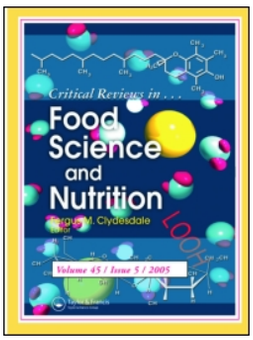

Critical Reviews in Food Science and Nutrition

ISSN: 1040-8398 (Print) 1549-7852 (Online) Journal homepage: http://www.tandfonline.com/loi/bfsn20

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To cite this article: Leandro de Morais Cardoso, Soraia Silva Pinheiro, Hércia Stampini Duarte Martino & Helena Maria Pinheiro-Sant'Ana (2017) Sorghum (*Sorghum bicolor* L.): Nutrients, bioactive compounds, and potential impact on human health, Critical Reviews in Food Science and Nutrition, 57:2, 372-390, DOI: 10.1080/10408398.2014.887057

To link to this article: https://doi.org/10.1080/10408398.2014.887057

Accepted author version posted online: 15 Apr 2015.
Published online: 15 Apr 2015.

CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
2017, VOL. 57, NO. 2, 372–390
http://dx.doi.org/10.1080/10408398.2014.887057

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Sorghum (*Sorghum bicolor* L.): Nutrients, bioactive compounds, and potential impact on human health

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ABSTRACT

Sorghum is the fifth most produced cereal in the world and is a source of nutrients and bioactive compounds for the human diet. We summarize the recent findings concerning the nutrients and bioactive compounds of sorghum and its potential impact on human health, analyzing the limitations and positive points of the studies and proposing directions for future research. Sorghum is basically composed of starch, which is more slowly digested than that of other cereals, has low digestibility proteins and unsaturated lipids, and is a source of some minerals and vitamins. Furthermore, most sorghum varieties are rich in phenolic compounds, especially 3-deoxyanthocyanidins and tannins. The results obtained in vitro and in animals have shown that phenolics compounds and fat soluble compounds (polycosanols) isolated from sorghum benefit the gut microbiota and parameters related to obesity, oxidative stress, inflammation, diabetes, dyslipidemia, cancer, and hypertension. The effects of whole sorghum and its fractions on human health need to be evaluated. In conclusion, sorghum is a source of nutrients and bioactive compounds, especially 3-deoxyanthocyanidins, tannins, and polycosanols, which beneficially modulate, in vitro and in animals, parameters related to noncommunicable diseases. Studies should be conducted to evaluate the effects of different processing on protein and starch digestibility of sorghum as well as on the profile and bioavailability of its bioactive compounds, especially 3-deoxyanthocyanidins and tannins. Furthermore, the benefits resulting from the interaction of bioactive compounds in sorghum and human microbiota should be studied.

KEYWORDS

Nutritional value; 3-deoxyanthocyanidins; tannins; noncommunicable diseases; oxidative stress; cancer

Abbreviations: ABCA1, ATP-binding cassette transporter A1; COX-2, cyclooxygenase-2; DP, degree of polymerization; GPx, glutathione peroxidase activity; HDL-c, high-density lipoprotein-cholesterol; HIF-1α, hypoxia-inducible factor 1α; HMG-CoA, 3-hydroxy-3-methylglutaryl CoA; IGF-1R, insulin-like growth factor 1; IL-1β, interleukin-1β; LDL-c, low-density lipoprotein-cholesterol; MUFA, monounsaturated fatty acids; NQO, NADH:quinone oxyreductase; NF- $\kappa\beta$, nuclear factor-$\kappa\beta$; PPAR-γ, peroxisome proliferator-activated receptor gamma; PUFA, polyunsaturated fatty acids; RES, reactive electrophilic species; RNS, reactive nitrogen species; ROS, reactive oxygen species; SOD, superoxide dismutase; TBARS, thiobarbituric acid reactive substances; TNF-α, tumor necrosis factor-α; VEGF, *vascular endothelial growth factor*

Introduction

Sorghum (*Sorghum bicolor* L.) is a cereal of the family *Poaceae*, native to Africa, and was domesticated between 3,000 and 5,000 years ago (U.S. Grains Council, 2004). It is the fifth most produced cereal in the world, and is preceded by wheat, rice, maize, and barley (Food and Agricultural Organization, 2010). Around the world, there are over 7,000 varieties of sorghum (Kangama and Rumei, 2005).

The sorghum crop is extremely important in Asia, Africa, and other semi-arid regions of the world, where it is mainly used in human feeding (Elkhalifa et al., 2005; Dillon et al., 2007; Afify et al., 2011). In Western countries such as the United States, Australia, and Brazil, sorghum is developed and cultivated primarily for animal feeding (Taleon et al., 2012). However, due to its high nutritional and functional potential, several studies on sorghum for human consumption have been conducted in these countries (Dykes et al., 2005; Maunder, 2005; Schober et al., 2005; Ciacci et al., 2007; Ferreira et al., 2009; Taylor, et al., 2014).

The sorghum grain has three distinct anatomical structures called the pericarp, endosperm, and germ. Some varieties have a fourth structure called the testa, located between the pericarp and the endosperm (Earp et al., 2004). The proportion and chemical composition of sorghum's anatomical structures depend on the variety and growing conditions (Waniska and Rooney, 2000). Generally, the pericarp (outer coating) and the testa are composed of non-starch polysaccharides, phenolic compounds (3-deoxyanthocyanidins, tannins, and phenolic acids, among others), and carotenoids. The starch, proteins, B-

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complex vitamins, and minerals are located in the endosperm (storage tissue). The germ (embryo) is composed of lipids, fat-soluble vitamins, B-complex vitamins, and minerals (Food Security Department, 1999; Waniska and Rooney, 2000; Earp et al., 2004; Slavin, 2004).

Sorghum is an excellent source of bioactive compounds that can promote benefits to human health. The results of in vitro and animal studies have shown that compounds isolated from sorghum, mainly phenolics, promote beneficial changes in parameters related to noncommunicable diseases such as obesity, diabetes, dyslipidemia, cardiovascular disease, cancer, and hypertension (Muriu et al., 2002; Shih et al., 2007; Kamath et al., 2007; Farrar et al., 2008; Awika et al., 2009; Yang et al., 2009; Kim and Park, 2012; Moraes et al., 2012a; Woo et al., 2012).

Given the high beneficial potential of sorghum on human health and the absence of a critical review about the subject, we summarize the recent findings concerning the nutrients and bioactive compounds of sorghum and its potential to modulate parameters related to human health, analyzing the limitations and positive points of recent studies and proposing directions for future research.

Methodology

Original articles published between 2005 and 2013 in scientific indexing bases (PubMed, Biological Abstracts, CAB Abstracts, Food Science and Technology Abstracts, LILACS, Scielo, MEDLINE, and Science Direct) were researched. In addition, some relevant scientific papers published in previous years were included.

The article search was performed by matching the terms sorghum and *Sorghum bicolor* L. with a group of terms related to chemical composition and nutritional value (starch, amylose, amylopectin, proteins, kafirins, dietary fibers, minerals, vitamins, mineral bioavailability, starch digestibility, phenolic compounds, phenolic acids, tannins, flavonoids, 3-deoxyanthocyanidins, flavones, flavanones, sterols, polycosanols, stilbenes, antioxidant profile, phytates, protease inhibitors: trypsin, chymotrypsin and amylase, and lectins) and another group related to chronic noncommunicable diseases (obesity, weight loss, dyslipidemia, cardiovascular disease, cholesterol, triacylglycerol, high-density lipoprotein-cholesterol (HDL-c), low-density lipoprotein-cholesterol (LDL-c), diabetes, fasting glucose, glycemic response, fasting insulin, insulinic response, cancer, oxidative stress, inflammation, interleukins, gut microbiota, and hypertension). The articles were screened and selected based on the title and abstract presented.

Chemical composition and nutritional value

The chemical composition and nutritional value of whole sorghum are similar to rice, corn, and wheat. The energy value of 100 g of sorghum grains varies between 296.1 and 356.0 kcal (Martino et al., 2012; U.S. Department of Agriculture, 2012). The main components of sorghum are the polysaccharides (starch and non-starch), followed by proteins and lipids (Martino et al., 2012; U.S. Department of Agriculture, 2012).

Polysaccharides

The content and composition of starch, the main polysaccharide of sorghum, are influenced by the genetic characteristics and growing conditions of the grain (Hill et al., 2012). In some varieties, starch ranges between 32.1 and 72.5 g/100 g and is composed mainly of amylopectin (81.0–96.5%) and amylose (3.5–19.0%) (Shegro et al., 2012; Udachan et al., 2012). The proportion of amylose and amylopectin affects the rheological proprieties (gelatinization, retrogradation, and gelling) and digestibility of the sorghum starch (Sang et al., 2008; Singh et al., 2010).

Sorghum has the lowest starch digestibility among cereals due to the strong association between the starch granules and proteins and tannins (Barros et al., 2012; Mkandawire et al., 2013; Rooney and Pflugfelder, 1986). Overall most of the starch granules are slowly digestible (30.0–66.2%) and the remainder is rapidly digestible (15.3–26.6%) or resistant (16.7–43.2%) (Sang et al., 2008; Mkandawire et al., 2013). The non-starch polysaccharides of sorghum (6.0 to 15.0 g/100 g) include insoluble fibers (75.0–90.0%), mainly arabinoxylans, and soluble fibers (10.0–25.0%) (Taylor and Emmambux, 2010; Martino et al., 2012; U.S. Department of Agriculture, 2012).

Proteins

Sorghum proteins are classified as prolamins and not prolamins. Prolamins correspond on average to 79% (77–82%) of the total proteins (7 to 15 g/100 g) and the remainder is albumins, globulins, and glutelins (Belton et al., 2006; Martino et al., 2012; U.S. Department of Agriculture, 2012; Afify et al., 2012b). The kafirins are the major prolamins of the sorghum and comprise three major classes: α-kafirins (66–84%), β-kafirins (8–13%) and γ-kafirins (9–21%) (Belton et al., 2006; Mokrane et al., 2010). Sorghum kafirins are stored in the endoplasmic reticulum in spherical protein bodies. The β and γ-kafirins are located in the peripheral protein bodies region while α and δ-kafirins are encapsulated in the inner region (Wu et al., 2013). This conformation determines the digestibility of sorghum proteins.

Overall, the digestibility of sorghum proteins, especially after cooked, is lower than cereals like wheat and maize (Duodu et al., 2003; Mokrane et al., 2010; Afify et al., 2012b; Moraes et al., 2012b). The kafirins of sorghum are resistant to peptidase due to the formation of intramolecular disulfide bonds; this is the main cause of the low digestibility (Belton et al., 2006). However, in varieties rich in tannins, the complexation of the kafirins with this phenolic compound can reduce the protein digestibility up to 50% (Taylor et al., 2007). Furthermore, other exogenous factors (interaction of the proteins with non-protein components such as starch, non-starch polysaccharides, phytic acid, and lipids) and endogenous factors (nature and organization of proteins inside the grain) contribute to this low digestibility (Duodu et al., 2002; Duodu et al., 2003; Ezeogu et al., 2005; Belton et al., 2006; Ezeogu et al., 2008; da Silva et al., 2011a).

Despite the reduction in protein digestibility of sorghum after cooking in wet heat, processing such as fermentation and germination may increase the digestibility up to 2 times

(Correia et al., 2008; Wedad et al., 2008; ELKhier and Abd-ALRaheem, 2011; Pranoto, et al.; Afify et al., 2012b). However, major recent efforts to improve the protein digestibility of sorghum aim to reduce the amount of kafirins, especially β and γ forms, and to increase the glutenins and albumins (Taylor and Taylor, 2011; da Silva et al., 2011b; Goodall et al., 2012; Kumar et al., 2012; Wu et al., 2013). The genetically modified varieties have in vitro digestibility from 23 to 102% higher than control varieties (da Silva et al., 2011a; Taylor and Taylor, 2011; Kumar et al., 2012).

The α-kafirins are the last proteins to be digested in the intestine and, because of their high abundance, the indigestibility reduces their nutritive value (Wu et al., 2013). The β and γ-kafirins are rich in cysteine, which forms disulfide bonds, and are therefore assumed to block the accessibility of α-kafirins to hydrolytic enzymes (Duodu et al., 2003; Wong et al., 2009). Thus, the higher digestibility in modified varieties can be attributed to increased enzyme susceptibility of the major storage protein, α-kafirin, because of changes in protein body morphology as well as to a reduction of the formation of disulfide bonds between β and γ-kafirins (Oria et al., 2000; Henley et al., 2010; Kumar et al., 2012; Mehlo et al., 2013).

Generally, sorghum proteins are rich in glutamic acid and nonpolar amino acids (proline, leucine, and alanine) and have lysine as the main limiting amino acid (De Mesa-Stonestreet et al., 2010; Mokrane et al., 2010; Moraes et al., 2012b). In addition, they may be deficient in 5 other essential amino acids (methionine, cysteine, isoleucine, valine, and threonine) (Moraes et al., 2012b). However, varieties obtained through breeding programs have 52–115% more lysine than conventional varieties (Henley et al., 2010; Taylor and Taylor, 2011; da Silva et al., 2011b; Kumar et al., 2012). Improved lysine contents were attributed to decreased levels of kafirin proteins and increased levels of lysine-rich, non-kafirin proteins in the grain endosperm (Shewry, 2007).

Unlike the major prolamins of wheat (gliadin), rye (secalin), and barley (hordein), the kafirins do not trigger an allergic response or an autoimmune reaction in humans (De Mesa-Stonestreet et al., 2010). In addition to the qualitative evidence based on the type of proteins found in sorghum, there is genetic evidence that it has characteristics that do not allow the expression of toxic peptides related to gliadin (Pontieri et al., 2013). Thus, sorghum is an effectively safe cereal for consumption by people with celiac disease.

Lipids

Sorghum has a reduced lipid content (1.24 to 3.07 g/100 g), which is mainly composed of unsaturated fatty acids (83–88%) (Afify et al., 2012a; Martino et al., 2012; U.S. Department of Agriculture, 2012). In most of the varieties of sorghum the polyunsaturated fatty acids (PUFA) are higher than monounsaturated fatty acids (MUFA) (Mehmood et al., 2008; Hadbaoui et al., 2010; Afify et al., 2012a). The major fatty acids of sorghum are linoleic (45.6–51.1%), oleic (32.2–42.0%), palmitic (12.4–16.0%), and linolenic acids (1.4–2.8%) (Mehmood et al., 2008; Hadbaoui et al., 2010; Afify et al., 2012a).

Table 1. Average content of minerals (mg/100 g) in sorghum grown in Brazil, United States and Ethiopia.

Minerals	Brazil [1] ($n = 8$)	United States [2] ($n = 1$)	Ethiopia [3] ($n = 31$)
Calcium	10.7	28.00	31.13
Iron	1.64	4.40	6.14
Potassium	—	350.00	188.80
Manganese	0.06	—	1.58
Sodium	nd	6.00	23.00
Potassium	217.87	287.00	289.34
Zinc	1.65	—	2.42
Magnesium	102.77	—	116.8
Copper	0.51	—	—
Sulfur	79.20	—	—
Aluminum	nd	—	—
Cadmium	nd	—	—
Chrome	nd	—	—
Lead	nd	—	—

[1]Martino, et al. (2012); [2]U.S. Department of Agriculture (2012); [3]Shegro, et al. (2012); nd: not detected, -: not analyzed.

Minerals and vitamins

Sorghum is a source of minerals (phosphorus, potassium, and zinc) whose content varies according to the place of cultivation (Table 1) (Martino et al., 2012; Shegro et al., 2012; Silva et al., 2012; U.S. Department of Agriculture, 2012). The bioavailability of most minerals of sorghum is still little known. However, it is known that zinc availability varies between 9.7% and 17.1% and iron availability ranges from 6.6% to 15.7% (Afify et al., 2011; Kruger et al., 2013). Studies have been conducted in order to increase the content and bioavailability of iron and zinc through biofortification, fortification, and genetic improvement of sorghum (Tripathi et al., 2010; Ashok Kumar et al., 2013; Kruger et al., 2013; Tripathi and Platel, 2013).

Information on the content of vitamins in sorghum is scarce. However, it is worth noting that it is a source of some B-complex vitamins (thiamine, riboflavin, and pyridoxine) and fat-soluble vitamins (D, E, and K) (Ochanda et al., 2010; Martino et al., 2012; U.S. Department of Agriculture, 2012; Cardoso et al., 2014).

Bioactive compounds

Phenolic compounds and their bioavailability

The phenolic compounds are the main bioactive compounds of sorghum and are present in all varieties of this cereal (Dykes and Rooney, 2006). Almost all classes of phenolics are found in sorghum (Awika and Rooney, 2004; Dykes et al., 2005); however, the classes of phenolic acids, tannins, and flavonoids are major.

The profile and content of phenolic compounds in sorghum are more diverse and higher than those observed in wheat, barley, rice, maize, rye, and oats (Ragaee et al., 2006). Sorghum varieties resistant to biotic and abiotic stresses were found to have on average higher contents of proanthocyanidins, 3-deoxyanthocyanidins, and flavan-4-ols than susceptible varieties (Dicko et al., 2005).

The bioavailability of phenolic compounds after dietary intake has been a topic of increasing research in recent years (Prior and Wu, 2006; Crozier et al., 2010; Yang et al., 2011; Hole et al., 2012; Faria et al., 2013). However, the results

obtained in humans are scarce and controversial. In addition, information about the bioavailability of phenolic compounds of sorghum, including tannins and 3-deoxyanthocyanidins, is not available yet.

The main difficulty in analyzing the bioavailability of phenolic compounds is the absence of standardized methods capable of identifying their metabolites. For example, the analysis of phenolic compounds in urine provides a more realistic bioavailability but does not include the possibility that their metabolites were sequestered by body tissues (Crozier et al., 2010). This limitation underestimates the bioavailability of phenolic compounds in food.

Different factors affect the bioavailability of phenolic compounds in humans, including environmental factors, food processing, food matrix, and interaction with other compounds and polyphenols (D'Archivio et al., 2010; Fernandes et al., In press). There is a need for extensive investigation about the alterations of phenolic compounds by the gastrointestinal tract and their subsequent absorption and metabolism, including distribution in tissues (Lafay and Gil-Izquierdo, 2008; D'Archivio et al., 2010). Studies have shown that catabolites of phenolic compounds not absorbed in the small intestine pass into the large intestine where they can affect the colon microbiota (Crozier et al., 2010; Faria et al., 2013).

Knowledge of the bioavailability of phenolic compounds in sorghum, including dietary factors able to modulate it, is essential for analysis of their functional potential in humans and, in the long term, for the implementation of therapeutic measures for health professionals.

Phenolic acids

The phenolic acids are classified as hydroxybenzoic acid derivatives and hydroxycinnamic acid derivatives (Fig. 1). These acids exhibit high antioxidant activity in vitro and thus may promote benefits to human health (Kamath et al., 2004).

The content of phenolic acids in some sorghum varieties ranged between 135.5 and 479.40 μg/g (Afify et al., 2012c; Chiremba et al., 2012), with major amounts of the protocatechuic (150.3 to 178.2 μg/g) and ferulic (120.5 to 173.5 μg/g) acids and small amounts of the p-coumaric (41.9 to 71.9 μg/g), syringic (15.7 to 17.5 μg/g), vanillic (15.4 to 23.4 μg/g), gallic (14.8 to 21.5 μg/g), caffeic (13.6 to 20.8 μg/g), cinnamic (9.8 to 15.0 μg/g), and p-hydroxybenzoic (6.1 to 16.4 μg/g) acids (Svensson et al., 2010; Afify et al., 2012c).

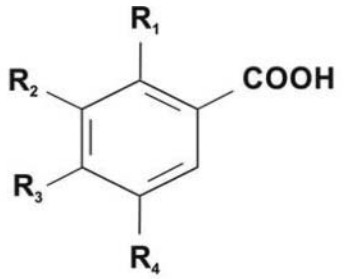
The phenolic acids in wines, fruits, and vegetables have a good bioavailability. In these matrices, the majority of phenolic acids are free or as conjugated forms that can be hydrolyzed in the upper intestinal tract (Hole et al., 2012). On the other hand, phenolic acids in cereals, including in sorghum, are mostly bound to arabinoxylans chains or lignin (Dykes and Rooney, 2006; Abdel-Aal et al., 2012; Hole et al., 2012). These bound phenolic acids are not hydrolyzed by human digestive enzymes that decrease their bioavailability, but are fermented by the microbiota of the colon (Saura-Calixto, 2010; Hole et al., 2012).

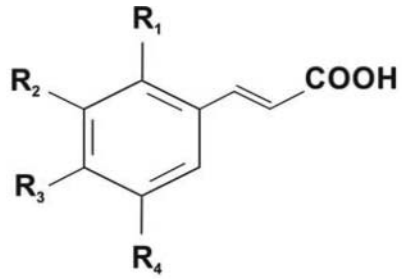
Knowledge about techniques for improving the bioavailability of phenolic acids in sorghum is incipient. The microorganisms and processing of grains can play a key role in improving this bioavailability. The study results demonstrated that cereal fermentation with specific probiotic strains and cooking processes can significantly increase the content-free phenolic acids (Lafay and Gil-Izquierdo, 2008; Saura-Calixto, 2010; Hole et al., 2012; N'Dri et al., 2013), thereby improving their bioavailability. The effects of other types of processing on the profile of phenolic acids in sorghum need to be studied.

Tannins (proanthocyanidins)

Tannins, secondary metabolites found in many plant species, are phenolic compounds that often act as a defense mechanism against pathogens and predators (Kaufman et al., 2013). Overall, these compounds are absent in other major cereals, such as rice, wheat, and maize, but are present in sorghum varieties that have pigmented testa (Awika, 2003; Dykes and Rooney, 2006; Wu et al., 2012). The presence and content of condensed tannins in sorghum are controlled by the genes S and Tannin1, among others (Hahn and Rooney, 1986; Wu et al., 2012).

The tannins in sorghum vary as to the type, content, and distribution of the individual oligomers and polymers. They are





Hydroxybenzoic acids

	R_1	R_2	R_3	R_4
Gallic acid	H	OH	H	OH
Gentisic acid	OH	H	H	OH
Salicylic acid	OH	H	H	H
p-hydroxybenzoic acid	H	H	H	OH
Syringic acid	H	OCH_3	OH	OCH_3
Protocatequinic acid	H	OH	OH	H

Hydroxycinnamic acids

	R_1	R_2	R_3	R_4
Caffeic acid	H	OH	OH	H
Feluric acid	H	OCH_3	OH	H
o-coumaric acid	OH	H	H	H
p-coumaric acid	H	H	H	H
Sinapic acid	H	OCH_3	OCH_3	OCH_3
Vanillic acid	H	OCH_3	OCH_3	H

Figure 1. Structure of the major phenolic acids present in foods, including in sorghum.

classified as type I (no significant levels), type II (tannins that are extractable only in acidified methanol) and type III (tannins that are extractable in methanol and acidified methanol) (Price et al., 1978; Hahn and Rooney, 1986). Almost all of the tannins in sorghum are condensed and constituted by oligomers or polymers of catechins (flavan-3-ols and/or flavan-3,4-diols) (Awika and Rooney, 2004; Wu et al., 2012). In general, most sorghum tannins have a high molecular weight and a degree of polymerization (DP) higher than 10 (69–81%) (Awika et al., 2003).

The content of tannins in sorghum varies between 0.2 and 48.0 mg/g and is highest in sorghum with black testa (Awika et al., 2003; Martínez et al., 2009; Schons et al., 2011; Afify et al., 2012c; Dykes et al., 2013). However, this content, as well as the activity of tannins in sorghum, can be affected by the season (Mkandawire et al., 2013). Therefore, the effect of the environment on tannins should be considered during the selection and breeding of tannin containing sorghum genotypes when the aim is to achieve health benefits (Mkandawire et al., 2013).

The tannins reduced the availability of minerals, proteins, and starch of the sorghum (Al-Mamary et al., 2001; Taylor et al., 2007; Barros et al., 2012). This reduction correlates not only with the content of tannins in the grain, but also with DP (Kaufman et al., 2013; Mkandawire et al., 2013). It is attributed mainly to the tannins with higher molecular weight or more complex tannin structures (DP > 10) (Osman, 2004; Barros et al., 2013; Mkandawire et al., 2013). Polymeric tannins, for example, are the major contributors to resistant starch formation due to their stronger interaction with starch, especially amylose (Barros et al., 2013).

Despite the anti-nutritional effect, tannins are 15–30 times more effective than simple phenolics in radical scavenging ability (Hagerman et al., 1998). Thus, tannins have been extensively studied for health-promoting capabilities (Beecher, 2004). The functional benefits of sorghum are attributed mainly to oligomers, which have been extensively studied (Beecher, 2004). The oligomers of tannins in foods contribute up to 19% of the antioxidant capacity of the diet and promote benefits to human health due to immunomodulatory, anticancer, antioxidant, antirradical, anti-inflammatory, vasodilatory, cardioprotective, antithrombotic, and anti-UV actions (Waniska and Rooney, 2000; Dixon et al., 2005; Sharma et al., 2007; Floegel et al., 2010).

The oligomeric and polymeric proanthocyanidins are not absorbed by animals and humans (Serrano et al., 2009; Crozier et al., 2010). But minor quantities of dimers of B1 and B2 procyanidins are detected in human plasma (Holt et al., 2002; Donovan et al., 2007). However, so far, it is unclear whether this low bioavailability is also observed in tannins in sorghum. Most tannins in foods pass unaltered to the large intestine where part of them are catabolized by the colonic microbiota yielding a diversity of phenolic acids (Selma et al., 2009). The biological effects of tannins are generally attributed to their more readily absorbed colonic breakdown products, the phenolic acids, although there is a lack of detailed study in this area (Crozier et al., 2010).

As to phenolic acids, processing can improve the digestibility of tannins in sorghum. The processing of grain sorghum in dry heat (95°C for 20 min and 121°C for 30 minutes) can depolymerize the condensed tannins in sorghum (Barros et al., 2012), which can increase their bioavailability. The thermal processing can be a strategy to increase the bioavailability of tannins with a minimum reduction in the content of these compounds. Thus, the functional potential of sorghum rich in tannins can be maintained or even increased. Furthermore, the nutritional value of the grain may increase due to higher digestibility of starch and proteins resulting from the reduction of polymeric tannins. The depolymerization of tannins through other types of processing needs to be studied.

Flavonoids

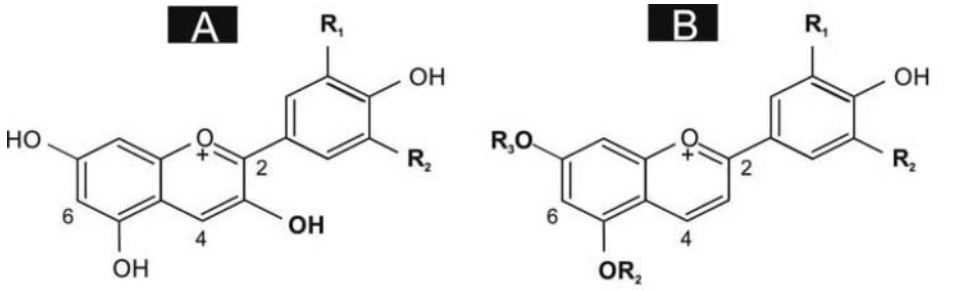
Most flavonoids of the sorghum are located in the outer layers of the grain. Thus, differences in the color and thickness of the pericarp and presence of the testa influence the concentration and profile of flavonoids (Awika et al., 2005; Dykes et al., 2009). In turn, the physical characteristics of the sorghum are determined by genetic and environmental factors (Taleon et al., 2012).

Three classes of flavonoids are in large quantities in sorghum: anthocyanins, flavones, and flavanones. Sorghum anthocyanins belong to the class of 3-deoxyanthocyanidins and correspond up to 79% of the flavonoids' content (Dykes and Rooney, 2006; Shih et al., 2007; Taleon et al., 2012). They have a differentiated structure due to the absence of a hydroxyl group at position C-3 and therefore they are more stable than other anthocyanins (Awika and Rooney, 2004; Shih et al., 2007; Awika, 2008; Dykes et al., 2009).

The main 3-deoxyanthocyanidins of the sorghum are non-methoxylated forms (luteolinidin and apigeninidin) (Awika et al., 2004) (Fig. 2). However, small quantities of methoxylated 3-deoxyanthocyanidins (5-methoxy-luteolinidin, 7-methoxy-luteolinidin, and 7-methoxy-apigeninidin) are observed in the sorghum as well as methoxylated 3-deoxyanthocyanins (5-methoxy-luteolinidin 5-glucoside, 5-methoxy-luteolinidin 7-glucoside, 7-methoxy-luteolinidin 5-glucoside, and 7-methoxy-apigeninidin 5-glucoside) and other non-methoxylated 3-deoxyanthocyanins (apigeninidin 5-glucoside and luteolinidin 5-glucoside) (Wu and Prior, 2005; Yang et al., 2009; Taleon et al., 2012; Cardoso et al., 2014). The content of sorghum 3-deoxyanthocyanidins correlates with its color and antioxidant activity (Awika and Rooney, 2004). Varieties with pericarp and black testa have 3 to 4 times more total 3-deoxyanthocyanidins (5.4 to 6.1 mg/g) than red and brown varieties (1.6 to 2.8 mg/g) (Awika et al., 2004).

The total flavones of the sorghum vary from 0 to 386 μg/g (on average, 87 μg/g), with a prevalence of aglycone forms of luteolin and apigenin (Dykes et al., 2009; Dykes et al., 2011). The main flavanones of sorghum are the aglycone forms of eriodictyol and naringenin (Dykes et al., 2009; Dykes et al., 2011). The smallest contents are found in white varieties and the largest contents are observed in those with lemon-yellow pericarp (474 to 1780 μg/g) (Dykes et al., 2011).

Information about the bioavailability of the 3-deoxyanthocyanidins, flavones, and flavanones in sorghum is not available in the literature so far. In other foods, including cereals, flavones and flavanones are highly available and are rapidly absorbed and excreted (Donovan et al., 2007; Crozier et al., 2009). The aglycone of flavones and flavanones, the forms most



Anthocyanins in foods

	R_1	R_2
Cyanidin	OH	H
Pelargonidin	H	H
Peonidin	OCH_3	H
Malvidin	OCH_3	OCH_3
Delfinidin	OH	OH
Petunidin	OCH_3	OH

3-Deoxyanthocyanins in sorghum

	R_1	R_2	R_3
Apigeninidin	H	H	H
5-methoxy-apigeninidin	H	H	CH_3
Apigeninidin 5-glycoside	H	Gcl	H
7-methoxy-apigenindin 5-glycoside	H	Glc	CH_3
Luteolinidin	OH	H	H
Luteolinidin 5-glycoside	OH	Glc	H
5-methoxy-luteolinidin	OH	CH_3	OCH_3
7-methoxy-luteolinidin	OH	H	CH_3
5-methoxy-luteolinidin 7-glycoside	OH	CH_3	CH_3
7-methoxy-luteolinidin 5-glycoside	OH	CH_3	CH_3
5-methoxy-luteolinidin 5-glycoside	OH	CH_3	CH_3

Figure 2. Structure of common anthocyanins in foods (A) and 3-deoxyanthocyanins in sorghum (B).

prevalent in sorghum, are rapidly absorbed (Spencer and Crozier, 2012; Urpi-Sarda et al., 2012).

The bioavailability of anthocyanins in foods is relatively low compared to flavones and flavanones (Yang et al., 2011) and is influenced by the nature of the sugar and also the structure of the anthocyanidin aglycone (Wu et al., 2005). Unlike flavonoids, where glycosides are hydrolyzed, anthocyanin glycosides are rapidly and efficiently absorbed in the small intestine (Fernandes et al., 2014; Prior and Wu, 2006). This fact indicates that the main aglycone forms present in sorghum can have low bioavailability.

The anthocyanins in foods appear to be rapidly absorbed and eliminated, reaching only low maximal concentrations in plasma and urine (Fernandes et al., 2014). In studies with animals and humans, the quantities of anthocyanins excreted in urine were less than 0.1% of intake (McGhie et al., 2003; Wu et al., 2005; Prior and Wu, 2006; Crozier et al., 2010). Although anthocyanin bioavailability in foods appears low, it could have been underestimated due to the fact that some major metabolites have been ignored or not analyzed due to analytical limitations (Manach et al., 2005). The difficulty in overcoming those analytical problems may contribute significantly to the low bioavailability of anthocyanins (Fernandes et al., 2014).

Between 60 and 90% of the anthocyanins may disappear from the gastrointestinal tract within 4 h after a meal (Prior and Wu, 2006). What happens to the bulk of the anthocyanins that disappear is not clear. Degradation accounts for a part of this disappearance, but differs for the various aglycones and may be modified further by the nature of the aglycone glycosylation, which further complicates our understanding of this process (Prior and Wu, 2006). Special attention is given to the contribution of the gastric mucosa to anthocyanin absorption as the result of the high content of intact anthocyanins (20–25%) detected in plasma few minutes after intake (Fernandes et al., 2014).

The contribution of intestinal tissue and the microbiota impact on absorption and anthocyanin bioavailability is also highlighted (Faria et al., 2013; Fernandes et al., 2014). It has been suggested that this is likely due to the spontaneous degradation under physiological conditions or following microbial metabolism (Fernandes et al., 2014; Woodward et al., 2009). In fact, colonic microbiota hydrolyzes glycosides into aglycones and degrades them to simple phenolic acids (Fernandes et al., 2014), which can be further fermented in the colon (Williamson and Clifford, 2010).

Stilbenes

Stilbenes are a small family of phenolic compounds derived from the phenylpropanoid pathway that have numerous implications in plant disease resistance and human health (Chong et al., 2009). The total content of stilbenes correlates with the color of the grain and is present in smaller quantities in white varieties. White sorghum contains traces of trans-piceid (up to 0.1 mg/kg) and trans-resveratrol is absent while in red sorghum, these two classes are present (Bröhan et al., 2011).

Polycosanols and phytosterols

Polycosanols and phytosterols are associated with the lipid fraction of the sorghum (Wang et al., 2008; Leguizamón et al., 2009; Zbasnik et al., 2009). Thus, these compounds have been studied mainly in lipids extracted from dry sorghum obtained after alcohol production.

One of the main components of the long-chained lipids extracted from sorghum grain kernels are polycosanols (33.4–44%) (Hwang, Keum T et al., 2004; Hwang, Keum Taek et al., 2005). Sorghum can be a major source of polycosanols that have physiological benefits. Total polycosanols content in unpolished sorghum grain was 74.5 mg/100 g in the dry kernel

while the content in the polished grain was 9.8 mg/100 g in the dry kernel (Hwang, Keum T et al., 2004; Hwang, Keum Taek et al., 2005).

The content of sorghum phytosterols (4.13 to 24.45 μg/g, dry weight basis) is affected by growing conditions (Chung et al., 2013). Sorghum grains are a relatively rich source of phytosterols when compared with fruits, vegetables, and other cereal grains commonly found in the food supply. Of the more than 200 sterols in vegetables, 3 have been identified in sorghum (sitosterol: 44.8 to 48.2%; campesterol: 26.1 to 38.0% and stigmasterol: 17.3% to 25.6%) (Singh et al., 2003; Wang et al., 2007; Delgado-Zamarreño et al., 2009; Leguizamón et al., 2009; Ye et al., 2010).

Phytochemicals with anti-nutritional activity

Like other cereals, sorghum has phytochemicals with anti-nutritional activity. Phytates are major anti-nutritional compounds identified in sorghum (Abdel-Rahman and Osman, 2011; Afify et al., 2011; Schons et al., 2011). In addition, some varieties have protease inhibitors (trypsin, chymotrypsin, and amylase) and lectins (Neucere, 1982; Abdel-Rahman and Osman, 2011; Raimi et al., 2012). These phytochemicals decrease the digestibility of proteins and carbohydrates, and mineral bioavailability.

Potencial impact of sorghum on the human health

The potential functional benefits to human health associated with the consumption of compounds isolated from sorghum, and especially the whole grain, are still unknown. The results of in vitro and animal studies have shown that phenolics or fat soluble compounds isolated from sorghum beneficially modulate the gut microbiota and parameters related to noncommunicable diseases such as obesity, diabetes, dyslipidemia, cardiovascular disease, cancer, and hypertension (Tables 2 and 3). The main mechanisms of action of the compounds isolated from sorghum on parameters related to noncommunicable diseases, as found in results of in vitro and animal studies, are presented in Fig. 3.

Oxidative stress

The chronic and excessive production of free radicals is crucial in the development of noncommunicable diseases (Hotamisligil, 2006; Lee et al., 2011). The activity of components isolated from sorghum against oxidative stress has been demonstrated in vitro (Table 2). These functional benefits are attributed to the phenolic compounds and are most evident when extracts from black or red sorghum were used (Burdette et al., 2010; Moraes et al., 2012a).

Phenolic compounds isolated from sorghum regulate the expression of phase II enzymes (Yang et al., 2009; Awika et al., 2009; González-Montilla et al., 2012). These enzymes modulate the defense system against oxidative stress by continuously converting highly reactive electrophilic species (RES) into non-toxic and excretable metabolites (Takabe et al., 2006; González-Montilla et al., 2012).

The main effect of sorghum on phase II enzymes is to increase the NADH:quinone oxyreductase (NQO) activity (Fig. 3). This effect is attributed to sorghum 3-deoxyanthocyanidins and depends on their profile but not on the content (Lewis, 2008; Awika et al., 2009; Yang et al., 2009; Suganyadevia et al., 2011b). Recent studies demonstrated that apigeninidin and luteolinidin did not show any significant NQO inducer activity (Awika et al., 2009; Yang et al., 2009). On the other hand, their 7-methoxylated forms were strong NQO inducers (Awika et al., 2009; Yang et al., 2009).

Varieties of black sorghum may exert greater effects on NQO due to the rich profile and high content of 3-deoxyanthocyanidins (Lewis, 2008; Yang et al., 2009; Awika et al., 2009; Suganyadevia et al., 2011b). However, sorghum varieties with different pericarp color can also induce the activity of NQO. For example, white sorghum (KARI-Mtama), which has low levels of pigments, extractable phenolics, and antioxidant capacity, has relatively strong NQO inducers (Awika et al., 2009; Yang et al., 2009). This fact demonstrated that sorghum is a source of other phytochemicals, pigmented or not, that might act synergistically with 3-deoxyanthocyanidins and produce high inducer activity. Conversely, sorghum tannins have a very poor ability to induce NQO and can inhibit the NQO activity caused by other phenolic compounds (Awika et al., 2009).

The effects of sorghum on the oxidative stress in vivo are little known (Table 3). The superoxide dismutase activity (SOD) increased in normolipidemic rats fed with black sorghum bran (rich in 3-deoxyanthocyanidins) (Lewis, 2008). This increase appears to be strictly related to the action of 3-deoxyanthocyanidins present in the bran. Furthermore, white (rich in phenolic acids), brown (rich in tannins) or black (rich in 3-deoxyanthocyanidins) sorghum brans suppressed the glutathione peroxidase activity (GPx) (Lewis, 2008). However, in the single animal study done so far using whole grains, normolipidemic rats that consumed different sorghum varieties (white, brown rich in tannin, and red without tannin) showed no change in the SOD activity (Moraes et al., 2012a). The absence of significant changes in the SOD activity (Moraes et al., 2012a) may reflect the lower content of bioactive compounds in whole sorghum grain compared with the bran. Thus, the amount of bioactive compounds consumed by the rats treated with whole grain may have been lower than those fed sorghum bran.

On the other hand, the normolipidemic animals fed with whole red sorghum evaluated by Moraes, et al. (2012a) had lower concentrations of thiobarbituric acid reactive substances (TBARS) in their livers. This reduction suggested that whole sorghum inhibited the RES and that it can reduce oxidative stress through other mechanisms not evaluated in this study, including the increase of other antioxidant enzymes (i.e., catalase, GPx and SOD) and total antioxidant capacity. Furthermore, the under or overexpression of genes and proteins related to the oxidative system also may have contributed to these results.

Cancer

Most cancers originate from DNA damage caused by carcinogens (toxics, mutagenic, and carcinogenic agents) that make up

Table 2. Description of the *in vitro* studies about the effects of the fractions isolated from sorghum on parameters related to chronic noncommunicable diseases.

Related pathology	Cell type (if any)	Sorghum fraction used and preparation form	Main results	References
Diabetes	Not applied	Extract of Sumac sorghum bran rich in 3-deoxyanthocyanidins and high antioxidant activity (10% bran diluted in ethanol 50%)	↓ Glycation of proteins in approximately 60%	Farrar, et al. (2008)
	Not applied	Extracts of five sorghum varieties (10% grain diluted in ethanol 70%)	↓ Activity of α-glucosidase of *B. stearothermophilus* ↓ Activity of human pancreatic and salivary α-amylases.	Kim, J.-S., et al. (2011)
Inflammation and cancer	Not applied	Extracts of bran of sorghum varieties rich in tannins and 3-deoxyanthocyanidins (10% bran diluted in ethanol 50%)	↓ Hyaluronidase activity	Bralley, et al. (2008)
	Skin sarcoma cells (Hs 63. T) LPS-induced	Extracts of sorghum rich in phenolic compounds (5% sorghum diluted in methanol)	↓ Nitric oxide, IL-6, TNF-α ↓ DNA synthesis	Hwang, J.-M., et al. (2013)
	LPS-induced peripheral blood mononuclear cells	Extracts of white, bronze, red and black sorghum (8.3% to 25% bran diluted in ethanol)	↓ IL-1β and TNF-α in blood mononuclear cells (black sorghum rich in 3-deoxyanthocyanidins)	Burdette, et al. (2010)
Oxidative stress and cancer	Hepatoma (Hepa1c1c7) and colon cancer (HT-29) cells	Extracts of red and black sorghum rich in 3-deoxyanthocyanidins	↑ NQO activity in Hepa1c1c7 cells ↓ Proliferation of HT 29 cells	Yang, L., et al. (2009)
	Cancer cells of esophagus (OE33) and colon (HT-29)	Extracts of 8 varieties of sorghum (with or without tannins)	↑ NQO activity (black and white varieties without tannins) ↓ Cell proliferation (black and white varieties without tannins)	Awika, et al. (2009)
	Hepatoma cells (Hepa1c1c7 cell)	Extract of black sorghum rich in 3-deoxyanthocyanidins (10% bran diluted in methanol 80%)	↑ NQO activity	González-Montilla, et al. (2012)
Cancer	Leukemia cells (HL-60)	Extract of sorghum rich in 3-deoxyanthocyanidins	↑ Cell apoptosis	Shih, C.-H., et al. (2007)
	Breast cancer cells (MCF-7)	Extract of red sorghum rich in 3-deoxyanthocyanidins (5% sorghum diluted in methanol HCl 1%)	↑ Cell apoptosis	Suganyadevia, et al. (2011a)
	Not applied	Extracts of sorghum rich in 3-deoxyanthocyanidins or tannins	↑ Human aromatase activity	Hargrove et al. (2011)
	Cancer cells of colon (HT 29) and liver (HEP G2)	Extract of red sorghum bran rich in 3-deoxyanthocyanidins (5% sorghum diluted in methanol HCl 1%)	↓ Cell proliferation	Suganyadevia, et al. (2011b)
	Leukemia cells (HL-60)	Extract of red sorghum bran rich in 3-deoxyanthocyanidins	↑ Activation of BAK and BAX, release of mitochondrial cytochrome C and apoptosis-inducing factor into the cytoplasm, and activation of caspase-9 and caspase-3 ↑ Cell apoptosis	Woo, et al. (2012)
	Breast cancer cells (MDA-MB 231 and MCF-7)	Extract of phenolic compounds of sorghum	↓ Phosphorylation of STAT5 and STAT3, and the expression or release of insulin-like growth factor 1 and VEGF proteins ↑ Expression of cyclin D, cyclin E, and pRb; Brk, p53, and hypoxia-inducible factor 1α	Park, Jin Hee, et al. (2012)
	Malignant cells of colonocytes	Extracts of white (rich in flavones), red and black sorghum (rich in 3-deoxyanthocyanidins)	↑ Luciferase and caspase-3 activity	Yang, L., et al. (2012)
	Breast cancer cells (MCF-7)	Extract of red sorghum bran rich in 3-deoxyanthocyanidins	↑ p53 gene expression ↓ Bcl-2 gene expression ↓ Cell proliferation	Suganyadevia, et al. (2013)
Hypertension	Not applied	Hydrolyzed proteins (α-kafirins) of sorghum	↓ Angiotensin I converting enzyme activity	Kamath, V., et al. (2007)

reactive intermediates, such as reactive oxygen species (ROS), reactive nitrogen species (RNS), and other reactive electrophilic metabolites (Shih et al., 2007; Sharma et al., 2010). The carcinogen rate in humans is strongly dependent on the activity of the phase I (cytochrome P-450) and II of the enzyme systems, which also removed endogenous and environmental carcinogens (Takabe et al., 2006).

The benefits of sorghum on phase II enzymes cited in the previous section, especially on NQO reductase, demonstrate its chemoprevention (Table 2 and Fig. 3). However, it is not possible to infer its effects in humans due to the lack of studies. There is epidemiological evidence that corroborates its potential to prevent cancer in humans. The substitution of sorghum by corn as a staple food of the diet increased the incidence of esophageal cancer in black South Africans (Isaacson, 2005). The mechanisms by which sorghum reduced the risk of esophageal cancer in humans are still unknown.

Table 3. Description of the *in vivo* studies about the effects of the isolated fractions from sorghum on parameters related to chronic noncommunicable diseases.

Related pathology	Animal	Fraction and doses used	Duration of the study	Observed effects (effective treatment)	References
Obesity	Male New Zealand white rabbits	Low or high tannin sorghum added to the diet (60% of the diet)	4 weeks	↓ Weight gain, feed conversion ratio, and activities of the α-amylase, trypsin and lipase (high tannin sorghum) ↑ Food consumption, fecal nitrogen excretion (high tannin sorghum)	Al-Mamary, et al. (2001)
	Male New Zealand white rabbits	White or black (high tannin) sorghum grain (approximately 35%) added to the diet	5 weeks	↓ Weight gain (high tannin sorghum)	Muriu, et al. (2002)
Dyslipidemia and cardiovascular risk	Mice	30% of whole sorghum (30%) added to the diet	4 weeks	↑ Fecal excretion of bile acid and plasma HDL-c	Cho, et al. (2000)
	Hamster	Sorghum lipids (0.5, 1.0 and 5.0%) added to the diet	4 weeks	↓ Non-HDL cholesterol in plasma, esterified cholesterol and cholesterol absorption in liver (0.5 to 5.0%) ≡ Plasma HDL-c, phospholipids and free cholesterol in liver (0.5 to 5.0%); ↑ Hepatic triacylglycerol (5%) and fecal excretion of sterols (cholesterol) (0.5 to 5.0%)	Carr, et al. (2005)
	Hamster	Sorghum lipids (0.5, 1.0 and 5.0%) added to the diet	4 weeks	↓ Non-HDL cholesterol in plasma, free and esterified cholesterol in liver; ≡ Hepatic phospholipid (5%); Hepatic gene expression of NPC1L1, SRB1, SREBP2, HMGR, LDLR, and CYP7A1 ↑ Fecal excretion of sterols (cholesterol) and liver triacylglycerol; ABCA1 gene expression	Hoi, et al. (2009)
	Hyperlipidemic rats	Extracts of phenolic compounds in dichloromethane and ethyl acetate.; Oral intake of 50 and 300 mg/kg	2 weeks	↓ Triacylglycerol, LDL-c and total cholesterol in plasma (50 and 300 mg/kg of extract in ethyl acetate) ↑ HDL-c in plasma (50 and 300 mg/kg of extract in ethyl acetate)	Chung, et al. (2011b)
Diabetes, dyslipidemia and cardiovascular risk	Diabetic rats	Extracts of phenolic compounds in acetonitrile. Oral intake of 100 and 250 mg / kg	2 weeks	↓ Glycaemia, triacylglycerol and total cholesterol in plasma (250 mg/kg) ↑ Insulin, urea, uric acid and creatinine in plasma (250 mg/kg)	Chung, et al. (2011a)
	Diabetic rats	Extract of phenolic compounds Oral intake of 400 and 600 mg / kg	2 weeks	↓ Triacylglycerol, total cholesterol, LDL-c, glycaemia, area under the curve for glucose in plasma (400 and 600 mg/kg), PEPCK and p38 expression ≡ Glutamic oxaloacetic transaminase and glutamic pyruvic transaminase in plasma; insulin, GLUT4 translocation and Akt phosphorylation ↑ AMPK expression	Kim, J. and Park (2012)
Dyslipidemia, cardiovascular risk and diabetes	Mice	Oral administration of 0.5% and 1% sorghum methanolic extract in mice fed a with high-fat diet	6 weeks	↓ Triacylglycerol, total cholesterol, LDL-c, glycaemia, insulin, area under the curve for glucose in plasma; adiponectina expression (0.5 to 1%) ↓ Tumor necrosis factor-α (1%). ≡ HDL-c, alanine and aspartate amino-transferase ↑ PPAR-γ expression (1%)	Park, et al. (2012)
	Mice	Modified AIN-93 M diet supplemented with 0%, 1% and 5% grain sorghum lipid	3 weeks	↑ *Bifidobacterium* (mainly a phylotype related to *B. animalis*) and HDL-c ↓ *Coriobacteriaceae* (mainly unclassified phylotypes yet) and non-HDL-c	Martínez, et al. (2009)
Inflammation	Mice	Application of ethanolic extract of white, bronze, red and black sorghum in the ear of the mice	–	↓ Ear edema of mice, generated induced inflammation (bronze and black sorghum) and myeloperoxidase activity (black sorghum)	Burdette, et al. (2010)

	Rats	Oral administration of 0.62 a 5g/kg of golden gelatinous sorghum rich in phenolic compounds	2 weeks	≡ Albumin, glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, alkaline phosphates, creatinin, total protein, albumin, blood urea nitrogen, chloride, sodium, potassium, and calcium; cell structure and formation (liver, kidney, spleen, lungs, and heart) ↓ Nitric oxide in Raw264.7 cells ↓ Inducible nitric oxide synthase and anti-cyclooxygenase (COX)-2, 12-O-tetradecanoylphorbol-13-acetate-induced ear edema	Shim, et al. (2013)
Inflammation, oxidative stress, diabetes, dyslipidemia	Normolipidemic Wistar rats	Whole sorghum (21.2 to 26.4%) added to the hyperlipidic di	5 weeks	↓ TBARS in liver, tumor necrosis factor-α in plasma (red sorghum without tannin) ≡ Glucose, fructosamine, cholesterol, HDL-c, triacylglycerol, alanine and aspartate amino-transferase, superoxide dismutase, IL-8 and IL-10	Moraes, et al. (2012a)
Cancer	Normolipidemic rats	Diets containing 6% of bran from white (contains phenolic acids), brown (contains tannins), or black sorghum (contains 3-deoxyanthocyanidins)	10 weeks	↓Number of aberrant crypts (black and brown sorghums) ↑Superoxide dismutase activy (black sorghum) and glutathione peroxidase activity (three genotypes)	Lewis (2008)
	Mice	Application of methanolic extract of sorghum rich in phenolic compounds by subcutaneous injection		↓ Cell growth and metastasis in breast cancer cells (MDA-MB 231 and MCF-7)	Park, Jin Hee, et al. (2012)

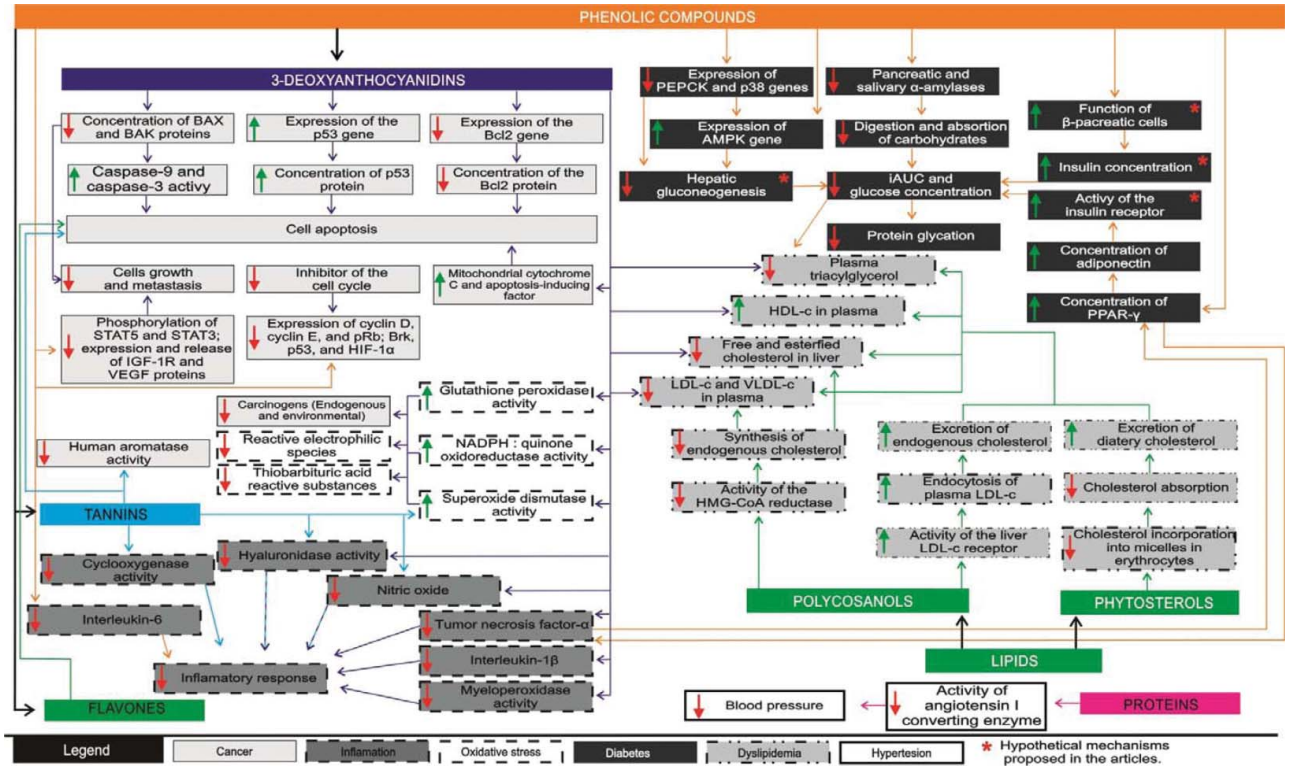


Figure 3. Main mechanisms of action of the sorghum on parameters related to noncommunicable diseases (diabetes, dyslipidemia, inflammation, cancer, oxidative stress and hypertension), proposed based on results of in vitro and animal studies.

Elimination of tumors in early stages is considered an integral part of anticancer effects. The results of the study have demonstrated that phenolic compounds from sorghum, especially 3-deoxyanthocyanidins, act directly against cancer cells due to the increase of the apoptosis and inhibition of the growth and metastasis of cancer cells of skin melanoma, colon, esophagus, liver, breast, and bone marrow (Shih et al., 2007; Yang et al., 2009; Awika et al., 2009; Suganyadevia et al., 2011a; Woo et al., 2012 Park, Jin Hee et al., 2012; Hwang et al., 2013). Sorghum 3-deoxyanthocyanidins are more cytotoxic to cancer cells than the respective analogous anthocyanidins present in other foods (cyanidin and pelargonidin) (Shih et al., 2007). In addition to 3-deoxyanthocyanidins, apoptosis of the colon cancer cells resulted from estrogenic activity of the flavones of sorghum (Yang et al., 2012).

The mechanisms by which sorghum's phenolic compounds induce in vitro apoptosis included the overexpression of genes and apoptotic proteins (BAX e BAK proteins and p53 gene expression), increase in enzymes' activity (caspase-9 and caspase-3 activy), and inhibition of anti-apoptotic factors (Bcl2 gene, anti-apoptotic Bcl2 proteins, mitochondrial cytochrome C, and apoptosis-inducing factor) (Suganyadevia et al., 2011b; Park, Jin Hee et al., 2012; Woo et al., 2012; Yang et al., 2012; 2013). Moreover, the sorghum phenolics inhibit the growth and metastasis of cancer cells by reducing the phosphorylation of STAT5 and STAT3, and the expression or the release of insulin-like growth factor 1 (IGF-1R) and vascular endothelial growth factor (VEGF) and increasing cell cycle inhibitors (expression of cyclin D, cyclin E, and pRb; Brk, p53, and HIF-1α - hypoxia-inducible factor 1α) (Suganyadevia et al., 2011a; Park et al., 2012; Woo et al., 2012). All of these events can inhibit cellular DNA synthesis, as was recently observed in skin melanoma cells (Hwang et al., 2013).

Furthermore, in addition to 3-deoxyanthocyanidins, sorghum has tannins that may have anticancer activity. Studies have shown that tannins isolated from other foods affect regulatory enzymes, blocking signal transduction pathways and inducing apoptosis; thus, they have attracted wide attention for cancer treatment (Huang et al., 2009). However, sorghum tannins still need to be better studied. In an recent study, sumac sorghum bran extract rich in tannins inhibited human aromatase (CYP19) activity in vitro more strongly than black sorghum bran extract rich in 3-deoxyanthocyanidins (Hargrove et al., 2011). This suggests that the tannins found in sumac sorghum are more potent inhibitors than the 3-deoxyanthocyanidins found in black sorghum, inhibiting and precipitating aromatase (Hargrove et al., 2011). This enzyme is key to the synthesis of estrogen and is an important target for chemotherapy of breast cancer dependent on this hormone (Dowsett et al., 2010).

The anticancer effects of sorghum in vivo have been little studied (Table 3). Recently, cellular growth and metastasis in breast cancer cells (MDA-MB 231 and MCF-7) in rats were reduced after the application of subcutaneously methanolic extract of sorghum rich in phenolic compounds (Park, Jin Hee et al., 2012). The results of the single study that evaluated the anticancer effects of sorghum showed that whole grains of the black and brown varieties (rich in 3-deoxyanthocyanidins and tannins, respectively) reduced the number of aberrant crypts of mice (Lewis, 2008). Furthermore, sorghum rich in tannins increased the colonocytes apoptosis.

Obesity and inflammation

Obesity is a pandemic that correlates with various noncommunicable diseases. The results of the studies demonstrate that sorghum rich in tannins reduces weight gain in animals (rats, pigs, rabbits, and poultry) (Al-Mamary et al., 2001; Muriu et al., 2002). The lower weight gain is undesirable in animals for slaughter, but can provide benefits against obesity in humans.

The lower weight gain in animals fed with sorghum rich in tannins results in part from the complexation of this compound to sorghum starch that helps lower caloric intake. Starch is the major component of cereals and the main source of calories in cereal products (Margareta Leeman et al., 2006). A recent study demonstrated that polymeric tannins from sorghum can naturally modify starch by interacting strongly with amylose forming resistant starch (Barros et al., 2013). Resistant starch cannot be digested in the small intestine and thus reaches the large intestine, delivering the health benefits of dietary fiber (Fuentes-Zaragoza et al., 2010). Furthermore, sorghum tannins can inhibit starch digestion by inhibiting saccharase and amylase enzymes (Nyamambi et al., 2000; Osman, 2004; Mkandawire et al., 2013).

Another important factor that may also have contributed to this lower weight gain was the complexation of tannins with proteins as well as digestive enzyme inhibition (trypsin, chymotrypsin, and lipases) (Nyamambi et al., 2000; Osman, 2004; Taylor et al., 2007; Ali et al., 2009; Frazier et al., 2010; Rahman and Osman, 2011; Barros et al., 2013). Proteins rich in proline bind more sorghum tannins than other proteins. In addition, a protein containing more proline repeats will bind more tannin than one with fewer such repeats (Medugu et al., 2010). Despite the evidence in animals, it is unknown whether sorghum (rich in tannins or not) modulates human weight. It is highlighted that the high consumption of sorghum rich in tannins can reduce the bioavailability of iron and zinc (Towo et al., 2006).

Obesity is characterized by a chronic low-grade inflammation (Gregor and Hotamisligil, 2011). Until recently, the role of fat itself in the development of the obesity and its consequences was considered to be a passive one and adipocytes were considered to be little more than storage cells for fat (Greenberg and Obin, 2006; Gregor and Hotamisligil, 2011). However, it is known that adipocytes and obesity play an important role on inflammatory mediators that signal this process. The discovery that obesity itself results in an inflammatory state in metabolic tissues opened a research field that examines the inflammatory mechanisms in obesity (Greenberg and Obin, 2006). This remarkable understanding allows a more clear definition of the role that adipocytes play in health and in obesity and how inflammatory mediators act as signaling molecules in this process (Gregor and Hotamisligil, 2011).

In an in vitro study, the extracts of sorghum rich in 3-deoxyanthocyanidins inhibited the secretion of interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α) and nitric oxide by human mononuclear cells activated with bacterial lipopolysaccharide (Burdette et al., 2010) (Fig. 3). These effects were not observed in varieties with tannins. However, in another study, sorghums rich in tannins were more effective than those rich in 3-deoxyanthocyanidins in inhibiting hyaluronidase, an important enzyme associated with inflammation (Bralley et al., 2008). The greater inhibitory effect of tannins can be attributed to their ability to complex the enzymes (competitive inhibition). However, in this study the tannins inhibited hyaluronidase through a competitive binding (Bralley et al., 2008) and this indicates that the tannins bind to binding sites of this enzyme.

The evaluation in vivo of the anti-inflammatory effects of sorghum is still incipient but the results are promising. The addition of whole red grains without tannins or its lipid fraction to a hyperlipidemic diet reduced the expression of TNF-α in rats (Moraes et al., 2012a; Park et al., 2012). The functional benefits in humans due to the consumption of whole sorghum and its fractions are still unknown, but they may result in part from the increased expression of adiponectin, which inhibits this inflammatory marker (Park et al., 2012). However, the sorghum extract of sorghum rich in tannins reduced the formation of edema in rats via the down-regulation of cyclooxygenase-2 (COX-2) expression, resulting in lower vascular permeability and edema with infiltration of neutrophils (Burdette et al., 2010; Shim et al., 2013). Thus, the results of in vitro and animal studies suggest that the anti-inflammatory effects of sorghum stem from its action on enzymes while 3-deoxyanthocyanidins act mainly on cytokines.

Dyslipidemia

In vitro and animal studies have shown that the lipidic and phenolic fractions from sorghum modulate parameters related to dyslipidemia and the risk of cardiovascular disease. These benefits result from the action of phytosterols, polycosanols, and phenolic compounds, which may modulate absorption, excretion, and synthesis of cholesterol.

The supplementation of the diet with sorghum lipids reduced the hepatic and plasma cholesterol of normolipidemic hamsters (Carr et al., 2005; Hoi et al., 2009) (Table 2). The phytosterols are one of the major bioactive compounds from sorghum lipid fraction able to inhibit the cholesterol absorption (Fig. 3). Studies demonstrated that phytosterols isolated from other foods inhibited cholesterol absorption in humans, leading to increased fecal excretion and reduced plasma LDL-c concentration (Amiot et al., 2011, 2013). These compounds reduce the amount of cholesterol captured in the gut enterocytes by inhibiting its incorporation into micelles, thereby lowering cholesterol absorption (Jesch and Carr, 2006).

The lipid fraction may also affect cholesterol absorption by altering the gut microbiota (Martínez et al., 2009). The addition of sorghum lipid fraction to the diet of hamsters increased the *Bifidobacterium spp* (mainly a phylotype related to *B. animalis*) and HDL-c, and reduced the family *Coriobacteriaceae* (mainly yet unclassified phylotypes) and non-HDL-c (Martínez et al., 2009). The correlation between the family *Coriobacteriaceae* and both non-HDL-c and cholesterol absorption suggest that this family could have a negative impact on cholesterol homeostasis by increasing cholesterol absorption. On the other hand, *Bifidobacterium* correlated with HDL-c and had no association with cholesterol absorption (Martínez et al., 2009). The mechanisms by which these bacteria affect cholesterol metabolism remain an important field of future research.

In addition to affecting the absorption of exogenous cholesterol, the sorghum lipidic fraction affects the synthesis and excretion of endogenous cholesterol. In one of the first in vitro studies about this subject, the sorghum lipid fraction inhibited in a dose-dependent manner the 3-hydroxy-3-methylglutaryl CoA (HMG-CoA) reductase activity, a key enzyme in cholesterol synthesis (Cho et al., 2000). However, the ability to reduce the in vivo cholesterol synthesis through HMG-CoA reductase requires further investigation. The polycosanols are one of the compounds present in the sorghum lipid fraction that can reduce the HMG-CoA reductase activity. These compounds, isolated from other food matrices, decrease the activity of this enzyme as well as increase the LDL receptor activity (Marinangeli et al., 2010).

Sorghum lipid fraction promotes the excretion of gut neutral sterols (i.e., cholesterol and its metabolites) and thus decreased the concentration of plasma cholesterol in normolipidemic hamsters (Hoi et al., 2009). It is not yet known whether sorghum bioactive compounds, including polycosanols and phytosterols, affect cholesterol metabolism through mechanisms similar to those proposed for compounds isolated from other plants. Therefore, possible metabolic pathways affected by the sorghum lipid fraction, including the expression of genes and proteins, are not still understood and poorly studied.

A single study published to date evaluated the effects of the sorghum lipid fraction on the molecular level of cholesterol metabolism in hamsters. This study observed the overexpression of a gene related to the synthesis of HDL-c (ABCA1 - ATP-binding cassette transporter A1) (Hoi et al., 2009). However, no changes were observed in the expression of genes related to cholesterol absorption (Niemann-Pick C1 like 1); cholesterol synthesis; (sterol regulatory element binding protein-2 and HMG-CoA reductase); and excretion of LDL-c and endogenous cholesterol (scavenger receptor class B type 1, low density lipoprotein receptor, cholesterol 7a-hydroxylase) (Hoi et al., 2009). This lack of effect can indicate that the intervention time used in the study (4 weeks) was not enough to cause changes in these genes.

In addition to the lipid fraction, sorghum phenolic compounds also affect the metabolism of cholesterol. However, the mechanisms involved in these functional benefits have not been elucidated. The results of recent studies have demonstrated that the oral intake of freeze-dried extracts of phenolic compounds of sorghum (50 to 600 mg/kg for 14 days) also reduced the plasma concentration of cholesterol and triacylglycerol in rats (Chung et al., 2011a; Chung et al., 2011b; Kim and Park, 2012). These functional benefits vary according to the sorghum variety and type of solvent used during preparation of the extracts (Chung et al., 2011a; Chung et al., 2011b).

Knowledge about the effects of whole sorghum on the lipid profile and the risk for developing cardiovascular disease in animals is incipient and in humans is nonexistent. In a study on mice, the addition of 30% whole sorghum to the diet increased the fecal excretion of bile acid and plasma HDL-c (Cho et al., 2000).

Diabetes

Recent results indicate that sorghum fractions modulate the glucose metabolism in animals due to the action of the phenolic compounds (Tables 2 and 3). However, it is not known whether the components isolated from sorghum and especially the whole grain are beneficial to humans. In studies with mice, the intake of extracts of sorghum phenolic compounds reduced the area under the curve of glucose and glycaemia (Chung et al., 2011a; Kim and Park, 2012; Park et al., 2012). Due to its strong effect on plasma glucose and insulin, the studies in animals have shown that phenolic extracts of sorghum exhibited a hypoglycemic effect similar to glibenclamida, an antidiabetic medication used in the control group (Chung et al., 2011a; Kim and Park, 2012).

The mechanisms by which sorghum phenolic compounds act involve metabolic pathways before and after absorption of carbohydrates that can contribute to the prevention and treatment of glycemic disorders in humans (Fig. 3). It was recently demonstrated that these extracts inhibited in vitro activity of the enzymes *B. stearothermophilus* α-glucosidase as well as human pancreatic and salivary α-amylase (Kim et al., 2011). Thus, the decrease in the rate of glucose digestion through inhibition of enzymes may be the first action mechanism of sorghum on human metabolism.

Study results suggest that phenolic compounds may also affect insulin-dependent pathways, including concentrations and sensitivity of this hormone in humans. The increase in insulin concentration was observed in diabetic mice that received extracts of phenolic compounds (Chung et al., 2011a). This increase indicates better functioning of the β cells and it has clinical relevance, especially for Type 2 diabetics, whose insulin synthesis is decreased. Furthermore, oral administration of the sorghum phenolic extracts can prevent and act as an adjuvant factor in the treatment of diabetes through an improvement in insulin sensitivity. This hypothesis is based on the fact that the extract of phenolic compounds from sorghum have induced antidiabetic effects in mice fed with a hiperlipidic diet through a mechanism that increased adiponectin and decreased TNF-α via overexpression of PPAR-γ, leading to improved insulin sensitivity (Park et al., 2012).

Furthermore, it is suggested that phenolic compounds reduce blood glucose concentration by inhibiting hepatic gluconeogenesis due to the down expression of the PEPCK and p38 genes and overexpression of the AMPK gene (Kim and Park, 2012). However, sorghum extract had no significant effect on glucose uptake by skeletal muscle determined by GLUT4 translocation and Akt phosphorylation (Kim and Park, 2012). It is not known whether sorghum exerts an effect on protein expression during glucose hepatic production and glucose uptake by skeletal muscle.

In addition to acting in basic processes of diabetes, the ethanolic extracts obtained from sorghum bran rich in phenolic compounds and with high antioxidant activity inhibit the glycation of proteins up to 60% (Farrar et al., 2008). However, sorghum bran extract with low antioxidant activity and content of phenolic compounds, as well as bran of rice, oats, and wheat, did not inhibit this process. The glycation products are associated with diabetes and insulin resistance and may increase the formation of reactive oxygen species and the activation of the nuclear factor-$\kappa\beta$ (NF- $\kappa\beta$) (Yamagishi, 2011).

Despite numerous in vitro evidence about the potential of bioactive compounds from sorghum to modulate

parameters related to diabetes, only one published study to date evaluated the effects of whole sorghum. However, in this study, normolipidemic rats that ingested from 1 to 5% of whole sorghum added to a hyperlipidemic diet showed no changes in blood glucose, glycated proteins, and triacylglycerol (Moraes et al., 2012a). The absence of significant changes in the study cited above may have resulted from a consumption of bioactive compounds less than those obtained in in vivo studies that used sorghum fractions. Therefore, these results indicate that consumption of whole sorghum may not promote significant changes in a short period of time during consumption of a nutritionally unbalanced diet. It is remarkable that the results do not refute the possibility that sorghum can promote preventive and therapeutic effects on other markers not analyzed in this study, including gene expression and conjugated protein to balanced and unbalanced diets.

Hypertension

Recently there is an indication in the scientific literature that sorghum can reduce blood pressure (Table 2). In this study, an isolate of sorghum α-kafirins inhibited in competitive and non-competitive ways the activity of the angiotensin I converting enzyme (Kamath et al., 2007).

Gut microbiota

The human gut is populated by an array of bacterial species, which develop important metabolic and immune functions, with a marked effect on the nutritional and health status of the host (Laparra and Sanz, 2010; Clemente et al., 2012). The functional benefits of phenolic compounds of foods on human health may result from direct action of the absorbed bioactive compounds (and their metabolites) or indirect effects mediated by non-absorbed compounds that modify the microbiota environment and, consequently, human metabolism or could act at the membrane border inducing signal transduction pathways (Fernandes et al., 2014). The probable effects of bioactive compounds sorghum on the gut microbiota are unknown. It is important to analyze these effects during interventions in humans.

There is scientific evidence that unabsorbed phenolic compounds and their metabolites contribute to the maintenance of gut health by the modulation of the gut microbial balance through the stimulation of the growth of beneficial bacteria and the inhibition of pathogen bacteria, exerting prebiotic-like effects (Larrosa et al., 2009; Requena et al., 2010; Clemente et al., 2012; Cardona et al., 2013). Among the compounds, tannins are of special interest due to their high abundance and because, even though they are not absorbed in the large intestine, they are metabolized by the colonic microbiota (Requena et al., 2010). Furthermore, sorghum has resistant starch and dietary fiber, which can modify gut microbiota (Scott et al., 2008; Martínez et al., 2010).

Although a great range of health-promoting activities of dietary phenolic compounds has been widely investigated, further scientific investigation is still needed in relation to their effect on modulation of gut microbiota (Requena et al., 2010; Cardona et al., 2013). Several studies demonstrated the effects of phenolic compounds from foods, including tannins and anthocyanins, on gut microbiota increasing the *Bifidobacterium spp* and *Lactobacillus spp* and decreasing the *Bacteroides spp, Clostridium spp, Propionibacterium spp, Salmonella typhimurium, Streptococcus mutans*, and *Escherichia Coli* (Dolara et al., 2005; Duarte et al., 2006; Lee et al., 2006; Tzounis et al., 2011; Hidalgo et al., 2012). The effects of sorghum, including varieties rich in tannins and 3-deoxyanthocyanidins, on gut microbiota are a field still to be explored. To date only one study has evaluated the relationship between bioactive compounds in sorghum in the gut microbiota of hamsters (Martínez et al., 2009).

Final considerations

Sorghum has a high nutritional value and is basically composed of starch, which is more slowly digested than that of other cereals, low digestibility proteins (mainly kafirins), unsaturated lipids, and is a source of some minerals (phosphorus, potassium, and zinc) and some B-complex vitamins (thiamine, riboflavin, and pyridoxine) and fat-soluble vitamins (D, E, and K). Furthermore, some varieties, especially the red, brown, and black colors, have a high content of phenolic compounds, especially 3-deoxyanthocyanidins and tannins, which are beneficial to human health.

The results of in vitro studies have demonstrated that compounds isolated from sorghum, particularly 3-deoxyanthocyanidins, tannins, and lipids, play a strong modulatory effect on gut microbiota and processes related to noncommunicable diseases (obesity, diabetes, dyslipidemia, cardiovascular disease, cancer, and hypertension). However, knowledge about the sorghum-specific bioactive compounds that promote these functional benefits is incipient.

Studies are needed to determine the preventive and therapeutic effects of sorghum whole grain and its fractions on human health, including gene and protein expression. It should be noted that the response of the human organism to these compounds may be dependent on their bioavailability. Thus, evaluating the bioavailability of sorghum's bioactive compounds is essential to determining the benefits of sorghum grains and bioactive compounds on human health.

The profile of bioactive compounds has been shown to be a determinant factor of the functional potential of sorghum varieties. In this context, the selection of varieties of sorghum and practical optimization should be performed to ensure the accumulation of bioactive components that will maximize the benefits of sorghum in humans. Furthermore, the behavior assessment of bioactive compounds in different processing conditions is essential to define the manner of use in which sorghum promotes maximum benefits to human health.

Funding

The authors thank the funding agency *FAPEMIG, CPNq* and *CAPES* for the financial support and for granting Doctor's and scientific initiation fellowships.

References

Abdel-Aal, E.-S. M., Choo, T.-M., Dhillon, S. and Rabalski, I. (2012). Free and bound phenolic acids and total phenolics in black, blue, and yellow barley and their contribution to free radical scavenging capacity. *Cereal Chem. J.* **89**:198–204.

Abdel-Rahman, I. E. and Osman, M. A. W. (2011). Effect of sorghum type (*Sorghum bicolor*) and traditional fermentation on tannins and phytic acid contents and trypsin inhibitor activity. *Food Agr. Environ.* **9**:163–166.

Afify, A. E.-M. M. R., El-Beltagi, H. S., Abd El-Salam, S. M. and Omran, A. A. (2011). Bioavailability of iron, zinc, phytate and phytase activity during soaking and germination of white sorghum varieties. *PLoS ONE* **6**:255–212.

Afify, A. E.-M. M. R., El-Beltagi, H. S., Abd El-Salam, S. M. and Omran, A. A. (2012a). Oil and fatty acid contents of white sorghum varieties under soaking, cooking, germination and fermentation processing for improving cereal quality. *Not. Bot. Horti. Agrobo.* **40**:86–92.

Afify, A. E.-M. M. R., El-Beltagi, H. S., Abd El-Salam, S. M. and Omran, A. A. (2012b). Protein solubility, digestibility and fractionation after germination of sorghum varieties. *PLoS ONE* **7**:e31154.

Afify, A. E.-M. M. R., El-Beltagi, H. S., El-Salam, S. M. A. and Omran, A. A. (2012c). Biochemical changes in phenols, flavonoids, tannins, vitamin E, β–carotene and antioxidant activity during soaking of three white sorghum varieties. *Asian Pac. J. Trop. Biomed.* **2**:203–209.

Al-Mamary, M., Molham, A.-H., Abdulwali, A.-A. and Al-Obeidi, A. (2001). *In vivo* effects of dietary sorghum tannins on rabbit digestive enzymes and mineral absorption. *Nutrit. Res.* **21**:1393–1401.

Ali, N. M. M., El Tinay, A. H., Elkhalifa, A. E. O., Salih, O. A. and Yousif, N. E. (2009). Effect of alkaline pretreatment and cooking on protein fractions of a high-tannin sorghum cultivar. *Food Chem.* **114**:646–648.

Amiot, M. J., Knol, D., Cardinault, N., Nowicki, M., Bott, R., Antona, C., Borel, P., Bernard, J.-P., Duchateau, G. and Lairon, D. (2011). Phytosterol ester processing in the small intestine: impact on cholesterol availability for absorption and chylomicron cholesterol incorporation in healthy humans. *J. Lipid Res.* **52**:1256–1264.

Amiot, M. J., Knol, D., Cardinault, N., Nowicki, M., Bott, R., Antona, C., Borel, P., Bernard, J.-P., Duchateau, G. and Lairon, D. (2013). Comparable reduction in cholesterol absorption after two different ways of phytosterol administration in humans. *Eur. J. Nutrit.* **55**:1–8.

Ashok Kumar, A., Reddy, B. V. S., Ramaiah, B., Sahrawat, K. L. and Pfeiffer, W. H. (2013). Gene effects and heterosis for grain iron and zinc concentration in sorghum [*Sorghum bicolor* (L.) Moench]. *Field Crop. Res.* **146**:86–95.

Awika, J. M. (2003). Antioxidant Properties of Sorghum. Texas A&M University, College Station, Texas.

Awika, J. M. (2008). Behavior of 3-deoxyanthocyanidins in the presence of phenolic copigments. *Food Res. Int.* **41**:532–538.

Awika, J. M., Dykes, L., Gu, L., Rooney, L. W. and Prior, R. L. (2003). Processing of sorghum (*Sorghum bicolor*) and sorghum products alters procyanidin oligomer and polymer distribution and content. *J. Agr. Food Chem.* **51**:5516–5521.

Awika, J. M., McDonough, C. M. and Rooney, L. W. (2005). Decorticating sorghum to concentrate healthy phytochemicals. *J. Agr. Food Chem.* **53**:6230–6234.

Awika, J. M. and Rooney, L. W. (2004). Sorghum phytochemicals and their potential impact on human health. *PhytoChem.* **65**:1199–1221.

Awika, J. M., Rooney, L. W. and Waniska, R. D. (2004). Properties of 3-deoxyanthocyanins from sorghum. *J. Agr. Food Chem.* **52**:4388–4394.

Awika, J. M., Yang, L., Browning, J. D. and Faraj, A. (2009). Comparative antioxidant, antiproliferative and phase II enzyme inducing potential of sorghum (*Sorghum bicolor*) varieties. *LWT - Food Sci. Technol.* **42**:1041–1046.

Barros, F., Awika, J. and Rooney, L. W. (2013). Effect of molecular weight profile of sorghum proanthocyanidins on resistant starch formation. *J. Sci. Food Agr.* n/a-n/a.

Barros, F., Awika, J. M. and Rooney, L. W. (2012). Interaction of tannins and other sorghum phenolic compounds with starch and effects on in vitro starch digestibility. *J. Agric. Food Chem.* **60**:11609–11617.

Beecher, G. R. (2004). Proanthocyanidins: Biological activities associated with human health. *Pharm. Biol.* **42**:2–20.

Belton, P. S., Delgadillo, I., Halford, N. G. and Shewry, P. R. (2006). Kafirin structure and functionality. *J. Cereal Sci.* **44**:272–286.

Bralley, E., Greenspan, P., Hargrove, J. L. and Hartle, D. K. (2008). Inhibition of hyaluronidase activity by select sorghum brans. *J. Med. Med. Food* **11**:307–312.

Bröhan, M., Jerkovic, V. and Collin, S. (2011). Potentiality of red sorghum for producing stilbenoid-enriched beers with high antioxidant activity. *J. Agric. Food Chem.* **59**:4088–4094.

Burdette, A., Garner, P. L., Mayer, E. P., Hargrove, J. L., Hartle, D. K. and Greenspan, P. (2010). Anti-inflammatory activity of select sorghum (*Sorghum bicolor*) brans. *J. Med. Food* **13**:1–9.

Cardona, F., Andrés-Lacueva, C., Tulipani, S., Tinahones, F. J. and Queipo-Ortuño, M. I. (2013). Benefits of polyphenols on gut microbiota and implications in human health. *J. Nutr. Biochem.* **24**:1415–1422.

Cardoso, L. d. M., Montini, T. A., Pinheiro, S. S., Pinheiro Sant'Ana, H. M., Martino, H. S. D. and Moreira, A. V. B. (2014). Effects of processing with dry heat and wet heat on the antioxidant profile of sorghum (*Sorghum bicolor* L.). *Food Chem.* **152**:201–217.

Carr, T. P., Weller, C. L., Schlegel, V. L., Cuppett, S. L., Guderian, D. M. and Johnson, K. R. (2005). Grain sorghum lipid extract reduces cholesterol absorption and plasma non-HDL cholesterol concentration in hamsters. *J. Nutrit.* **135**:2236–2240.

Chiremba, C., Taylor, J. R. N., Rooney, L. W. and Beta, T. (2012). Phenolic acid content of sorghum and maize cultivars varying in hardness. *Food Chem.* **134**:81–88.

Cho, S. H., Choi, Y. and Ha, T. Y. (2000). In vitro and in vivo effects of prosomillet, buckwheat and sorghum on cholesterol metabolism. *FASEB J.* **14**:249–249.

Chong, J., Poutaraud, A. and Hugueney, P. (2009). Metabolism and roles of stilbenes in plants. *Plant Sci.* **177**:143–155.

Chung, I.-M., Kim, E.-H., Yeo, M.-A., Kim, S.-J., Seo, M. C. and Moon, H.-I. (2011a). Antidiabetic effects of three Korean sorghum phenolic extracts in normal and streptozotocin-induced diabetic rats. *Food Res. Int.* **44**:127–132.

Chung, I.-M., Yeo, M.-A., Kim, S.-J., Kim, M.-J., Park, D.-S. and Moon, H.-I. (2011b). Antilipidemic activity of organic solvent extract from *Sorghum bicolor* on rats with diet-induced obesity. *Human Exp. Toxicol.* **30**:1865–1868.

Chung, I.-M., Yong, S.-J., Lee, J. and Kim, S.-H. (2013). Effect of genotype and cultivation location on β-sitosterol and α-, β-, γ-, and δ-tocopherols in sorghum. *Food Res. Int.* **51**:971–976.

Ciacci, C., Maiuri, L., Caporaso, N., Bucci, C., Del Giudice, L., Rita Massardo, D., Pontieri, P., Di Fonzo, N., Bean, S. R., Ioerger, B. and Londei, M. (2007). Celiac disease: In vitro and in vivo safety and palatability of wheat-free sorghum food products. *Clin. Nutr.* **26**:799–805.

Clemente, Jose.C., Ursell, Luke.K., Parfrey, Laura.W. and Knight, R. (2012). The impact of the gut microbiota on human health: an integrative view. *Cell* **148**:1258–1270.

Correia, I., Nunes, A., Barros, A. S. and Delgadillo, I. (2008). Protein profile and malt activity during sorghum germination. *J. Sci. Food Agr.* **88**:2598–2605.

Crozier, A., Del Rio, D. and Clifford, M. N. (2010). Bioavailability of dietary flavonoids and phenolic compounds. *Mol. Aspect Med.* **31**:446–467.

Crozier, A., Jaganath, I. B. and Clifford, M. N. (2009). Dietary phenolics: chemistry, bioavailability and effects on health. *Nat. Prod. Rep.* **26**:1001–1043.

D'Archivio, M., Filesi, C., Varì, R., Scazzocchio, B. and Masella, R. (2010). Bioavailability of the polyphenols: status and controversies. *Int. J. Mol. Sci.* **11**:1321–1342.

da Silva, L. S., Jung, R., Zhao, Z.-y., Glassman, K., Taylor, J. and Taylor, J. R. N. (2011a). Effect of suppressing the synthesis of different kafirin sub-classes on grain endosperm texture, protein body structure and protein nutritional quality in improved sorghum lines. *J. Cereal Sci.* **54**:160–167.

da Silva, L. S., Taylor, J. and Taylor, J. R. (2011b). Transgenic sorghum with altered kafirin synthesis: kafirin solubility, polymerization, and protein digestion. *J. Agric. Food Chem.* **59**:9265–9270.

De Mesa-Stonestreet, N. J., Alavi, S. and Bean, S. R. (2010). Sorghum proteins: the concentration, isolation, modification, and food applications of kafirins. *J. Food Sci.* **75**:90–104.

Delgado-Zamarreño, M., Bustamante-Rangel, M., Martínez-Pelarda, D. and Carabías-Martínez, R. (2009). Analysis of β-sitosterol in seeds and nuts using pressurized liquid extraction and liquid chromatography. *Anal. Sci.* **25**:765–768.

Dicko, M. H., Gruppen, H., Barro, C., Traore, A. S., van Berkel, W. J. and Voragen, A. G. (2005). Impact of phenolic compounds and related enzymes in sorghum varieties for resistance and susceptibility to biotic and abiotic stresses. *J. Chem. Ecol.* **31**:2671–2688.

Dillon, S. L., Shapter, F. M., Henry, R. J., Cordeiro, G., Izquierdo, L. and Lee, L. S. (2007). Domestication to crop improvement: genetic resources for sorghum and saccharum (*Andropogoneae*). *Ann. Bot.* **100**:975–989.

Dixon, R. A., Xie, D.-Y. and Sharma, S. B. (2005). Proanthocyanidins—a final frontier in flavonoid research? *New Phytol.* **165**:9–28.

Dolara, P., Luceri, C., Filippo, C. D., Femia, A. P., Giovannelli, L., Caderni, G., Cecchini, C., Silvi, S., Orpianesi, C. and Cresci, A. (2005). Red wine polyphenols influence carcinogenesis, intestinal microflora, oxidative damage and gene expression profiles of colonic mucosa in F344 rats. *Mutation Res./λατνεμαδνυΦ σισενεγατυμ φο σμσιναηχεμ ραλυχελομ δνα* **195**:642–732.

Donovan, J. L., Manach, C., Faulks, R. M. and Kroon, P. A. (2007). Absorption and metabolism of dietary plant secondary metabolites. **In**: Plant Secondary Metabolites, pp. 303–351. Blackwell Publishing Ltd.

Dowsett, M., Cuzick, J., Ingle, J., Coates, A., Forbes, J., Bliss, J., Buyse, M., Baum, M., Buzdar, A. and Colleoni, M. (2010). Meta-analysis of breast cancer outcomes in adjuvant trials of aromatase inhibitors versus tamoxifen. *J. Clin. Oncol.* **28**:509–518.

Duarte, S., Gregoire, S., Singh, A. P., Vorsa, N., Schaich, K., Bowen, W. H. and Koo, H. (2006). Inhibitory effects of cranberry polyphenols on formation and acidogenicity of *Streptococcus mutans* biofilms. *FEMS Microbiol. Lett.* **257**:50–56.

Duodu, K. G., Nunes, A., Delgadillo, I., Parker, M. L., Mills, E. N. C., Belton, P. S. and Taylor, J. R. N. (2002). Effect of grain structure and cooking on sorghum and maize in vitro protein digestibility. *J. Cereal Sci.* **35**:161–174.

Duodu, K. G., Taylor, J. R. N., Belton, P. S. and Hamaker, B. R. (2003). Factors affecting sorghum protein digestibility. *J. Cereal Sci.* **38**:117–131.

Dykes, L., Peterson, G. C., Rooney, W. L. and Rooney, L. W. (2011). Flavonoid composition of lemon-yellow sorghum genotypes. *Food Chem.* **128**:173–179.

Dykes, L. and Rooney, L. W. (2006). Sorghum and millet phenols and antioxidants. *J. Cereal Sci.* **44**:236–251.

Dykes, L., Rooney, L. W., Waniska, R. D. and Rooney, W. L. (2005). Phenolic compounds and antioxidant activity of sorghum grains of varying genotypes. *J. Agric. Food Chem.* **53**:6813–6818.

Dykes, L., Rooney, W. L. and Rooney, L. W. (2013). Evaluation of phenolics and antioxidant activity of black sorghum hybrids. *J. Cereal Sci.* **58**:278–283.

Dykes, L., Seitz, L. M., Rooney, W. L. and Rooney, L. W. (2009). Flavonoid composition of red sorghum genotypes. *Food Chem.* **116**:313–317.

Earp, C. F., McDonough, C. M. and Rooney, L. W. (2004). Microscopy of pericarp development in the caryopsis of *Sorghum bicolor* (L.) Moench. *J. Cereal Sci.* **39**:21–27.

Elkhalifa, A. E. O., Schiffler, B. and Bernhardt, R. (2005). Effect of fermentation on the functional properties of sorghum flour. *Food Chem.* **92**:1–5.

ELKhier, M. K. S. and Abd-ALRaheem, A. A. (2011). Effect of fermentation period on the chemical composition, in vitro protein digestibility and tannin content in two Sorghum cultivars (Dabar and Tabat) in Sudan. *J. Appl. Biosci.* **39**:2602–2606.

Ezeogu, L. I., Duodu, K. G., Emmambux, M. N. and Taylor, J. R. N. (2008). Influence of cooking conditions on the protein matrix of sorghum and maize endosperm flours. *Cereal Chem. J.* **85**:397–402.

Ezeogu, L. I., Duodu, K. G. and Taylor, J. R. N. (2005). Effects of endosperm texture and cooking conditions on the in vitro starch digestibility of sorghum and maize flours. *J. Cereal Sci.* **42**:33–44.

Faria, A., Fernandes, I., Mateus, N. and Calhau, C. (2013). Bioavailability of Anthocyanins. **In**: Natural Products, pp. 2465–2487. Ramawat, K. G. and Mérillon, J.-M., Eds., Springer, Berlin Heidelberg.

Farrar, J. L., Hartle, D. K., Hargrove, J. L. and Greenspan, P. (2008). A novel nutraceutical property of select sorghum (*Sorghum bicolor*) brans: inhibition of protein glycation. *Phytotherapy Res.* **22**:1052–1056.

Fernandes, I., Faria, A., Calhau, C., de Freitas, V. and Mateus, N. (2014). Bioavailability of anthocyanins and derivatives. *J. Funct. Foods.* **7**:54–66.

Ferreira, S. M. R., Luparelli, P. C., Schieferdecker, M. E. M. and Vilela, R. M. (2009). Cookies sem glúten a partir da farinha de sorgo. *Archivos Latinoamericanos Nutr.* **59**:433–440.

Floegel, A., Kim, D.-O., Chung, S.-J., Song, W. O., Fernandez, M. L., Bruno, R. S., Koo, S. I. and Chun, O. K. (2010). Development and validation of an algorithm to establish a total antioxidant capacity database of the US diet. *Int. J. Food Sci.s Nutr.* **61**:600–623.

Food and Agricultural Organization. (2010). FAOSTAT. In). Rome, Italy.

Food Security Department. (1999). Sorghum: Post-harvest Operations. United Kingdom: Natural Resources Institute, United Kingdom.

Frazier, R. A., Deaville, E. R., Green, R. J., Stringano, E., Willoughby, I., Plant, J. and Mueller-Harvey, I. (2010). Interactions of tea tannins and condensed tannins with proteins. *J. Pharm. Biomed. Anal.* **51**:490–495.

Fuentes-Zaragoza, E., Riquelme-Navarrete, M. J., Sánchez-Zapata, E. and Pérez-Álvarez, J. A. (2010). Resistant starch as functional ingredient: A review. *Food Res. Int.* **43**:931–942.

González-Montilla, F. M., Chávez-Santoscoy, R. A., Gutiérrez-Uribe, J. A. and Serna-Saldivar, S. O. (2012). Isolation and identification of phase II enzyme inductors obtained from black Shawaya sorghum [*Sorghum bicolor* (L.) Moench] bran. *J. Cereal Sci.* **55**:126–131.

Goodall, M. A., Campanella, O. H., Ejeta, G. and Hamaker, B. R. (2012). Grain of high digestible, high lysine (HDHL) sorghum contains kafirins which enhance the protein network of composite dough and bread. *J. Cereal Sci.* **56**:352–357.

Greenberg, A. S. and Obin, M. S. (2006). Obesity and the role of adipose tissue in inflammation and metabolism. *Am. J. Clin. Nutr.* **83**:461–465.

Gregor, M. F. and Hotamisligil, G. S. (2011). Inflammatory mechanisms in obesity. *Ann. Rev. Immunol.* **29**:415–445.

Hadbaoui, Z., Djeridane, A., Yousfi, M., Saidi, M. and Nadjemi, B. (2010). Fatty acid, tocopherol composition and the antioxidant activity of the lipid extract from the sorghum grains growing in Algeria. *Mediterr. J. Nutr. Met.* **3**:215–220.

Hagerman, A. E., Riedl, K. M., Jones, G. A., Sovik, K. N., Ritchard, N. T., Hartzfeld, P. W. and Riechel, T. L. (1998). High molecular weight plant polyphenolics (tannins) as biological antioxidants. *J. Agric. Food Chem.* **46**:1887–1892.

Hahn, D. and Rooney, L. (1986). Effect of genotype on tannins and phenols of sorghum. *Cereal Chem.* **63**:4–8.

Hahn, D. H. and Rooney, L. W. (1986). Effect of genotype on tannins and phenols of sorghum. *Cereal Chem. J.* **63**:4–8.

Hargrove, J. L., Greenspan, P., Hartle, D. K. and Dowd, C. (2011). Inhibition of aromatase and α-amylase by flavonoids and proanthocyanidins from *Sorghum bicolor* bran extracts. *J. Med. Food* **14**:799–807.

Henley, E. C., Taylor, J. R. N. and Obukosia, S. D. (2010). The importance of dietary protein in human health: combating protein deficiency in sub-saharan africa through transgenic biofortified sorghum. **In**: Advances in Food and Nutrition Research, Vol. 60, pp. 21–52. Steve, L. T. ed., Academic Press.

Hidalgo, M., Oruna-Concha, M. J., Kolida, S., Walton, G. E., Kallithraka, S., Spencer, J. P. E., Gibson, G. R. and de Pascual-Teresa, S. (2012). Metabolism of anthocyanins by human gut microflora and their influence on gut bacterial growth. *J. Agric. Food Chem.* **60**:3882–3890.

Hill, H., Slade Lee, L. and Henry, R. J. (2012). Variation in sorghum starch synthesis genes associated with differences in starch phenotype. *Food Chem.* **131**:175–183.

Hoi, J. T., Weller, C. L., Schlegel, V. L., Cuppett, S. L., Lee, J.-Y. and Carr, T. P. (2009). Sorghum distillers dried grain lipid extract increases cholesterol excretion and decreases plasma and liver cholesterol concentration in hamsters. *J. Funct. Foods* **1**:381–386.

Hole, A. S., Rud, I., Grimmer, S., Sigl, S., Narvhus, J. and Sahlstrøm, S. (2012). Improved bioavailability of dietary phenolic acids in whole grain barley and oat groat following fermentation with probiotic *Lactobacillus acidophilus, Lactobacillus johnsonii*, and *Lactobacillus reuteri*. *J. Agric. Food Chem.* **60**:6369–6375.

Holt, R. R., Lazarus, S. A., Sullards, M. C., Zhu, Q. Y., Schramm, D. D., Hammerstone, J. F., Fraga, C. G., Schmitz, H. H. and Keen, C. L. (2002). Procyanidin dimer B2 [epicatechin-(4β-8)-epicatechin] in human plasma after the consumption of a flavanol-rich cocoa. *Am. J. Clin. Nutr.* **76**:798–804.

Hotamisligil, G. S. (2006). Inflammation and metabolic disorders. *Nature* **444**:860–867.

Huang, W.-Y., Cai, Y.-Z. and Zhang, Y. (2009). Natural phenolic compounds from medicinal herbs and dietary plants: potential use for cancer prevention. *Nutr. Cancer* **62**:1–20.

Hwang, J.-M., Choi, K.-C., Bang, S.-J., Son, Y.-O., Kim, B.-T., Kim, D.-H., Choi, G., Kim, D., Shi, X. and Lee, J.-C. (2013). Anti-oxidant and anti-inflammatory properties of methanol extracts from various crops. *Food Sci. Biotechnol.* **22**:265–272.

Hwang, K. T., Kim, J. E. and Weller, C. L. (2005). Policosanol contents and compositions in wax-like materials extracted from selected cereals of Korean origin. *Cereal Chem.* **82**:242–245.

Hwang, K. T., Weller, C. L., Cuppett, S. L. and Hanna, M. (2004). Policosanol contents and composition of grain sorghum kernels and dried distillers grains. *Biol. Syst. Eng.: Papers Publ.* **81**:345–349.

Isaacson, C. (2005). The change of the staple diet of black South Africans from sorghum to maize (corn) is the cause of the epidemic of squamous carcinoma of the oesophagus. *Med. Hypotheses* **64**:658–660.

Jesch, E. D. and Carr, T. P. (2006). Sitosterol reduces micellar cholesterol solubility in model bile. *Nutr. Res.* **26**:579–584.

Kamath, V., Niketh, S., Chandrashekar, A. and Rajini, P. S. (2007). Chymotryptic hydrolysates of α-kafirin, the storage protein of sorghum (*Sorghum bicolor*) exhibited angiotensin converting enzyme inhibitory activity. *Food Chem.* **100**:306–311.

Kamath, V. G., Chandrashekar, A. and Rajini, P. S. (2004). Antiradical properties of sorghum (*Sorghum bicolor* L. Moench) flour extracts. *J. Cereal Sci.* **40**:283–288.

Kangama, C. O. and Rumei, X. (2005). Introduction of sorghum (*Sorghum bicolor* (L.) Moench) into China. *Afr. J. Biotechnol.* **4**:575–579.

Kaufman, R. C., Herald, T. J., Bean, S. R., Wilson, J. D. and Tuinstra, M. R. (2013). Variability in tannin content, chemistry and activity in a diverse group of tannin containing sorghum cultivars. *J. Sci. Food Agric.* **93**:1233–1241.

Kim, J.-S., Hyun, T. K. and Kim, M.-J. (2011). The inhibitory effects of ethanol extracts from sorghum, foxtail millet and proso millet on α-glucosidase and α-amylase activities. *Food Chem.* **124**:1647–1651.

Kim, J. and Park, Y. (2012). Anti-diabetic effect of sorghum extract on hepatic gluconeogenesis of streptozotocin-induced diabetic rats. *Nutr. Metabol.* **9**:1–7.

Kruger, J., Taylor, J. R. N., Du, X., De Moura, F. F., Lönnerdal, B. and Oelofse, A. (2013). Effect of phytate reduction of sorghum, through genetic modification, on iron and zinc availability as assessed by an in vitro dialysability bioaccessibility assay, Caco-2 cell uptake assay, and suckling rat pup absorption model. *Food Chem.* **141**:1019–1025.

Kumar, T., Dweikat, I., Sato, S., Ge, Z., Nersesian, N., Chen, H., Elthon, T., Bean, S., Ioerger, B. P., Tilley, M. and Clemente, T. (2012). Modulation of kernel storage proteins in grain sorghum (*Sorghum bicolor* (L.) Moench). *Plant Biotechnol. J.* **10**:533–544.

Lafay, S. and Gil-Izquierdo, A. (2008). Bioavailability of phenolic acids. *PhytoChem. Rev.* **7**:301–311.

Laparra, J. M. and Sanz, Y. (2010). Interactions of gut microbiota with functional food components and nutraceuticals. *Pharm. Res.* **61**:219–225.

Larrosa, M., Yañéz-Gascón, M. a. J., Selma, M. a. V., González-Sarrías, A., Toti, S., Cerón, J. J. n., Tomás-Barberán, F., Dolara, P. and Espín, J. C. (2009). Effect of a low dose of dietary resveratrol on colon microbiota, inflammation and tissue damage in a DSS-induced colitis rat model. *J. Agric. Food Chem.* **57**:2211–2220.

Lee, H. C., Jenner, A. M., Low, C. S. and Lee, Y. K. (2006). Effect of tea phenolics and their aromatic fecal bacterial metabolites on intestinal microbiota. *Res. Microbiol.* **157**:876–884.

Lee, S., Park, Y., Zuidema, M. Y., Hannink, M. and Zhang, C. (2011). Effects of interventions on oxidative stress and inflammation of cardiovascular diseases. *World J. Cardiol.* **3**:18–24.

Leguizamón, C., Weller, C., Schlegel, V. and Carr, T. (2009). Plant sterol and policosanol characterization of hexane extracts from grain sorghum, corn and their DDGS. *J. Am. Oil Chem. Soc.* **86**:707–716.

Lewis, J. B. (2008). Effects of Bran from Sorghum Grains Containing Different Classes and Levels of Bioactive Compounds in Colon Carcinogenesis. Texas A&M University, USA.

Manach, C., Williamson, G., Morand, C., Scalbert, A. and Rémésy, C. (2005). Bioavailability and bioefficacy of polyphenols in humans. I. Review of 97 bioavailability studies. *Am. J. Clin. Nutr.* **81**:230S–242S.

Margareta Leeman, A., Karlsson, M. E., Eliasson, A.-C. and Björck, I. M. (2006). Resistant starch formation in temperature treated potato starches varying in amylose/amylopectin ratio. *Carbohyd. Polym.* **65**:306–313.

Marinangeli, C. P. F., Jones, P. J. H., Kassis, A. N. and Eskin, M. N. A. (2010). Policosanols as nutraceuticals: fact or fiction. *Crit. Rev. Food Sci. Nutr.* **50**:259–267.

Martínez, I., Kim, J., Duffy, P. R., Schlegel, V. L. and Walter, J. (2010). Resistant starches types 2 and 4 have differential effects on the composition of the fecal microbiota in human subjects. *PLoS ONE* **5**:1–11.

Martínez, I., Wallace, G., Zhang, C., Legge, R., Benson, A. K., Carr, T. P., Moriyama, E. N. and Walter, J. (2009). Diet-induced metabolic improvements in a hamster model of hypercholesterolemia are strongly linked to alterations of the gut microbiota. *Appl. Environ. Microbiol.* **75**:4175–4184.

Martino, H. S. D., Tomaz, P. A., Moraes, E. A., Conceição, L. L., Oliveira, D. S., Queiroz, V. A. V., Rodrigues, J. A. S., Pirozi, M. R., Pinheiro-Sant'Ana, H. M. and Ribeiro, M. R. (2012). Chemical characterization and size distribution of sorghum genotypes for human consumption. *Rev. Inst. Adolfo. Lutz.* **71**:337–344.

Maunder, B. (2005). Sorghum: The global grain of the future. National Grain Sorghum Producers, Lubbock, TX.

McGhie, T. K., Ainge, G. D., Barnett, L. E., Cooney, J. M. and Jensen, D. J. (2003). Anthocyanin glycosides from berry fruit are absorbed and excreted unmetabolized by both humans and rats. *J. Agric. Food Chem.* **51**:4539–4548.

Medugu, C., Kwari, I., Igwebuike, J., Nkama, I. and Mohammed, I. (2010). Performance and economics of production of broiler chickens fed sorghum or millet as replacement for maize in the semi-arid zone of Nigeria. *Agric. Biol. J. North. Am.* **1**:321–325.

Mehlo, L., Mbambo, Z., Bado, S., Lin, J., Moagi, S. M., Buthelezi, S., Stoychev, S. and Chikwamba, R. (2013). Induced protein polymorphisms and nutritional quality of gamma irradiation mutants of sorghum. *Mutation Res./λατνεμαδνυΦ σισενεγατυμ φο σμσιναηχεμ ραλυχελομ δνα* **195**:642–732.

Mehmood, S., Orhan, I., Ahsan, Z., Aslan, S. and Gulfraz, M. (2008). Fatty acid composition of seed oil of different *Sorghum bicolor* varieties. *Food Chem.* **109**:855–859.

Mkandawire, N. L., Kaufman, R. C., Bean, S. R., Weller, C. L., Jackson, D. S. and Rose, D. J. (2013). Effects of sorghum (*Sorghum bicolor* (L.) Moench) tannins on α-amylase activity and in vitro digestibility of starch in raw and processed flours. *J. Agric. Food Chem.* **61**:4448–4454.

Mokrane, H., Amoura, H., Belhaneche-Bensemra, N., Courtin, C. M., Delcour, J. A. and Nadjemi, B. (2010). Assessment of Algerian sorghum protein quality [*Sorghum bicolor* (L.) Moench] using amino acid analysis and in vitro pepsin digestibility. *Food Chem.* **121**:719–723.

Moraes, É. A., Natal, D. I. G., Queiroz, V. A. V., Schaffert, R. E., Cecon, P. R., de Paula, S. O., Benjamim, L. d. A., Ribeiro, S. M. R. and Martino, H. S. D. (2012a). Sorghum genotype may reduce low-grade inflammatory response and oxidative stress and maintains jejunum morphology of rats fed a hyperlipidic diet. *Food Res. Int.* **49**:553–559.

Moraes, É. A., Queiroz, V. A. V., Shaffert, R. E., Costa, N. M. B., Nelson, J. D., Ribeiro, S. M. R. and Martino, H. S. D. (2012b). In vivo protein quality of new sorghum genotypes for human consumption. *Food Chem.* **134**:1549–1555.

Muriu, J. I., Njoka-Njiru, E. N., Tuitoek, J. K. and Nanua, J. N. (2002). Evaluation of sorghum (Sorghum bicolor) as replacement for maize in the diet of growing rabbits (Oryctolagus cuniculus). *Asian-Aust. J. Animal Sci.* **15**:565–569.

N'Dri, D., Mazzeo, T., Zaupa, M., Ferracane, R., Fogliano, V. and Pellegrini, N. (2013). Effect of cooking on the total antioxidant capacity and phenolic profile of some whole-meal African cereals. *J. Sci. Food Agr.* **93**:29–36.

Neucere, J. N. (1982). Lectins in grain sorghum [*Sorghum bicolor* (L.) Moench]. *J. Agr. Food Chem.* **30**:603–604.

Nyamambi, B., Ndlovu, L. R., Read, J. S. and Reed, J. D. (2000). The effects of sorghum proanthocyanidins on digestive enzyme activity in vitro and in the digestive tract of chicken. *J. Sci. Food Agric.* **80**:2223–2231.

Ochanda, S. O., Onyango, C., Mwasaru, A., Ochieng, J. and Mathooko, F. (2010). Effects of malting and fermentation treatments on group B-vitamins of red sorghum, white sorghum and pearl millets in Kenya. *J. Appl. Biosci.* **34**:2128–2134.

Oria, M. P., Hamaker, B. R., Axtell, J. D. and Huang, C.-P. (2000). A highly digestible sorghum mutant cultivar exhibits a unique folded structure of endosperm protein bodies. *Proc. Natl. Acad. Sci. USA* **97**:5065–5070.

Osman, M. A. (2004). Changes in sorghum enzyme inhibitors, phytic acid, tannins and in vitro protein digestibility occurring during Khamir (local bread) fermentation. *Food Chem.* **88**:129–134.

Park, J. H., Darvin, P., Lim, E. J., Joung, Y. H., Hong, D. Y., Park, E. U., Park, S. H., Choi, S. K., Moon, E.-S., Cho, B. W., Park, K. D., Lee, H. K., Kim, M.-J., Park, D.-S., Chung, I.-M. and Yang, Y. M. (2012). Hwanggeumchal sorghum induces cell cycle arrest, and suppresses tumor growth and metastasis through Jak2/STAT pathways in breast cancer xenografts. *PLoS ONE* **7**:40531–40531.

Park, J. H., Lee, S. H., Chung, I.-M. and Park, Y. (2012). Sorghum extract exerts an anti-diabetic effect by improving insulin sensitivity via PPAR-γ in mice fed a high-fat diet. *Nutr. Res. Pract.* **6**:322–327.

Pontieri, P., Mamone, G., De Caro, S., Tuinstra, M. R., Roemer, E., Okot, J., De Vita, P., Ficco, D. B. M., Alifano, P., Pignone, D., Massardo, D. R. and Del Giudice, L. (2013). Sorghum, a healthy and gluten-free food for celiac patients as demonstrated by genome, biochemical, and immunochemical analyses. *J. Agric. Food Chem.* **61**:2565–2571.

Pranoto, Y., Anggrahini, S. and Efendi, Z. (2013). Effect of natural and Lactobacillus plantarum fermentation on in-vitro protein and starch digestibilities of sorghum flour. *Food BioSci*. **2**:46–52

Price, M. L., Van Scoyoc, S. and Butler, L. G. (1978). A critical evaluation of the vanillin reaction as an assay for tannin in sorghum grain. *J. Agric. Food Chem.* **26**:1214–1218.

Prior, R. L. and Wu, X. (2006). Anthocyanins: structural characteristics that result in unique metabolic patterns and biological activities. *Free Radical Res.* **40**:1014–1028.

Ragaee, S., Abdel-Aal, E.-S. M. and Noaman, M. (2006). Antioxidant activity and nutrient composition of selected cereals for food use. *Food Chem.* **98**:32–38.

Rahman, I. E. A. and Osman, M. A. W. (2011). Effect of sorghum type (Sorghum bicolor) and traditional fermentation on tannins and phytic acid contents and trypsin inhibitor activity. *J. Food Agric. Environ.* **9**:163–166.

Raimi, O., Olaitan, S., Fajana, O. and Sanni, J. (2012). Effect of germination time on fat and protein contents, and α-amylase activity of Guinea Corn (*Sorghum vulgare*). *Pakistan J. Food Sci.* **22**:86–89.

Requena, T., Monagas, M., Pozo-Bayón, M. A., Martín-Álvarez, P. J., Bartolomé, B., del Campo, R., Ávila, M., Martínez-Cuesta, M. C., Peláez, C. and Moreno-Arribas, M. V. (2010). Perspectives of the potential implications of wine polyphenols on human oral and gut microbiota. *Trend Food Sci. Technol.* **21**:332–344.

Rooney, L. and Pflugfelder, R. (1986). Factors affecting starch digestibility with special emphasis on sorghum and corn. *J. Animal Sci.* **63**:1607–1623.

Sang, Y., Bean, S., Seib, P. A., Pedersen, J. and Shi, Y.-C. (2008). Structure and functional properties of sorghum starches differing in amylose content. *J. Agric. Food Chem.* **56**:6680–6685.

Saura-Calixto, F. (2010). Dietary Fiber as a Carrier of Dietary Antioxidants: An Essential Physiological Function. *J. Agric. Food Chem.* **59**:43–49.

Schober, T. J., Messerschmidt, M., Bean, S. R., Park, S.-H. and Arendt, E. K. (2005). Gluten-free bread from sorghum: quality differences among hybrids. *Cereal Chem. J.* **82**:394–404.

Schons, P. F., Ries, E. F., Battestin, V. and Macedo, G. A. (2011). Effect of enzymatic treatment on tannins and phytate in sorghum (*Sorghum bicolor*) and its nutritional study in rats. *Int. J. Food Sci. Technol.* **46**:1253–1258.

Scott, K. P., Duncan, S. H. and Flint, H. J. (2008). Dietary fibre and the gut microbiota. *Nutr. Bull.* **33**:201–211.

Selma, M. a. V., Espín, J. C. and Tomás-Barberán, F. A. (2009). Interaction between phenolics and gut microbiota: role in human health. *J. Agric. Food Chem.* **57**:6485–6501.

Serrano, J., Puupponen−Pimiä, R., Dauer, A., Aura, A. M. and Saura-Calixto, F. (2009). Tannins: current knowledge of food sources, intake, bioavailability and biological effects. *Mol. Nutr. Food Res.* **53**:310–329.

Sharma, S., Kelly, T. K. and Jones, P. A. (2010). Epigenetics in cancer. *Carcinogenesis* **31**:27–36.

Sharma, S. D., Meeran, S. M. and Katiyar, S. K. (2007). Dietary grape seed proanthocyanidins inhibit UVB-induced oxidative stress and activation of mitogen-activated protein kinases and nuclear factor-κB signaling in in vivo SKH-1 hairless mice. *Mol. Cancer Ther.* **6**:995–1005.

Shegro, A., Shargie, N., Biljon, A. and Labuschagne, M. (2012). Diversity in starch, protein and mineral composition of sorghum landrace accessions from Ethiopia. *J. Crop Sci. Biotechnol.* **15**:275–280.

Shewry, P. R. (2007). Improving the protein content and composition of cereal grain. *J. Cereal Sci.* **46**:239–250.

Shih, C.-H., Siu Ng, R., Wong, E., Chiu, L. C. M., Chu, I. K. and Lo, C. (2007). Quantitative analysis of anticancer 3-deoxyanthocyanidins in infected sorghum seedlings. *J. Agric. Food Chem.* **55**:254–259.

Shih, P.-H., Yeh, C.-T. and Yen, G.-C. (2007). Anthocyanins induce the activation of phase ii enzymes through the antioxidant response element pathway against oxidative stress-induced apoptosis. *J. Agric. Food Chem.* **55**:9427–9435.

Shim, T., Kim, T., Jang, K., Ko, J. and Kim, D. (2013). Toxicological evaluation and anti-inflammatory activity of a golden gelatinous sorghum bran extract. *Biosci. Biotechnol. Biochem.* **77**:697–705.

Silva, C. S. d., Queiroz, V. A. V., Simeone, M. L. F., Guimarães, C. d. C., Schaffert, R. E., Rodrigues, J. A. S. and Miguel, R. d. A. (2012). Teores de minerais em linhagens de sorgo para uso na alimentação humana. In XXIX Congresso Nacional de Milho e Sorgo, (pp.2776–2782). Água de Lindóia.

Singh, H., Sodhi, N. S. and Singh, N. (2010). Characterisation of starches separated from sorghum cultivars grown in India. *Food Chem.* **119**:95–100.

Singh, V., Moreau, R. A. and Hicks, K. B. (2003). Yield and phytosterol composition of oil extracted from grain sorghum and its wet-milled fractions. *Cereal Chem. J.* **80**:126–129.

Slavin, J. (2004). Whole grains and human health. *Nutr. Res. Rev.* **17**:99–110.

Spencer, J. P. and Crozier, A. (2012). Flavanoids and Related Compounds: Bioavailability and Function (Vol. 29): CRC Press, Boca Raton, FL, USA.

Suganyadevia, P., Saravanakumara, K. M. and Mohandasb, S. (2011a). Evaluation of antiproliferative activity of red sorghum bran anthocyanin on a human breast cancer cell line (MCF-7). *Int. J. Breast Cancer* **2011**:1–6.

Suganyadevia, P., Saravanakumara, K. M. and Mohandasb, S. (2011b). Identification of 3- deoxyanthocyanins from red sorghum (*Sorghum bicolor*) bran and its biological properties. *Afr. J. Pure Appl. Chem.* **5**:181–193.

Suganyadevia, P., Saravanakumara, K. M. and Mohandasb, S. (2013). The antiproliferative activity of 3-deoxyanthocyanins extracted from red sorghum (*Sorghum bicolor*) bran through P53-dependent and Bcl-2 gene expression in breast cancer cell line. *Life Sci.* **92**:379–382.

Svensson, L., Sekwati-Monang, B., Lutz, D. L., Schieber, A. and Gänzle, M. G. (2010). Phenolic acids and flavonoids in nonfermented and fermented red sorghum (*Sorghum bicolor* (L.) Moench). *J. Agric. Food Chem.* **58**:9214–9220.

Takabe, W., Matsukawa, N., Kodama, T., Tanaka, K. and Noguchi, N. (2006). Chemical structure–dependent gene expression of proteasome subunits via regulation of the antioxidant response element. *Free Radical Res.* **40**:21–30.

Taleon, V., Dykes, L., Rooney, W. L. and Rooney, L. W. (2012). Effect of genotype and environment on flavonoid concentration and profile of black sorghum grains. *J. Cereal Sci.* **56**:470–475.

Taylor, J., Bean, S. R., Ioerger, B. P. and Taylor, J. R. N. (2007). Preferential binding of sorghum tannins with γ-kafirin and the influence of tannin binding on kafirin digestibility and biodegradation. *J. Am. Coll. Nutr.* **46**:22–31.

Taylor, J. and Taylor, J. R. N. (2011). Protein biofortified sorghum: effect of processing into traditional African foods on their protein quality. *J. Agric. Food Chem.* **59**:2386–2392.

Taylor, J. R. N., Belton, P. S., Beta, T. and Duodu, K. G. (2014). Increasing the utilisation of sorghum, millets and pseudocereals: Developments in the science of their phenolic phytochemicals, biofortification and protein functionality. *J. Cereal Sci.* **59**:257–275.

Taylor, J. R. N. and Emmambux, M. (2010). Developments in our understanding of sorghum polysaccharides and their health benefits. *Cereal Chem.* **87**:263–271.

Towo, E., Matuschek, E. and Svanberg, U. (2006). Fermentation and enzyme treatment of tannin sorghum gruels: effects on phenolic compounds, phytate and in vitro accessible iron. *Food Chem.* **94**:369–376.

Tripathi, B., Chetana, and Platel, K. (2010). Fortification of sorghum (*Sorghum vulgare*) and pearl millet (*Pennisetum glaucum*) flour with zinc. *J. Trace Elem. Med. Biol.* **24**:257–262.

Tripathi, B. and Platel, K. (2013). Feasibility in fortification of sorghum (*Sorghum bicolor* L. Moench) and pearl millet *(Pennisetum glaucum*) flour with iron. *LWT—Food Sci. Technol.* **50**:220–225.

Tzounis, X., Rodriguez-Mateos, A., Vulevic, J., Gibson, G. R., Kwik-Uribe, C. and Spencer, J. P. (2011). Prebiotic evaluation of cocoa-derived flavanols in healthy humans by using a randomized, controlled, double-blind, crossover intervention study. *Am. J. Clin. Nutr.* **93**:62–72.

U.S. Department of Agriculture, A. R. S. (2012). USDA National Nutrient Database for Standard Reference (25th ed.). Washington, DC.

U.S. Grains Council. (2004). Sorghum Handbook: White Sorghum, the New Food Grain. U.S. Grains Council, Washington, DC.

Udachan, I. S., Sahu, A. K. and Hend, F. M. (2012). Extraction and characterization of sorghum (Sorghum bicolor L. Moench) starch. *Int. Food Res. J.* **19**:315–319.

Urpi-Sarda, M., Rothwell, J., Morand, C. and Manach, C. (2012). Bioavailability of flavanones. **In**: Flavanoids and Related Compounds: Bioavailability and Function, pp. 1–44. Spencer, J. P. E. and Crozier, A., Eds., CRC Press, London, U.K.

Wang, L., Weller, C. L., Schlegel, V. L., Carr, T. P. and Cuppett, S. L. (2007). Comparison of supercritical CO2 and hexane extraction of lipids from sorghum distillers grains. *Eur. J. Lipid Sci. Technol.* **109**:567–574.

Wang, L., Weller, C. L., Schlegel, V. L., Carr, T. P. and Cuppett, S. L. (2008). Supercritical CO_2 extraction of lipids from grain sorghum dried distillers grains with solubles. *Bioresource Technol.* **99**:1373–1382.

Waniska, R. D. and Rooney, L. W. (2000). Structure and chemistry of the sorghum caryopsis. **In**: Sorghum: Production, Agronomy, Chemistry and Utilization, pp. 649–688. Smith, W. and Frederiksen, R. A., eds., Wiley & Sons, New York.

Wedad, H. A., El Tinay, A. H., Mustafa, A. I. and Babiker, E. E. (2008). Effect of fermentation, malt-pretreatment and cooking on antinutritional factors and protein digestibility of sorghum cultivars. *Pakistan J. Nutr.* **7**:335–341.

Williamson, G. and Clifford, M. N. (2010). Colonic metabolites of berry polyphenols: the missing link to biological activity? *Br. J. Nutr.* **104**:48–66.

Wong, J. H., Lau, T., Cai, N., Singh, J., Pedersen, J. F., Vensel, W. H., Hurkman, W. J., Wilson, J. D., Lemaux, P. G. and Buchanan, B. B. (2009). Digestibility of protein and starch from sorghum (*Sorghum bicolor*) is linked to biochemical and structural features of grain endosperm. *J. Cereal Sci.* **49**:73–82.

Woo, H. J., Oh, I. T., Lee, J. Y., Jun, D. Y., Seu, M. C., Woo, K. S., Nam, M. H. and Kim, Y. H. (2012). Apigeninidin induces apoptosis through activation of Bak and Bax and subsequent mediation of mitochondrial damage in human promyelocytic leukemia HL-60 cells. *Process Biochem.* **47**:1861–1871.

Woodward, G., Kroon, P., Cassidy, A. and Kay, C. (2009). Anthocyanin stability and recovery: implications for the analysis of clinical and experimental samples. *J. Agric. Food Chem.* **57**:5271–5278.

Wu, X., Pittman, H. E., Mckay, S. and Prior, R. L. (2005). Aglycones and sugar moieties alter anthocyanin absorption and metabolism after berry consumption in weanling pigs. *J. Nutr.* **135**:2417–2424.

Wu, X. and Prior, R. L. (2005). Identification and characterization of anthocyanins by high-performance liquid chromatography—electrospray ionization—tandem mass spectrometry in common foods in the United States: vegetables, nuts, and grains. *J. Agric. Food Chem.* **53**:3101–3113.

Wu, Y., Li, X., Xiang, W., Zhu, C., Lin, Z., Wu, Y., Li, J., Pandravada, S., Ridder, D. D., Bai, G., Wang, M. L., Trick, H. N., Bean, S. R., Tuinstra, M. R., Tesso, T. T. and Yu, J. (2012). Presence of tannins in sorghum grains is conditioned by different natural alleles of Tannin1. *Proc. Natl. Acad. Sci. USA* **109**:10281–10286.

Wu, Y., Yuan, L., Guo, X., Holding, D. R. and Messing, J. (2013). Mutation in the seed storage protein kafirin creates a high-value food trait in sorghum. *Nature Commun.* **4**.

Yamagishi, S.-i. (2011). Role of advanced glycation end products (AGEs) and receptor for AGEs (RAGE) in vascular damage in diabetes. *Exp. Gerontol.* **46**:217–224.

Yang, L., Allred, K. F., Geera, B., Allred, C. D. and Awika, J. M. (2012). Sorghum phenolics demonstrate estrogenic action and Induce apoptosis in nonmalignant colonocytes. *Nutr. Cancer* **64**:419–427.

Yang, L., Browning, J. D. and Awika, J. M. (2009). Sorghum 3-deoxyanthocyanins possess strong phase II enzyme inducer activity and cancer cell growth inhibition properties. *J. Agric. Food Chem.* **57**:1797–1804.

Yang, M., I Koo, S., O Song, W. and K Chun, O. (2011). Food matrix affecting anthocyanin bioavailability: review. *Curr. Med. Chem.* **18**:291–300.

Ye, J.-C., Chang, W.-C., Hsieh, D. J.-Y. and Hsiao, M.-W. (2010). Extraction and analysis of β-sitosterol in herbal medicines. *J. Med. Plants Res.* **7**:522–527.

Zbasnik, R., Carr, T., Weller, C., Hwang, K. T., Wang, L., Cuppett, S. and Schlegel, V. (2009). Antiproliferation properties of grain sorghum dry distiller's grain lipids in caco. *J. Agric. Food Chem.* **57**:10435–10441.