

Viswanath, V., A. Urooj, and N. G. Malleshi. 2009. Evaluation of antioxidant and antimicrobial properties of finger millet (Eleusine coracana). *Food Chemistry* 114 (1):340–6. doi: 10.1016/j.foodchem.2008.09.053.

Wang, D., M. L. Wise, F. Li, and M. Dey. 2012. Phytochemicals attenuating aberrant activation of beta-catenin in cancer cells. *PLoS One* 7 (12):e50508. doi: 10.1371/journal.pone.0050508.

Wang, P., H. D. Chen, Y. D. Zhu, J. McBride, J. S. Fu, and S. M. Sang. 2015. Oat avenanthramide-C(2c)is biotransformed by mice and the human microbiota into bioactive metabolites1-3. Journal of Nutrition 145:239–45. doi: 10.3945/jn.114.206508..

Wang, Y., S. V. Harding, P. Eck, S. J. Thandapilly, T. H. Gamel, E. S. M. Abdel-Aal, G. H. Crow, S. M. Tosh, and N. P. Ames. 2016. High-molecular-weight beta-glucan decreases serum cholesterol differentially based on the CYP7A1 rs3808607 polymorphism in mildly hypercholesterolemic adults. Journal of Nutrition 146:720–7. doi: 10.3945/jn.115.223206..

Wang, Y., S. V. Harding, S. J. Thandapilly, S. M. Tosh, P. J. H. Jones, and N. P. Ames. 2017. Barley beta-glucan reduces blood cholesterol levels via interrupting bile acid metabolism. British Journal of Nutrition 118:822–9. doi: 10.1017/S0007114517002835..

Waniska, R. D., J. H. Poe, and R. Bandyopadhyay. 1989. Effects of growth conditions on grain molding and phenols in sorghum caryopsis. Journal of Cereal Science 10 (3):217–25. doi: 10.1016/S0733-5210(89)80051-7.

Wei, Y. M., G. Q. Zhang, X. Z. Hu, and S. H. Ouyang. 2003. Studies on the amino acid and mineral content of buckwheat protein fractions. *Nahrung* 47:114–6. doi: 10.1002/food.200390020..

Weickert, M. O., M. Mohlig, C. Schofl, A. M. Arafat, B. Otto, H. Viehoff, C. Koebnick, A. Kohl, J. Spranger, and A. F. Pfeiffer. 2006. Cereal fiber improves whole-body insulin sensitivity in overweight and obese women. *Diabetes Care* 29:775–80. doi: 10.2337/diacare.29.04.06.dc05-2374..

Whelton, P. K., and D. C. Lisandro. 2019. Cardiovascular disease risk estimation in China. *Ann Intern Med* 170 (5):340–1.

Williams, C. M., and K. G. Jackson. 2002. Inulin and oligofructose: Effects on lipid metabolism from human studies. *British Journal of Nutrition* 87 (S2):S261–S4. doi: 10.1079/BJN/2002546.

Wilson, T. A., R. J. Nicolosi, B. Delaney, K. Chadwel, V. Moolchandani, T. Kotyla, S. Ponduru, G. H. Zheng, R. Hess, N. Knutson, et al. 2004. Reduced and high molecular weight barley beta-glucans decrease plasma total and non-HDL-cholesterol in hypercholesterolemic Syrian golden hamsters. Journal of Nutrition 134:2617–22. doi: 10.1093/jn/134.10.2617..

Wong, J. M. 2007. Carbohydrate digestibility and metabolic effects. Journal of Nutrition 137:2539S. doi: 10.1093/jn/137.11.2539S..

Wood, P. J. 2010. REVIEW: Oat and rye β-glucan: Properties and function. *Cereal Chemistry* 87 (4):315–30. doi: 10.1094/CCHEM-87-4-0315.

Wood, P. J., J. T. Braaten, F. W. Scott, K. D. Riedel, M. S. Wolynetz, and M. W. Collins. 1994. Effect of dose and modification of viscous properties of oat gum on plasma glucose and insulin following an oral glucose load. British Journal of Nutrition 72:731–43. doi: 10.1079/bjn19940075..

Yang, H., D. Ming, and S. Laura. 2020. Intake of whole grain foods and risk of type 2 diabetes: results from three prospective cohort studies. *BMJ* 370 (1):2206–18.

Yang, R. P., S. H. Shan, C. Zhang, J. Y. Shi, H. Q. Li, and Z. Y. Li. 2020. Inhibitory effects of bound polyphenol from foxtail millet bran on colitis-associated carcinogenesis by the restoration of gut microbiota in a mice model. Journal of Agricultural and Food Chemistry 68:3506–17. doi: 10.1021/acs.jafc.0c00370..

Yao, Y., Z. X. Shi, and G. X. Ren. 2014. Antioxidant and immunoregulatory activity of polysaccharides from quinoa (Chenopodium quinoa Willd.). International Journal of Molecular Sciences 15: 19307–18. doi: 10.3390/ijms151019307..

Ze, X., S. H. Duncan, P. Louis, and H. J. Flint. 2012. Ruminococcus bromii is a keystone species for the degradation of resistant starch in the human colon. *ISME Journal* 6:1535–43. doi: 10.1038/ismej.2012.4..

Zhao, J., and P. C. Cheung. 2013. Comparative proteome analysis of Bifidobacterium longum subsp. infantis grown on β-glucans from different sources and a model for their utilization. Journal of Agricultural and Food Chemistry 61:4360–70. doi: 10.1021/jf400792j..

Zhou, Z. K., K. Robards, S. Helliwell, and C. Blanchard. 2004. The distribution of phenolic acids in rices. *Food Chemistry.* 87 (3):401–6. doi: 10.1016/j.foodchem.2003.12.015.

Žilić, S. 2016. Phenolic compounds of wheat their content, antioxidant capacity and bioaccessibility. *MOJ Food Processing & Technology* 2: 85–9. doi: 10.15406/mojfpt.2016.02.00037.