2015

Sorghum: an underutilized cereal whole grain with the potential to assist in the prevention of chronic disease

Anita Stefoska-Needham
University of Wollongong, an442@uowmail.edu.au

Eleanor Beck
University of Wollongong, eleanor@uow.edu.au

Stuart K. Johnson
Curtin University

Linda C. Tapsell
University of Wollongong, ltapsell@uow.edu.au

Publication Details

Stefoska-Needham, A., Beck, E. J., Johnson, S. K. & Tapsell, L. C. (2015). Sorghum: an underutilized cereal whole grain with the potential to assist in the prevention of chronic disease. Food Reviews International, 31 (4), 401-437.

Sorghum: an underutilized cereal whole grain with the potential to assist in the prevention of chronic disease

Abstract

Sorghum is an important cereal grain food, grown globally, that is rich in nutrients, dietary fiber and bioactive components, yet is considered of low value to humans and often used as an animal feed. This review provides an overview of key sorghum grain components, including starches, dietary fiber, protein, lipids and phytochemicals, with functional properties that have potential to impact on health. While acknowledging the impact of the whole food will reflect the synergy between the components, studies of these components implicate effects on energy balance, glycemic control, lipids, gut microbiota and cell-mediated immune responses including anti-oxidant and anti-inflammatory effects. For these to be confirmed as contributory effects from sorghum consumption, evidence from quality randomized controlled trials is required. If proven effective, there may be a role for sorghum grain-based diets to assist in the prevention of chronic diseases such as diabetes, obesity and heart disease. Future research addressing effects of sorghum consumption may help drive a paradigm shift from sorghum as a low value food to a potentially health-promoting, highly-valued human grain food.

Disciplines

Medicine and Health Sciences | Social and Behavioral Sciences

Publication Details

Stefoska-Needham, A., Beck, E. J., Johnson, S. K. & Tapsell, L. C. (2015). Sorghum: an underutilized cereal whole grain with the potential to assist in the prevention of chronic disease. Food Reviews International, 31 (4), 401-437.

Sorghum: an underutilized cereal whole grain with the potential to assist in the prevention of chronic disease

Anita Stefoska-Needham, Eleanor J. Beck, Stuart K. Johnson, Linda C. Tapsell

Anita Stefoska-Needham, Eleanor J. Beck, Linda C. Tapsell
School of Medicine, Illawarra Health & Medical Research Institute, University of Wollongong, NSW Australia.
Stuart K. Johnson
Food Science and Technology Program, School of Public Health, Faculty of Health Sciences, International Institute of Agri-Food Security, Curtin University, Perth, Western Australia, Australia.

Corresponding author
Anita Stefoska-Needham
School of Medicine, Illawarra Health & Medical Research Institute, University of Wollongong, NSW 2522 Australia.
T: +61 458850088; an442@uowmail.edu.au

Abstract

Sorghum is an important cereal grain food, grown globally, that is rich in nutrients, dietary fiber and bioactive components, yet is considered of low value to humans and often used as an animal feed. This review provides an overview of key sorghum grain components, including starches, dietary fiber, protein, lipids and phytochemicals, with functional properties that have potential to impact on health. While acknowledging the impact of the whole food will reflect the synergy between the components, studies of these components implicate effects on energy balance, glycemic control, lipids, gut microbiota and cell-mediated immune responses including anti-oxidant and anti-inflammatory effects. For these to be confirmed as contributory effects from sorghum consumption, evidence from quality randomized controlled trials is required. If proven effective, there may be a role for sorghum grain–based diets to assist in the prevention of chronic diseases such as diabetes, obesity and heart disease. Future research addressing effects of sorghum consumption may help drive a paradigm shift from sorghum as a low value food to a potentially health-promoting, highly-valued human grain food.

Running head: Sorghum grain to assist in prevention of chronic disease
Key words: sorghum, whole grain, cereal, health, nutrition

INTRODUCTION

Cereal whole grains are significant contributors to energy, nutrients and dietary fiber in the human diet and are important for health. Numerous prospective studies demonstrate that regular consumption of whole grains lowers the risk of heart disease and diabetes by 20-30%,[1,2] improves blood glucose regulation,[3] achieves better weight management over time,[4,5] and lowers the risk of certain types of cancer.[6] A critical appraisal of the body of evidence is reflected in multiple national dietary guidelines that inform the community to eat more "grain foods particularly whole grain cereals" and to reduce consumption of refined grains.[2,7]

Sorghum (*Sorghum bicolor (L.) Moench*) is an example of a so-called ancient whole grain cereal that is better known to Western societies as an animal feed rather than a human food source. Sorghum is grown around the world, and ranks fifth in global cereal production after maize, rice, wheat and barley.[8] In many countries of Africa, Asia and Central America, sorghum is widely cultivated due to its adaptability to semi-arid and arid conditions and high temperatures. In these regions it is a major contributor to the staple diets of local populations.[9] In countries such as Australia and the United States, the primary use of sorghum has been as livestock feed and more recently in biofuel production.[9] Increasingly, the nutritional and agronomic advantages of sorghum, combined with a growing consumer movement dedicated to "healthy living", has peaked commercial interests in developed economies on how to make sorghum-based food products more accessible to consumers who remain largely unaware of their potential health benefits.

The starting point for exposing health benefits of foods is often their nutritional properties. In the case of sorghum, as with plant foods generally, the phytochemical component is of particular interest and this reflects recent developments in the nutritional sciences. The type of phytochemicals in some sorghum varieties have been purported to reduce the risk of certain types of cancer, cardiovascular disease, obesity and diabetes.[10] Sorghum also has decreased starch and protein digestibility *in vitro*, and is high in dietary fiber and resistant starch and this array of qualities may play a role in mechanisms that reduce disease risk (Table 1[10-17]). Not least, is the fact that sorghum is gluten-free and is suitable for people with coeliac disease and other intolerances.[18]

In a traditional nutrition sense, the value of sorghum grain has been considered to be slightly inferior compared to other cereal grains on the basis of lower protein and starch digestibility and consequently, reduced metabolizable energy. This consideration is especially relevant to many of the world's poorest and most food-insecure communities where sorghum is a core food. In these cases sorghum is combined with legumes and other cereals to increase macro- and micro- nutrient density of sorghum-based foods and diets,[19,20] and bio-fortified transgenic sorghum lines have been developed.[21] Paradoxically, these properties of lower digestibility and reduced available energy may prove to be better suited in populations where over-weight and obesity related chronic diseases, such as metabolic syndrome, diabetes, heart disease and cancer are major public health issues.[22]

Over the past decade, Awika and Rooney,[10] Dicko et al.[23] and Taylor and Emmambux[24] have exposed the potential role of sorghum in human health and in disease prevention. They have argued for a paradigm shift from perceiving sorghum as a low-value cereal grain to a health-promoting, environmentally sustainable food for inclusion in the global human diet. In order to achieve commercial adoption of this position, food innovation is required that would extend the range of sorghum-based products available to consumers. At the same time, quality human clinical trials are required to provide evidence of effects.

The research needs to be conducted in a food-health paradigm that considers not only the effects of individual grain constituents and their involvement in physiological processes, but also the effects of consuming sorghum-based foods within the broader context of whole diets. Because sorghum has been largely used as an animal feed in Western societies, much of the research has been done on livestock, but a wide range of studies have emerged that provide the basis for moving into human clinical studies. With this backdrop, the aims of this paper are to 1) provide a general overview of sorghum components and the related mechanisms of action which may impact on health 2) provide a narrative review of the scientific evidence for effects of sorghum consumption on health outcomes.

NUTRITIONAL AND CHEMICAL COMPOSITION OF THE SORGHUM GRAIN

Sorghum is a self-pollinating, summer plant belonging to the grass family of Poaceae. Sorghum grain is similar to maize with respect to chemical composition, with its key components being: starch, proteins, lipids, non-starch polysaccharides and phytochemicals such as phenolic compounds, phytosterols and policosanols. Sorghum grain also contains dietary fiber, including resistant starch, and micronutrients including vitamins and minerals, oil bodies and waxes.

The proximate nutritional composition of sorghum whole grain is similar to wheat whole grain; energy density is 1377 *vs* 1418 kJ/100 g dry weight, total carbohydrate 74.6 *vs* 71.1, fat 3.3 *vs* 2.5 and protein 11.3 *vs* 13.7 g/100 g dry weight, respectively (Table 2[25,26]). However, sorghum has lower starch digestibility relative to other grains such as maize, rice, wheat and barley, although the degree of digestibility depends on the method of processing.[11,27] The nutritional quality of sorghum proteins is diminished because they are more resistant to digestion[27] and have low levels of essential amino acids such as lysine, tryptophan and threonine.[28] In contrast, there are high levels of leucine that were previously implicated, but now not accepted, as a cause of niacin deficiency and consequently endemic pellagra in some sorghum-eating populations.[29-32]

As with cereals more broadly, sorghum is a source of B-complex vitamins (such as thiamin, riboflavin, vitamin B6, biotin, and niacin) that are diminished with grain refining processes including decortication.[33] The mineral composition in sorghum is similar to millet, higher compared to maize but lower than wheat, and is predominantly composed of potassium and phosphorus (Table 2).[34] Sorghum-based foods are a good source of both iron and zinc, although anti-nutrients such as phytates may diminish bioavailability,[35,36] a problem not unique to sorghum but common to other grains and plant foods in general. A complete nutrient analysis of sorghum is detailed in Table 2.

COMPONENTS OF SORGHUM WITH POTENTIAL FOR FUNCTIONAL PROPERTIES

Starches

Sorghum grain is a good source of starch, containing approximately 71% of dry whole grain weight.[26] The starch is encapsulated in granules that are located predominantly in the endosperm (storage tissue), though uniquely some are present in the pericarp (outer layer of grain).[26] Sorghum starch is comprised of both amylose and amylopectin polysaccharides (branched polymers of glucose) with very low percentages of amylose present in the starch of waxy sorghum varieties compared to 24-33% in non-waxy sorghum starch.[24] Sorghum starch granules are enmeshed in a strong protein matrix in the endosperm[1], a unique structural aspect of sorghum grain.(27) Disulphide-bond cross-linking involving kafirins in the protein matrix forms a protective network around the starch granules reducing starch digestibility.(12)

The lower starch digestibility reported for sorghum foods is not an intrinsic property of the sorghum starch granules themselves, but appears mainly to be a consequence of the interactions of the starch with the endosperm protein matrix, as well as with cell wall material and polyphenolic compounds, such as condensed tannins and flavonoids.(37-41) These interactions inhibit carbohydrate-hydrolyzing enzymes, such as α-glucosidase and α-amylase, thereby lowering starch digestibility.(42) The presence of the protein matrix has also been associated with reduced starch gelatinization during cooking resulting in partially-gelatinized sorghum starch granules that may resist enzymatic degradation *in vivo*.(27) Sorghum starch has amongst the highest gelatinization temperatures, ranging from 66-81 °C, depending upon cultivars, and is higher than that of maize, wheat and barley.(24,43) However, the extent of gelatanization of starch granules as a result of processing cannot easily predict *in vivo* digestibility and physiological effects such as glycemic responses. Factors such as the precise ratios of amylose to amylopectin, their arrangement within the starch granule, further degradation of other polymer molecules and post-processing conditions also influence the postprandial effects of a starchy food.(44)

Recent publications report on the *in vitro* starch digestibility of different sorghum foods, including sorghum-refined maize snack-like extrudates,(45) wholegrain sorghum-refined wheat flour flat bread(46) and wholegrain sorghum-durum semolina pasta.(14) These *in vitro* studies confirm that sorghum foods can be formulated and processed to deliver slowly digested starch

---

[1] Sorghum starch granules are densely packed in the *corneous endosperm* but exist in a more open structure in the *floury endosperm* of the grain caryopsis.

(SDS), with the potential to assist in improving blood glucose control, however these predicted positive results require rigorous testing in humans.

Resistant Starch and Non-Starch Polysaccharides

Sorghum foods also contain varying amounts of resistant starch (RS) depending on factors such as processing, cooking, cooling, food storage, gelatinization, and cultivar.(14,15,40,46) Physiologically, RS resists hydrolysis by enzymatic digestion in the small intestine(47) and enters the colon where it is partially or completely fermented to produce beneficial short-chain fatty acids (SCFA).(48) Here, the RS can act as a prebiotic(49,50) by stimulating the proliferation of beneficial bacteria already in residence in the gastrointestinal tract (GIT). To date these effects have not been widely researched with respect to sorghum foods and sorghum-based diets.

Non-starch polysaccharides (NSPs) have been associated with lower blood plasma cholesterol levels, reduced small intestine transit time, and improved bowel function.(51,52) NSPs are the major component of dietary fiber in sorghum grain and are mainly located in the pericarp and endosperm cell walls, constituting 2-7% of the total weight of the grain depending upon cultivar.(13,53) Sorghum NSPs are both cellulose and non-cellulosic consisting of arabinose, xylose, mannose, galactose, glucose, and uronic acid monomers.(24,54) The non-cellulosic polysaccharides are primarily water-insoluble glucuronoarabinoxylans (GAX) along with β-glucans,(55) although naturally occurring β-glucans in sorghum are lower than that of barley and oats.(15,56) The GAX in sorghum are very abundant and are highly substituted with glucoronic acid residues, and acetyl and feruloyl compounds. Sorghum contains other non-carbohydrate cell-wall components that form part of the dietary fiber fraction such as lignins, at levels up to 20% of the total cell wall contents by dry weight.(57) The total dietary fiber content of different sorghum cultivars ranges from 7.6% in low-tannin sorghums to 9.2% in high tannin varieties,[13] and its level in sorghum-based meals can be manipulated by cooking and fermentation.[58] The effect of consumption of sorghum NSPs has not been investigated in humans.

Proteins

Protein is the second largest constituent of sorghum grain (6-18%) after starch.[59] Sorghum endosperm proteins are found in both a matrix and as protein bodies that are enveloped by the matrix. Sorghum proteins are classified as albumins, globulins, kafirins, cross-linked kafirins and glutelins.[60] Of these, kafirins are the main protein,[61] comprising 50-70% of total protein content.[27] The kafirins are prolamin storage proteins with limiting levels of some amino acids, in particular lysine,[62] a disadvantage not unique among cereal grains. The kafirins differ in structure from the gliadin and glutenin storage proteins in wheat. They do not elicit damage to the mucosa of the small intestine of people with coeliac disease,[18] making sorghum a viable ingredient for gluten-free foods such as bread. However, the inability of sorghum kafirins to make elastic dough and the difficulty in making bread of high consumer acceptability presents challenges and has driven research into the manufacture of quality sorghum-based gluten-free food products.[46,63]

Sorghum kafirins are poorly digested due to the formation of cross-linking especially when moist cooked, resulting in protease resistance.[27] *In vitro* and animal studies have also shown that sorghum protein digestibility may be reduced by other protein-protein, protein-phenol and carbohydrate-phenol complexes that have been identified.[54,64-66] Cornu and Delpeuch[67] reported that the nitrogen digestibility in humans on a diet of 80% sorghum decreased from 65.4% to 60.5% when the decorticated sorghum in the diet was replaced by whole grain sorghum, suggesting that higher fiber sorghum varieties may have lower protein digestibility. Rather than a fiber effect per se, this more likely relates to the higher polyphenol content that naturally occurs in whole grain sorghum and the resultant binding of phenols to dietary protein.(54) In sorghum-consuming communities, where protein malnutrition is an issue, efforts to increase protein digestibility are imperative and lactic acid fermentation, decortication and extrusion have been shown to improve digestibility and consequent amino acid availability.(45,66,68)

Sorghum grain also contains a broad range of bioactive peptides, recently reviewed by Lin et al.(69) These are of current interest to researchers due to their potential biological role in human physiological processes including pathogenesis. The peptide bioactivities include antioxidant, antihypertensive, anticancer, antimicrobial, and opioid activities as well as immunomodulatory and cholesterol-lowering effects. The specific bioactive peptides isolated in sorghum include but are not limited to: amylase inhibitors,(70) protease inhibitors,(71) cationic peroxidase,(72) 2-kDa antiviral peptide(73) and xylanase inhibitors.(69) To date, research linking cereal grains with potential bioactive peptide activity has been limited, however there are more sorghum studies appearing in the literature.(69,74) Overall, there is much to consider in translating this knowledge to human clinical trials, in particular the study populations of interest and the health/disease outcomes that might be researched.

Lipids

Sorghum grain contains approximately 3-4% lipids, the majority of which are neutral triglycerides, rich in unsaturated fatty acids and mostly present in the germ.(16)

The predominant fatty acids are oleic acid (31.1–48.9%), linoleic acids (27.6–50.7%), linolenic acid (1.7–3.9%), stearic acid (1.1–2.6%), palmitic acid (11.7–20.2%) and palmitoleic acid (0.4–0.6%).[26,75,76] Two less common saturated fatty acids, octanedioic (C8:0) and azelaic acid (C9:0), have been identified in some sorghum varieties.[75] This lipid composition has generated interest in sorghum as a source of edible oil, representing a potentially valuable dietary source of monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA), with higher PUFA levels than MUFA.[75] This desirable lipid composition is conducive to mechanisms that lower lipid levels in humans and therefore to potentially lower risk factors associated with heart disease.

Based on research in hamsters, Carr et al.[77] suggested that the primary cholesterol-lowering mechanism of sorghum lipid extracts appears to be a reduction in cholesterol absorption with a concomitant increase in fecal sterol excretion. Specifically, policosanols (a mixture of long-chained primary alcohols) in the sorghum lipid extracts appear to inhibit endogenous cholesterol synthesis.[77] Sorghum also contains plant sterols that may reduce cholesterol absorption to collectively lower plasma and liver cholesterol concentrations.[77] These results were recently supported by Lee et al.[78] in a hamster model of hypercholesterolemia, investigating the effects of whole kernel grain sorghum oil (rich in plant sterols) and wax (high in policosanols). The authors report that the sorghum oil played a more significant role in modulating cholesterol, most likely by inhibiting absorption, however subtle interactions by the wax may have contributed to the effect.[78]

The policosanols in sorghum wax (found on the surface of the grain kernel) are comprised of mainly docosanol (C22), tetracosanol (C24), hexacosanol (C26), octacosanol (C28), triacontanol (C30), and dotriacontanol (C32).[79] In sorghum, C28 and C30 are the most abundant policosanols.[17] A mixture of C28 and C30 from sugar cane wax has been shown to improve blood lipid levels,[80] however reports on the human effects of sorghum-derived policosanols have not been published to date.

An alternative mechanism for the cholesterol lowering effect of sorghum lipid extract was reported by Martinez et al.[81] from research done with hamsters. They reported that sorghum lipid extract acts as a "prebiotic" to improve the host cholesterol metabolism through effects on gut microbiota. *Bifidobacteria* significantly increased in the hamsters fed grain sorghum lipid extract and was positively associated with HDL plasma cholesterol levels.[81] In humans, this shift in *bifidobacteria* is associated with improved overall health, including reduced gut infections and suppression of colon cancer initiation.[82-84]

Finally, sorghum lipids may also possess antiproliferation properties. Zbasnik et al.[85] extracted lipids from sorghum dry distiller's grain (a by-product of the ethanol industry) and observed an anti-proliferative effect on human colon carcinoma cells. They suggested that the effect may have been a result of synergistic interactions of vitamin E (predominantly gamma-tocopherol), triacylglycerides, free fatty acids (predominantly linoleic acid), policosanols, aldehydes, and sterols (predominantly campesterol and stigmasterol) that were identified in the extracts.[85] Although sorghum dry distiller's grain is primarily used for animal feed, it is chemically and microbiologically safe as a human food ingredient, therefore further research in humans is relevant.

Phytochemicals

Most sorghum varieties, except white sorghums, have a high concentration of phytochemicals, particularly phenolic compounds, which exhibit high antioxidant activity and are linked to health benefits.[10,86,87] In fact, bran of some sorghum grain varieties reportedly has the highest antioxidant activity of all cereal crop fractions, even higher than many fruits and vegetables.[10] Specifically, sorghum bran has up to two orders of magnitude higher antioxidant activity than oat bran and wheat cereal, and an order of magnitude higher than rice bran although the precise amount is highly dependent on the variety of sorghum (Figure 1[10,25]).

Phenolic compounds The phenolic compounds in some sorghum grain varieties are more abundant and diverse than in any other cereal grain.[88] Sorghum grain varieties that have a pigmented testa and thick pericarps have the highest levels.[89] The phenolic compounds are concentrated in the bran component of the grain (in particular the testa and pericarp) and can be categorized into three main groups; 1) phenolic acids (hydrobenzoic acids and hydrocinnamic acids), 2) monomeric polyphenolic flavonoids (flavanols, flavanones, flavones, flavan-4-ols and anthocyanins), and 3) polymeric polyphenolic condensed tannins (also known as proanthocyanidins or procyanidins).

The phenolic compounds in sorghum grain exhibit high antioxidant activity through their ability to scavenge free radicals.[88] The degree of antioxidant activity is correlated to the content of phenolic compounds in a specific sorghum cultivar and this in turn is influenced by its genotype and growing environment.[89] Levels of phenolic compounds and the activity of enzymes which synthesize or catabolize phenols in sorghum grain, strongly influence food product properties such as flavor and color, and are therefore important determinants of sorghum for food use.[23] In general, sorghum processing decreases antioxidant activity mainly as a result of reducing levels of measurable phenolic compounds.[90-92] This may be as a result of thermal degradation or lowered extractability during the analytical procedures used for their measurement.[91] However, some processes including steeping, germination, fermentation[93] and roasting of steamed grain[94] have been reported to increase the level of polyphenolics.

These may be related to improved extractability through breakdown of the food matrix which might also result in higher bioavailability.

It has been postulated that sorghum grain phytochemicals may provide overall disease protection *in vivo* through not only antioxidative but also hypoglycemic, and hypolipidemic mechanisms.(95,96) However, the extent of these health beneficial effects is unclear since only limited clinical research has been reported. Reduction in oxidative stress is implicated in these protective processes,(97) therefore sorghum polyphenolic compounds may be relevant in disrupting the cascade of pathophysiological changes that lead to metabolic disease. *In vitro*, sorghum bran extracts with a high phenolic content and thus high antioxidant properties were shown to inhibit albumin glycation, whereas wheat, rice, oat and low-phenolic sorghum bran extracts (such as white sorghum) did not.(98) Albumin glycation is the non-enzymatic process that results in formation of advanced glycation end-products (AGEs). AGEs have been associated with metabolic diseases such as diabetes and atherosclerosis. Human clinical investigations are warranted to further test these effects *in vivo*, especially since sorghum bran extracts have been suggested for use in food ingredients, food supplements or nutraceutical products.

Flavonoids The anthocyanin flavonoids found in pigmented sorghums, but not in white sorghums, are of particular interest to researchers since some are unique to sorghum grain and they have potent antioxidant properties.(99) The 3-deoxyanthocyanins (3-DA and derivatives) are the major class of flavonoid and are located in the pericarp.(88,100) 3-DAs lack the hydroxyl group in the 3-position of the C-ring and include the apigenidin and luteolinidin that are largely responsible for the pigmentation of certain sorghum grain varieties, namely red and black sorghums.(101) A recent *in vitro* analysis of red sorghum flour extracts showed strong free radical scavenging activity as measured by an oxygen radical absorbance capacity (ORAC) assay and protection against LDL-oxidation, contributing to the evidence base for the potential of red sorghum as a valuable health-promoting food grain.[102] However, understanding the bioavailability of sorghum anthocyanins for the putative health-promoting effects in humans is a much-needed focus of future research.

In-vitro research investigating effects of specific sorghum anthocyanins is emerging. A study utilizing the human epithelial larynx carcinoma cell line (Hep-2) by Devi et al.[103] demonstrated that anthocyanins extracted from red sorghum bran, specifically luteolinidin and apigenindin, induced significant anti-proliferative activity. Powerful anti-proliferative effects were also observed against colon cancer cells when black, red, and white sorghum extracts, rich in 3-DA were tested.[104,105] Yang et al.[106] proposed that these protective effects result from estrogen-induced apoptosis of the non-malignant colonocytes that were strongly influenced by the flavones, apigenin and luteolin. In breast cancer cell lines, 3-DA isolated from red sorghum bran have been shown to have strong anti-proliferative properties and to be cytotoxic.[107] Sorghum chloroform extracts have particularly strong anti-inflammatory effects *in vitro* (in both cell-free and cell-mediated experimental systems) through almost complete suppression of lipopolysaccharide-mediated production of nitric oxide, tumor-necrosis factor-α, and interleukin-6. These effects are correlated to flavonoid concentration in the extracts.[108]

Tannins Tannin sorghums contain high molecular weight *condensed tannins* that are oligomers or polymers composed of flavan-3-ol nuclei, found in the pigmented testa of the sorghum grain.[109] Condensed tannins exhibit strong antioxidant activity *in vitro* via free radical scavenging activity, chelation of transition metals and inhibition of pro-oxidative enzymes. The antioxidant activity of sorghum tannins is higher than that of tannins extracted from any other crop.[88,99,110] In animal studies, sorghum tannins have been shown to be 15-30 fold more effective at quenching peroxyl radicals than simple phenolics.[111]

The presence of tannins in sorghum grain may reduce the nutritive value and lower metabolizable energy of the grain. Several mechanisms have been proposed to explain this "anti-nutritional" effect as reviewed by Awika and Rooney.[10] These include: binding of proteins and carbohydrates into insoluble complexes that resist digestive enzyme breakdown;[112-115] binding of digestive enzymes directly, inhibiting their enzymatic activity;[116,117] and inhibition of intestinal brush border bound amino acid transporters,[118] particularly by tannin sorghums with higher degrees of polymerization,[119] resulting in reduced digestive enzyme activity. These effects were also reflected in animal feeding trials that demonstrated the feeding efficiency of tannin sorghums was 5 to 10% lower than non-tannin sorghums, depending on the animal species, the method of grain processing and diet type. In general, animals consumed more feed yet experienced the same or slightly less weight gain when tannin sorghum formed the basis of their diets.[116,117,120] Such effects in a Western diet, where food is ubiquitous, may be beneficial if these results are to be translatable to humans.

Antioxidant tannins may be key protective components in sorghum foods for the mitigation of oxidative stress-induced diseases, with anti-proliferative and anti-inflammatory effects as their key mechanisms of action. For example, brans from tannin sorghum varieties (naturally high in tannins, such as brown sorghum) and non-tannin sorghum varieties (black, red and white-grained) have demonstrated significant anti-inflammatory potential *in-vitro* on the basis of strong inhibition of hyaluronidase activity (enzymes involved in cancer metastasis, osteoarthritis and skin aging).[121] The inhibition of the hyaluronidases correlated positively with total phenolic content and antioxidant capacity of the extracts, with greater effects observed in sorghum bran extracts than those of wheat and rice bran. In two experimental inflammatory systems using blood cells and a mouse-model, Burdette et al.[122] also demonstrated that the anti-inflammatory activity of ethanolic extracts of different sorghum brans correlated with their phenolic content and antioxidant activity. At present, it is not possible to extrapolate these *in vitro* effects to *in vivo* effects after realistic consumption of sorghum by humans. However, the research provides mechanistic models for further investigation.

Grimmer et al.[123] demonstrated the potent anti-mutagenic activity of higher molecular weight compared to lower molecular weight tannins isolated in sorghum-derived polyphenol extracts. Gomez-Cordoves et al.[124] also demonstrated that sorghum tannins induce anti-carcinogenic effects against human melanoma cells *in vitro* through increased melanogenic activity (a protective effect against UV irradiation damage to human skin) and therefore reduced formation of human melanoma cells. Collectively, these cell line studies demonstrate the bioactive potency of sorghum grain constituents, in particular the tannins, although *in vivo* studies have not occurred.

EXPERIMENTAL RESEARCH ON SORGHUM CONSUMPTION

Despite the diversity of bioactive components in sorghum, human studies investigating specific effects of sorghum consumption on protective health benefits are severely limited. Although numerous studies have been conducted with human subjects (Table 3[19,29,35,58,67,125-153]), the majority have addressed micronutrient metabolism (such as interactions between leucine, molybdenum, and niacin),[129] iron absorption from cereals,[35] dietary fiber effects,[140] protein digestibility[144] and oral rehydration therapies.[148] This review therefore summarizes the experimental evidence that suggests protective health effects of sorghum consumption, targeting studies that investigate effects on energy balance, glycemic control, lipids, oxidative stress and cell-mediated responses.

Effects on energy balance

Sorghum may be a valuable lower-calorie grain alternative in Western diets where overweight and obesity rates continue to rise and represent major public health burdens.[22] Sorghum's energy value is approximately 1377 kJ/100 g however the available energy for human metabolism may be lower than this estimate due to the described low starch and protein digestibility rates. This postulation is partly based on evidence from numerous feeding studies that show animals (from rodents to livestock species) fed whole grain sorghum, in particular the slowly digested high tannin sorghum varieties, have reduced weight gain.[116,117,120,154,155]

In general, dietary fiber and whole grain intakes have been associated with reduced risks of obesity, overweight and with lowered waist-to-hip ratio.[156,157] Effects of dietary fiber on appetite and satiety have been proposed as major mechanisms for these reductions. Whole grain sorghum, with high fiber and slowly digestible starches, may increase satiety in humans due in part, to effects on glycemic index of foods. It is believed that many communities in Africa who prefer to eat foods made from tannin sorghums do so because they impart stronger feelings of satiety and satiation compared to other cereals.[10] Sorghum's satiety effects in humans have not yet been investigated through controlled dietary trials.

Sorghum contains resistant starch (RS) and fermentation of RS in the colon is linked to a number of positive effects including those on the gut microbiome.[50,158] Studies specific to energy control with sorghum intake are limited however a recent study by Shen et al.,[159] evaluated the effects of sorghum RS on changes to body weight, blood lipids and intestinal flora in 60 overweight and obese rats receiving treatment for 8 weeks. Results demonstrated that overweight rats fed a high-fat diet containing 30% sorghum RS gained less weight than rats fed a comparator diet devoid of sorghum RS ($p<0.05$). However, there was no significant difference ($p>0.05$) in weight measures in the obese rats who were administered the same test diets. Thus sorghum RS did not overcome weight gain caused by high fat diets, but it did have an ameliorating effect. Significant changes ($p<0.05$) to the synthesis and secretion of serum leptin and adiponectin, two adipose-derived hormones that are involved in the regulation of food intake and body weight, were also reported in the sorghum RS groups, as were improvements to the intestinal flora ($p<0.05$) (as measured by increased populations of *Bifidobacterium* and *Lactobacillus* and reduced populations of *Enterobacteriaceae*). This is an important study that demonstrates mechanisms by which sorghum RS may assist in the prevention and treatment of obesity. The study also identified positive lipid changes. Triglycerides, total cholesterol and LDL-cholesterol in both the overweight and obese rats consuming sorghum RS-enriched diets were significantly lower than the control groups ($p<0.05$). HDL-cholesterol levels were significantly higher in the sorghum RS groups ($p<0.05$). It remains to be seen whether these effects can be translated to the human condition. At this stage, the human studies demonstrate only possible mechanisms but the positive results in animal models identify that whole grain sorghum may be useful in managing energy balance to assist with control of over-weight and obesity.

Effects on glycemic control

Sorghum foods have demonstrated slow starch digestibility *in vitro* and in animal feeding trials, suggesting favorable effects on post-prandial glycemic and insulinemic responses in humans. Numerous animal feeding studies have shown that sorghum in the diet effectively improves glucose metabolism compared to sorghum-free diets.[111,160-162] A limitation in some of these studies is that the specific type of sorghum extract is not defined, thus it cannot be determined whether effects are linked to phenolic, fiber or macronutrient contents. Furthermore, whether the concentrations of sorghum extracts are physiologically relevant, that is, capable of eliciting these blood glucose attenuation effects in humans after a realistic dose, is not yet clear.

A recent study by Cervantes-Pahm et al.(163) reported on the use of a pig model to investigate the comparative nutrient and energy digestibility of a range of grains widely used for human consumption, including wholegrain sorghum. In this study, the apparent ileal digestibility of sorghum starch was lower than for corn.(163) The authors attributed this to the high level of resistant starch in sorghum, which appeared to be fully fermented in the pig hindgut since ~100% starch disappearance was reported. The low apparent ileal digestibility of its starch in pigs suggests that sorghum may be of value for reducing the glycemic index of human foods.(163) Caution in extrapolating these pig trials to human health is needed, since in this study raw grains were used, whereas in human food the grains are invariably cooked, changing the structure and digestion properties of the starch.

Dixit et al.(164) have even gone as far as to specifically recommend sorghum grain is regularly consumed in the modern Indian diet to assist in the reduction of Type 2 diabetes and cardiovascular disease in this population. Despite the positive recommendation, only four *in vivo* human studies exploring these effects have been reported in the literature, each with limitations and inconsistencies.(135-138) The most recent of these human studies investigated the effects of consuming muffins made from grain sorghum on plasma glucose and insulin levels.(138) In a randomized-crossover design, 10 male subjects consumed muffins containing 50 g of total starch (TS) from either grain sorghum flour or whole wheat flour (although the available carbohydrate was not reported), with all additional ingredients the same across both treatments. Glucose and insulin levels were measured at baseline (15 minutes prior to consumption), time-point 0 (onset of consumption) and 15, 30, 45, 60, 75, 90, 120, and 180 minutes after consumption. Additionally, levels of rapidly digestible starch (RDS), SDS, RS and TS in muffins were analyzed. Results indicated that RDS, SDS and RS contents were significantly higher in sorghum muffins compared to wheat muffins ($p<0.05$). Plasma glucose incremental area under the curve (iAUC) reduced by ~26% and glucose measures at the 45 to 120 minute intervals were significantly lower for the sorghum muffin ($p<0.05$). Also, plasma insulin iAUC reduced significantly and insulin measures at the 15 to 90 minute intervals were significantly lower for the sorghum muffins ($p<0.05$), reducing by ~55%. Lack of information on the available carbohydrate in each test muffin is a limitation but this study shows the potential of sorghum-based foods to attenuate blood glucose and insulin responses.

In a similar study, Lakshmi and Vimala[(136)] also demonstrated that the consumption of whole grain sorghum meals compared with consumption of the same meals based on dehulled sorghum and other recipes prepared with wheat and rice (as controls), resulted in significantly lower glycemic responses ($P<0.05$) in 6 subjects with Type 2 diabetes mellitus.[(136)] These observations may have been in part due to the difference in fiber content of the meals that ranged from 2.2 g to 4.8 g in whole grain sorghum treatment meals and 1.8 g to 2.7 g in dehulled sorghum treatment meals. Also, the different cooking methods utilized in the treatment meal recipes (pan-fried, boiled, fermented-steamed) may have had an effect on starch digestibility and therefore carbohydrate metabolism.

Further glucose control studies by Mani et al.[(135)] evaluated the glycemic index (GI) of six traditional Indian meals, one of which was based on sorghum. The test meals were consumed as baked bread (prepared from flours of sorghum or finger millet or pearl millet) or as pressure-cooked meals (based on kodo millet, consumed as is or with added whole mung beans or with added mung bean dal). No fats were added in the preparation of the test meals. Testing was undertaken in 36 subjects with Type 2 diabetes mellitus. Glucose responses were measured one and two hours after consumption of the test foods (50 g available carbohydrate) and compared to a 50 g glucose load. The mean GI of the sorghum bread was relatively high at 77% +/- 8 (SE), but not as high as the finger millett bread which had a GI of 104% +/- 13 (SE), equivalent to the glucose load . The pearl millet bread had the lowest GI of all six test meals, producing a GI of 55% +/- 13 (SE). No significant difference was observed in blood glucose level after each of the test foods at the 1 hour and 2 hour time-points when compared with the corresponding blood glucose response to the 50 g glucose load. The study identifies sorghum's digestibility in this meal format (baked bread) may not be as slow as *in-vitro* studies may suggest.

Abdelgadir et al.[(137)] investigated the influence of six traditional Sudanese carbohydrate-rich meals (prepared from wheat, sorghum, millet and maize flours) on glucose and insulin responses in a randomized crossover design with 10 subjects with Type 2 diabetes mellitus (6 males and 4 females). Millet porridge had the most favorable (lowest) post-prandial glucose and insulin responses followed by wheat pancakes, then sorghum porridge and sorghum flat bread, whereas maize porridge induced higher glucose and insulin responses (as measured by mean incremental AUCs). Consideration of the method and time of preparation, particularly the duration of fermentation and the degree of milling, as well as the nature of starch and fiber content is important when interpreting these findings. That is, inadequate reporting of the precise physico-chemical properties of the final products limits generalizability in food studies. Overall, the glucose and insulin response studies using sorghum in humans have used small sample sizes with ambiguous results.

Effects on serum lipids

Mechanisms for the role of sorghum grain components in cardiovascular protection have been investigated.[10] Only one study has been conducted with human subjects (10 males and 6 females) to investigate the effects of consuming sorghum foods on serum lipid levels as an indicator of cardiovascular disease risk.[134] In this study, a significant reduction ($p<0.05$) in total cholesterol, triglycerides and HDL cholesterol was observed after daily consumption of 100 g of unrefined sorghum in the form of pancakes over 3 weeks. However, the content of subjects' background diets was not adequately reported, making assessment of dietary confounders difficult.

Most of the research identifying beneficial effects of sorghum consumption still lies with animal models.[111,159,161,165-167] Klopfenstein et al.[168] concluded that sorghum bran was effective in lowering serum and liver cholesterol levels in hamsters. This effect was repeated in another hamster model of hypercholesterolemia, when grain sorghum lipid extract included in the diet significantly reduced plasma non-HDL and liver esterified cholesterol levels while increasing HDL levels.[77] In all these studies, total cholesterol levels were reduced in animals consuming sorghum-based diets compared to sorghum-free control diets. In a single negative finding, Lee et al.[169] found that while sorghum consumption increased HDL-cholesterol levels, total cholesterol and LDL-cholesterol levels were increased in a rat model. However, the lack of a control group in this research makes conclusions difficult.

Sorghum tannins have not been broadly investigated in relation to their effects on cardiovascular disease risk factors, unlike tannins from some other foods and beverages such as red wine and tea. There may be an anticoagulant effect of sorghum tannins, yet to be tested in humans, as evidenced in cultured mullet fish that were fed tannin-containing sorghum distillery residues.[170] The sorghum residue significantly improved blood thinning and erythrocyte membrane integrity of the fish blood cells in cooler water temperatures over the winter months, enabling normal blood viscosity and prevention of red blood cell hemolysis induced by typical oxidation processes. The authors suggest that the antioxidant activity of the tannins and polyphenols present in the sorghum residue contributed to the prevention of red blood cell hemolysis. A translation to humans studies has yet to be conducted.

Effects on oxidative stress biomarkers and plasma antioxidant capacity

A randomized, controlled, crossover human study, involving 22 healthy adults, was conducted to assess the acute effects of consuming pasta containing red or white wholegrain sorghum flour (30% sorghum, 70% semolina) on plasma total polyphenols, antioxidant capacity and oxidative stress markers compared to a wheat control made from 100% semolina.[139] Compared to baseline, the 2 hour post-prandial levels of plasma polyphenols, antioxidant capacity and superoxide dismutase (SOD) activity were significantly ($P<0.001$) higher following the red sorghum pasta (RSP) meal while the protein carbonyl level was significantly lower ($P=0.035$). Furthermore, net changes in polyphenols, antioxidant capacity and SOD activity were significantly ($P<0.001$) higher while protein carbonyls were significantly ($P=0.035$) lower following consumption of the RSP meal than the control meal. Pasta containing red wholegrain sorghum flour, but not white sorghum flour, enhanced antioxidant status and improved markers of oxidative stress in healthy subjects. The increase in plasma polyphenols by the RSP meal may be attributed to its higher content of polyphenols. The potential limitations of this study include the short duration and use of only one postprandial blood collection. Furthermore, subjects in this study were healthy and their results may differ to people with oxidative-stress induced disease such as diabetes and obesity. Studies in subjects with mild to moderate oxidative-stress induced disease and who consume a sorghum-enriched diet daily over an extended period of time are required to further investigate potential antioxidant effects of sorghum consumption.

Effects on cell-mediated immune responses

Cell mediated immune responses have been linked to cancer development. Epidemiological evidence dating back to the early 1980s has correlated consumption of sorghum with reduced incidence of esophageal cancer, warranting closer attention to the potential chemopreventive properties of sorghum chemical components. Data from various sorghum-consuming countries in Africa and Asia has demonstrated lower esophageal cancer incidences compared to regions where wheat and maize were the major cereals consumed.[171-174] However, contamination of maize in these communities by the *Fusarium* fungi, which convert nitrates to nitrites, known carcinogens, has been identified as a more likely cause of increased rates with maize consumption. Nevertheless, such epidemiological observations have driven research efforts towards understanding potential cell-mediated chemopreventive properties of sorghum grain components and their mechanisms of action not just against esophageal cancer, but other cancers of the gastrointestinal tract and beyond. Currently research is in its infancy, with growing numbers of cancer cell line studies exploring anti-inflammatory, anti-mutagenic and anti-proliferative effects that are important in prevention of carcinogenesis. Some animal studies have also shown that phenolic extracts derived from sorghum, on the basis of high antioxidant activity particularly from red, black and tannin sorghum varieties, have been able to effectively induce cell arrest and suppress tumor growth in vivo.[175,176] Many more *in vitro* and animal studies are required before antioxidant effects of sorghum extract, aimed at cancer prevention and treatment can be justified in clinical trials. The role of sorghum consumption in cancer prevention is more likely to be examined in epidemiological studies with mechanistic studies contributing to the discussion on the plausibility of findings.

Future Research Directions

A possible role for sorghum in prevention and treatment of metabolic disease requires greater investigation. Initial research would investigate acute responses such as blood glucose, insulin and appetite responses to sorghum consumption. *In vitro* inhibition of glucose release by sorghum extracts (bran, phenolic and lipid extracts) and a small number of human studies have demonstrated a lower glycemic response to sorghum-based foods however results were inconsistent. Sorghum's lipid profile, rich in unsaturated fatty acids, may provide additional lipid-lowering effects. As a fiber rich food, sorghum is likely to impart satiating qualities. Specifically, designing studies that combine objective measures (physiological effects such as glucose, insulin, appetite hormones) with subjective analysis of appetite utilizing visual analogue scales (questions about hunger, desire to eat, satisfaction, fullness and subsequent food intake) are important.[(177)] It is also important to consider that for functional foods to deliver their potentially subtle benefits, repeated consumption is required.[(178)]

Substantiating potentially beneficial effects of sorghum foods on chronic lifestyle related disease risk factors requires rigorous scientific investigation in human studies whereby consistent results from randomized controlled trial (RCTs) are reported, contributing to the highest level of evidence for practice.[(179)] To date there appears to be fewer than five RCTs investigating sorghum metabolic disease-related effects in humans, and all interventions are short-term and have some experimental design shortcomings. Future RCTs should aim to directly examine a specific effect on chronic disease biomarkers or health outcomes between a control and sorghum-intervention diet, for a minimum of 3-6 months, enabling evidence for longer-term effects to emerge.[(180)] Specifically, studies should investigate lipid profiles, longer-term markers of glycemic control, and body weight. While much of the research to date focuses on extracts and components, the impact of the whole food reflecting the synergy between the components needs to be considered. It is also important to study the content of the background diet in these RCTs as background diet can confound results and may interfere with the ability to attribute effects to the dietary variable of interest.[(180)] In addition, for translation to practice, the impact of sorghum-based foods on chronic lifestyle related disease must be seen in the context of the whole diet, carefully monitored throughout trials.

The evidence for a relationship between the antioxidant activity of sorghum and health benefits of its consumption is of particular importance due to the role oxidative stress plays in chronic disease development. To date, several *in-vitro* and animal model studies have highlighted the potential of sorghum grain components, such as polyphenols, to scavenge free radicals.[(176,181-184)] Unfortunately, these studies are limited in their ability to attribute direct antioxidant effects of sorghum, as they do not account for metabolic transformations and interactions that influence bioavailability and biological activity of the polyphenols in the body after ingestion. For example, it is unclear what transformations polyphenols undergo *in vivo*, from the oral cavity, through the gastrointestinal tract and after absorption and metabolism.[(185)] Thus, test regimens from such *in-vitro* and animal studies need to be repeated in humans with mild to moderate oxidative-stress induced disease. Disease indicators, such as oxidative stress and inflammatory markers, can be measured in subjects who consume a sorghum-enriched diet daily over an extended period of time.

Finally, while the development of an evidence base for a link between sorghum consumption and chemoprevention is in its infancy, some evidence for strong anti-oxidant and anti-inflammatory effects that may mitigate cell proliferation, mutagenesis and carcinogenesis has been reported. Cell-line and animal studies have demonstrated the potential for such cell-mediated effects, but require substantiation in humans. Determining whether the concentration of sorghum grain extracts used in these studies may be feasibly consumed through dietary intake of sorghum-based foods is critical. Notwithstanding, the study of food effects on cancer is highly complex and clinical trials are problematic for ethical reasons. Even so, knowledge generated through various forms of experimental research adds to a general understanding of how the sorghum food matrix may be beneficial.

Conclusions

There is an emerging body of scientific literature on sorghum (*Sorghum bicolor*) as an underutilized cereal whole grain that may contribute to the prevention of chronic lifestyle related diseases, particularly in regions where associated morbidity and mortality rates are significant public health burdens.[22] This review identifies that sorghum grain components may have an impact on metabolic disease processes through the delivery of slowly digestible starches, resistant starch, dietary fiber, polyphenols (including phenolic acids, flavonoids and condensed tannins), policosanols, unsaturated fatty acids and the food attribute of a high antioxidant capacity. However, the vast majority of studies utilized extracts or purified compounds, and were conducted in animal models. Few studies in humans have been reported, and there is a need to study sorghum as a whole grain, and in the context of a healthy diet.

High quality clinical research investigating effects of sorghum consumption in humans is the next step to build on the promising in-vitro and animal research conducted to date. Human evidence for the long-term effects of consuming sorghum as part of a healthy diet is necessary to provide future directions for consumers, the food industry, growers, health professionals, and government-based grain advocacy organizations. If proven effective, the quality evidence from trials involving humans could position sorghum as an important driver for economic development in many of the world's most food insecure regions, particularly parts of Africa, where sorghum is often the only viable grain food. This same evidence from human studies could also act as a catalyst for the uptake and demand for sorghum by food industry and consumers where the food supply is more plentiful and obesity is a problem.

Table 1. Sorghum's nutritional and functional attributes associated with metabolic disease effects

Component/Property	Proposed benefits
Slow starch digestibility[11,12] (slowly digestible starches; interactions with endosperm & polyphenolic compounds that reduce starch hydrolysis)	Potential to attenuate blood glucose & insulin responses & increase satiety through reduction of glycemic index of sorghum-based foods. This has relevance in appetite regulation, weight management & risk reduction of obesity-related diseases such as diabetes
High antioxidant activity[10] (phenolic acids, monomeric polyphenolic flavonoids, polymeric polyphenolic condensed tannins)	Potential to reduce oxidative stress that plays an important role in the pathogenesis of many chronic diseases such as diabetes, atherosclerosis, some cancers, aging, arthritis & neurological diseases
High fiber[13] (including resistant starch, ranging from 2.2 g[14] – 6.5 g[15] / 100 g dry matter)	Offers benefits to gut microbiome, metabolic disease risk & gastrointestinal health
High unsaturated fatty acid content of lipid[16] (oleic acid, linoleic acid, linolenic acid and policosanols in wax[17])	Improving dyslipidemia & thus promoting heart health

Table 2. Nutritional Composition of Sorghum, Wheat and Corn

(per 100g dry weight, edible portion)[25,26]

	Sorghum,White,Whole	Wheat, Durum, Whole	Corn, Yellow
Proximates			
Energy (kcal / kJ)	329/1377	339/1418	365/1527
Protein (g)	10.62	13.68	9.42
Total lipid (fat) (g)	3.46	2.47	4.74
Carbohydrate, by difference (g)	72.09	71.13	74.26
Fiber (g)	6.7#	10.7*	7.3
Lipids			
Fatty acids, total saturated (g)	0.610	0.454	0.667
Fatty acids, total monounsaturated (g)	1.131	0.344	1.251
Fatty acids, total polyunsaturated (g)	1.558	0.978	2.163
Cholesterol (mg)	0	0	0
Minerals			
Calcium, Ca (mg)	13	34	7
Iron, Fe (mg)	3.36	3.52	2.71
Magnesium, Mg (mg)	165	144	127
Phosphorus, P (mg)	289	508	210
Potassium, K (mg)	363	431	287
Sodium, Na (mg)	2	2	35
Zinc, Zn (mg)	1.67	4.16	2.21
Copper, Cu (mg)	1.080	0.553	0.314
Manganese, Mn (mg)	1.630	3.012	0.485
Selenium, Se (mg)	12.2	89.4	15.5
Vitamins			
Vitamin C, total ascorbic acid (mg)	0	0	0
Thiamin, B1 (mg)	0.332	0.419	0.385
Riboflavin, B2 (mg)	0.096	0.121	0.201
Niacin, B3 (mg)	3.688	6.738	3.627
Pantothenic acid, B5 (mg)	1.250	0.935	0.424
Vitamin B6 (mg)	0.440	0.419	0.622
Folate, DFE (μg)	20	43	19
Vitamin B-12 (μg)	0	0	0
Vitamin A, RAE (μg)	0	0	11
Vitamin D (IU)	0	0	0
Vitamin E (alpha-tocopherol) (mg)	0.50	0.71*	0.49
Amino Acids			
Tryptophan (g)	0.124	0.176	0.067
Threonine (g)	0.346	0.366	0.354
Isoleucine (g)	0.433	0.533	0.337
Leucine (g)	1.491	0.934	1.155
Lysine (g)	0.229	0.303	0.265
Methionine (g)	0.169	0.221	0.197
Cystine (g)	0.127	0.286	0.170
Phenylalanine	0.546	0.681	0.463
Tyrosine (g)	0.321	0.357	0.383
Valine (g)	0.561	0.594	0.477
Arginine (g)	0.355	0.483	0.470
Histidine (g)	0.246	0.322	0.287
Alanine (g)	1.033	0.427	0.705
Aspartic acid (g)	0.743	0.617	0.655
Glutamic acid (g)	2.439	4.743	1.768
Glycine (g)	0.346	0.495	0.386
Proline (g)	0.852	1.459	0.822
Serine (g)	0.462	0.667	0.447

** value is for whole grain wheat flour # value is for white sorghum (fiber in other types of sorghum ranges from 8.8 - 11.1 g/100g)*

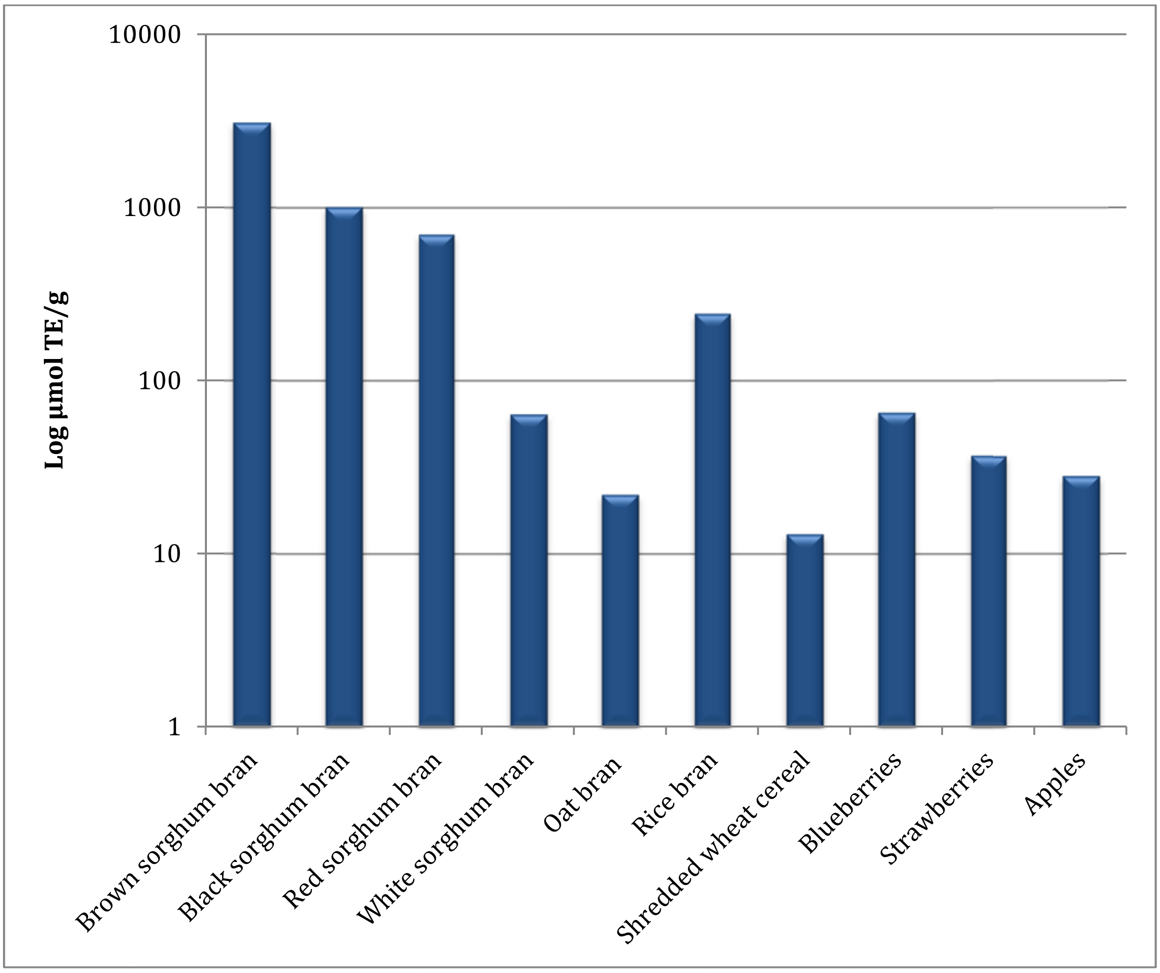

Figure 1. Antioxidant activity in sorghum bran fractions (dry basis) relative to other cereals and common fruits measured by Oxygen Radical Absorbance Capacity (ORAC) and expressed as µmol Tocopherol Equivalents (TE). Compiled from previously reported data.[10,25]

Table 3: Human Studies incorporating sorghum-based test meals

Lead Author/Year	Focus of investigations	Subjects/Experiment	Results
Nutrient & vitamin metabolism			
Gopalan et al. (1960)[29]	Role of amino acid imbalance (relative excess of leucine) in the pathogenesis of pellagra.	13 healthy & pellagrin subjects. 5g dietary leucine administered daily & changes in urinary excretion of N-methyl nicotinamide (NMN) measured.	Leucine increased urinary excretion of NMN in all subjects. Isocaloric replacement of rice by sorghum (jowar) resulted in increased urinary NMN excretion in all patients.
Deosthale et al. (1974)[125]	Sorghum molybdenum (Mo) consumption effects on copper (Cu) & uric acid excretion.	4 adult males (age not specified). Low (0.21 µg/g) & high (1.39 µg/g) Mo-containing grains were used in diets controlled for calories, protein, minerals, sulfur.	Uric acid increased only in high Mo intakes (10-15 mg Mo/day). Urinary Cu excretion was sig.ly increased with increasing levels of Mo. Faecal Cu excretion was unchanged.
Krishnaswamy et al. (1976)[126]	Vitamin B6, leucine absorption.	6 healthy males (25-35 yrs). Metabolic interrelations between excess dietary leucine & vitamin B6 studied.	Vit. B6 counteracted effects of leucine on urinary quinolinic acid excretion, in-vitro nicotinamide nucleotide synthesis by erythrocytes; corrected abnormalities of 5-hydroxytryptamine metabolism induced by excess leucine.
Obizoba (1979)[127]	Mineral & vitamin metabolism.	5 healthy women (19-25 yrs). Fed 4 iso-nitrogeneous mixed plant protein diets various blends based on whole wheat, navy bean & 3 sorghum flour varieties (Purdue normal, high lysine & Nigeria normal).	Various effects on measured Ca, Mg, Fe, Niacin, riboflavin, folic acid levels were reported & related to the contents in the test diet.
Wang et al. (1991)[128]	Fiber effects on niacin status/ niacin utilization.	10 healthy adult subjects. 28 g per day of ready-to-eat cereal (whole-ground sorghum flour) or cereal from decorticated sorghum flour (bran removed, polished). Urine, stool & fasting blood samples collected.	Whole grain sorghum cereal decreased fecal transit time, lowered urinary NMN excretions, but raised blood serum levels of NMN & nicotinamide when compared to polished grain sorghum cereal.
Schmid et al. (2007)[129]	Dietary intake analysis of mothers & their children in South India.	218 mothers (> 15 yrs) & their children (< 5 yrs) in South India. Comparison of dietary intake of subjects with & without intervention to manage malnutrition.	Mothers had sig. higher intakes of energy & protein in summer, & sig. higher intakes of energy, protein & Fe in rainy season. No differences in children. In mothers, sorghum contributed 29% energy, 33% protein, 53% iron.
Iron (Fe) status/absorption			
Derman et al. (1980)[130]	Fe absorption from maize & sorghum.	21 male & female South African subjects, healthy & Fe-deficient. Ages not specified. Study compared thin gruel, sorghum & wheat beers.	Ten times as much Fe was absorbed from the traditional maize & sorghum beer as from gruel made from the same ingredients.
Radhakrishnan et al. (1980)[131]	Fe bioavailability.	12 healthy & 13 anemic subjects. Ages not specified. Diets based on high & low tannin sorghum.	In 12 healthy subjects, Fe absorption from the low & high tannin varieties was similar. In 6 anemic subjects, Fe absorption from low tannin sorghum was sig. higher. In the other 7 anemic subjects, there was no difference observed.
Gillooly et al. (1984)[132]	Fe absorption.	53 Fe-deficient Indian females (age not specified). 6 different experiments. Systematically examined effects on Fe absorption of polyphenol & phytate in sorghum.	When amounts of both compounds were reduced to low levels by pearling, there was a sig. increase in Fe absorption.
Haidar et al. (1999)[133]	Fe deficiency anaemia (IDA) status.	1449 pregnant & lactating subjects (15-49 yrs) in Ethiopia.	Overall status of IDA determined by hemoglobin level was 18.4 % with higher rates in maize, milk & sorghum staple areas.
Hurrell et al. (2003)[35]	Fe absorption.	34 males & 44 females (21-38 yrs). Measured the influence of phytic acid degradation on Fe absorption from cereal porridges.	Phytate degradation improves Fe absorption from cereal porridges prepared with water but not with milk, except from high-tannin sorghum.
Cardiovascular effects			
Suhasini et al. (1991)[134]	Effect of unrefined sorghum or maize on serum lipids.	6 males & 10 females (23-26 yrs). Grp 1 ate 100g unrefined sorghum. Grp 2 ate 50g of unrefined maize.	Both diets showed sig. reduction in serum total cholesterol & triglyceride levels with simultaneous increase in HDL cholesterol value over 3 weeks.
Diabetes/glycemia/oxidative stress research			
Mani et al. (1993)[135]	Determination of glycemic index of commonly consumed	36 subjects (Type 2 DM). Glucose responses were measured 1 & 2 hrs after consumption of test foods (50g available	The mean glycemic index of the sorghum meal was 77% +/- 8 (SE), indicating a relatively high glycemic index. No sig. difference was observed in blood glucose

	foods in India.	carbohydrate) & compared to a 50g glucose load. 6 foods tested, 1 based on sorghum.	level at the 1 h & 2 h time-points when compared with the corresponding reference.
Lakshmi et al. (1996)[136]	Glucose & insulin responses to sorghum-based meals.	3 males & 3 females with Type 2 DM (45-60 yrs). Consumption of whole grain sorghum meals compared with the same meals based on dehulled sorghum & other recipes prepared with wheat & rice.	The consumption of whole grain meals resulted in sig. lower glycemic responses (P<0.05) in 6 subjects, in part due to differences in fiber content & cooking methods.
Abdelgadir et al. (2005)[137]	Glucose & insulin responses to 6 traditional Sudanese meals from wheat, sorghum, millet & maize flours.	Glucose & insulin responses in a randomized crossover design with 10 subjects with Type 2 diabetes mellitus (6 males & 4 females).	Millet porridge had the lowest post-prandial glucose & insulin responses followed by wheat pancakes, sorghum porridge & sorghum flat bread. Maize porridge induced higher glucose & insulin responses (as measured by mean iAUC).
Poquette et al. (2013)[138]	Glucose & insulin responses to sorghum-based meals.	Randomized-crossover design, 10 males consumed muffins containing 50g of total starch from either grain sorghum flour or whole wheat flour. Plasma glucose & insulin measured over 3 hrs.	Plasma glucose & insulin iAUC reduced by ~26% & 55% respectively. Glucose & insulin measures were sig.ly lower for the sorghum muffins (p<0.05) at different time points.
Khan et al. (2014)[139]	Plasma total polyphenols, antioxidant capacity & oxidative stress responses to sorghum pasta meal.	Randomized-crossover design, 22 males and females consumed pasta containing red or white wholegrain sorghum flour (30% sorghum, 70% semolina) or a wheat control made from 100% semolina. One blood collection at 2 h time-point.	Plasma polyphenols, antioxidant capacity and superoxide dismutase (SOD) activity were significantly (P < 0.001) higher following red sorghum pasta (RSP) meal & protein carbonyl level was significantly lower (P = 0.035) following consumption of the RSP meal than the control meal (wheat).

Specific fiber effects

Cornu et al. (1981)[67]	Effect of fiber in sorghum on N digestibility.	12 healthy Cameroonian adult males whose habitual diet is based on a sorghum meal (2.4-4.2 g of crude fiber / 100 g DM). Subjects received successive diets of 3.3, 4.8, 5.4 g of crude fiber / 100 g of DM.	Increased fiber intake resulted in a sig. rise in quantity of fecal matter excreted (N & formic insoluble substances), but a reduction in urinary N losses.
MacLean et al. (1983)[58]	Effect of decortication & extrusion on the digestibility of sorghum.	9 children (7-24 mo). Sorghum provided 8% protein & 62% carbohydrate (kCal) in diet. Lysine was supplemented to 3% of protein. Casein provided 6.4% protein (kCal) in the control diet.	N absorption from sorghum & control not different but N retention lower than control. Fecal weights & energy losses showed minor differences. Decortication & extrusion improve protein quality & digestibility of sorghum.
Fedail et al. (1984)[140]	Effect of sorghum & wheat bran on the colonic functions.	10 males (22-24 yrs) healthy Sudanese subjects. Comparative study of normal diet, diet of 20 g/day sorghum bran, & 20 g/day wheat bran, for 3 wks. Wet stool wt, gut transit time, & freq. of bowel evac. noted.	The mean stool weight on normal diet was 136.6 ± 43.1 g/day, on sorghum bran 173.3 ± 48.4 g/day, & on wheat bran 219.1 ± 98.3 g/day (p < 0.001). Both brans produced a similar number of bowel evacuations, stool weight & transit time.
Cornu et al. (1986)[141]	Effects of fiber on digestibility of sorghum lipids.	12 healthy Cameroonian adult males whose habitual diet is based on a sorghum meal (2.4-4.2 g of crude fiber / 100 g DM). Subjects received successive diets of 3.3 (A), 4.8 (B), 5.4 (C) g crude fiber / 100 g of DM.	Reduced lipid digestibility occurred in all diets. No difference was observed between A & B fiber diets but dropped with diet C. Lipid losses increased more rapidly than N losses with increasing fiber content. No sig. changes in concentrations of fecal fat.

Protein digestibility

Kurien et al. (1960)[142]	Metabolism of N, calcium & phosphorus.	7 boys (10-11 yrs). Effect on metabolism of N, Ca & P of replacing 25%, 50% or 100% of rice in a poor Indian diet by Sorghum Vulgare was studied. Daily intake of N was constant in all diets.	Protein digestibility coefficients of protein & mean daily N retention diminished as sorghum increased. Sorghum led to: 1) higher Ca intake, but Ca retention decreased 2) higher P intake, which resulted in higher P retention.
Nicol et al. (1978)[143]	Utilization of protein in cassava, rice & sorghum (Sativa) based diets	19 Nigerian men, 13 different feeding trials, each of 6 men. Net protein utilization (NPU) of diets based on rice, sorghum or cassava, was compared to a minimal protein diet. Endogenous N excretion measured.	The NPU of a diet based on home-pounded, winnowed sorghum flour was higher than that of a diet based on milled whole-meal sorghum due to the low digestibility of the latter diet.
MacLean et al. (1981)[144]	Protein quality & digestibility of sorghum	13 children (6-30 mo). Protein quality & digestibility of 2 high lysine (2.9-3.0 g/100 g protein) & 2 conventional varieties (lysine content 2.1-2.2 g/100 g protein) of whole grain sorghum milled were assessed.	Weight loss or poor weight gain was reported. No difference by variety in N absorption or retention. Stool weight & energy loss 2.5-3x control values. Total conc. essential amino acids was low as were conc. Lys & Thr. Lys was the limiting amino acid.

Weaning or therapeutic foods

Dibari et al. (2013)[145]	Acceptability/safety of new ready-to-use therapeutic foods (RUTF) before use.	41 HIV/TB patients (>18 yrs) in Kenya. Cross-over RCT comparing soy/maize/sorghum RUTF (SMS-RUTFh) to control -10 d measures of product intake.	SMS-RUTFh is acceptable & can be safely clinically trialed, if close monitoring of vomiting & nausea is included.
Bisimwa et al. (2012)[146]	Fortified soybean-maize-sorghum paste Vs fortified corn soy blend porridge in underweight infants.	6 mo Congolese infants randomly assigned to lipid-based ready-to-use complementary foods (RUCF, n = 691) or fortified corn soy blend (UNIMIX, n = 692) for 6 mo. Hemoglobin, triglyceride, & cholesterol noted.	No sig. differences in the concentrations of hemoglobin, serum triglyceride, & serum cholesterol were found between the 2 grps.

Human oral rehydration solutions based on sorghum

Mustafa et al. (1995)[147]	Oral rehydration therapy for acute diarrhea using cereal-based solutions.	96 (children (6-40 mo) in Sudan. Comparative RCT (32 rice, 34 sorghum, 30 control). Safety & efficacy of rice or sorghum cereal-based oral rehydration solutions (ORS) relative to std. WHO ORS formulation.	Cereal-based ORS shortened the duration of diarrhea, reduced stool vol. & the freq. of diarrhoea & vomiting, & the mean total ORS intake. These effects were more marked with the sorghum-based ORS than with the rice-based ORS.
Molla et al. (1989)[148]	Food-based oral rehydration solution (maize, millet, wheat, sorghum, rice, potato).	266 children (1-5 yrs), history of acute diarrhea for ≤ 48 h. Digestibility of food-based ORS was assessed by stool pH, glucose content before & after acid hydrolysis & osmolality.	The mean stool output over the first 24 h in std ORT was sig. higher than food-based ORT. Food-based ORT showed substantial reduction in stool output.
Pelleboer et al. (1990)[149]	Oral rehydration therapy for acute diarrhea.	64 Nigerian children (2.5 mo–5 yrs). Comparative RCT - subjects consumed either the WHO recommended oral rehydration solution (WHO-ORS) or a solution, containing 60 g/l sorghum powder.	No sig. differences in amt. of fluid used, no. of stools & duration of diarrhea. No sig. difference in weight gain. 7 children died, 2 (6%) in the sorghum-ORS grp & 5 (17%) in the WHO-ORS grp. Sorghum-ORS was well accepted & tolerated.

Consumer/sensory/acceptability studies

Kayitesi et al. (2010)[19]	Consumer opinions of marama /sorghum composite porridge.	30 males & 22 females. Descriptive sensory analysis, consumer testing, texture analysis, pasting & color.	The 100% sorghum porridge & the composite porridge with full-fat flour were the most acceptable to consumers.
Vazquez-Araujo (2012)[150]	Consumer input for developing human food products made with sorghum.	Adults n=34 focus grps; n=1002 national survey; n=160 conjoint analysis	Heath aspects of grain products were the most appealing for consumers, whereas conjoint analysis showed that sensory attributes were the principal drivers for purchase intent.
Muhihi et al. (2013)[151]	Sensory study: sorghum ugali (stiff porridge).	Overweight & obese Tanzanian adults. Pre-& post-tasting questionnaires were administered. A 10-point LIKERT scale used to rate attributes of 3 test foods. Sorghum ugali was consumed by 23% of participants.	All of the test foods were highly rated for smell, taste, color, appearance & texture. Taste was rated highest for unrefined maize ugali. Whole grain carbohydrates are highly acceptable.

Effects on immune status in people with HIV

Motswagole et al. (2013)[152]	Effects of a sorghum meal on the immune status of adults with HIV.	132 HIV+ adults. Double-blind randomized placebo-controlled trial in Botswana. Micronutrient fortified sorghum meal including Vit. A (n = 67) or control (n = 65). Serum retinol, Fe, Zn, albumin, CD4 cell count & HIV viral load assessed over 12 mo.	Fortified sorghum meal did not influence serum retinol, CD4 cell count & HIV viral load.
Ayuba et al. (2014)[153]	Effects of supplementation with sorghum herbal preparation (Jobelyn®) on immune status.	61 HIV+ adults in Nigeria – 2 trials. 10 HIV+ patients not receiving antiretroviral therapy (ARVT). Patients consumed 500 mg Jobelyn® daily for 8 wks. Control with 51 HIV+ patients receiving ARVT.	Consumption of Jobelyn® contributed to improved hemoglobin levels & increased CD4 cell counts HIV+ patients.

References

1. Flight, I.; Clifton, P. Cereal grains and legumes in the prevention of coronary heart disease and stroke: a review of the literature. Eur J Clin Nutr. **2006**, *60*(10), 1145-1159.
2. National Health and Medical Research Council. *Australian Dietary Guidelines.* Canberra, Australia: National Health and Medical Research Council; 2013.
3. Sahyoun, N.R.; Jacques, P.F.; Zhang, X.L.; Juan, W.; McKeown, N.M. Whole-grain intake is inversely associated with the metabolic syndrome and mortality in older adults. Am J Clin Nutr. **2006**, *83*, 124-131.
4. Venn, B.J.; Mann, J.I. Cereal grains, legumes and diabetes. Eur J Clin Nutr. **2004**, *58*(11), 1443-1461.
5. Williams, P.G.; Grafenauer, S.J.; O'Shea, J.E. Cereal grains, legumes, and weight management: a comprehensive review of the scientific evidence. Nutr Rev. **2008**, *66*(4), 171-182.
6. McIntosh, G.H. Cereal Foods, Fibres and the Prevention of Cancers. Aust J Nutr Diet. **2001**, *58*(Suppl2), S35-S48.
7. U.S. Department of Agriculture; U.S. Department of Health and Human Services. *Dietary Guidelines for Americans.* Washington DC: U.S. Department of Agriculture, U.S. Department of Health and Human Services; 2010.
8. Food and Agriculture Organisation of the United Nations. Production – Sorghum 2012. 2012; http://faostat.fao.org/site/339/default.aspx. Accessed 22 May, 2014.
9. Taylor, J.R.N.; Schober, T.J.; Bean, S.R. Novel food and non-food uses for sorghum and millets. J Cereal Sci. **2006**, *44*(3), 252-271.
10. Awika, J.M.; Rooney, L.W. Sorghum phytochemicals and their potential impact on human health. Phytochemistry. **2004**, *65*(9), 1199-1221.
11. Ezeogu, L.I.; Duodu, K.G.; Taylor, J.R.N. Effects of endosperm texture and cooking conditions on the *in vitro* starch digestibility of sorghum and maize flours. J Cereal Sci. **2005**, *42*(1), 33-44.
12. Ezeogu, L.I.; Duodu, K.G.; Emmanbux, M.N.; Taylor, J.R.N. Influence of cooking conditions on the protein matrix of sorghum and maize endosperm flours. Cereal Chem. **2008**, *85*, 397–402.
13. Bach Knudsen, K.E.; Munck, L. Dietary fibre contents and compositions of sorghum and sorghum-based foods. J Cereal Sci. **1985**, *3*(2), 153-164.
14. Khan, I.; Yousif, A.; Johnson, S.K.; Gamlath, S. Effect of sorghum flour addition on resistant starch content, phenolic profile and antioxidant capacity of durum wheat pasta. Food Res Int. **2013**, *54*(1), 578-586.
15. Niba, L.L.; Hoffman, J. Resistant starch and b-glucan levels in grain sorghum (Sorghum bicolor M.) are influenced by soaking and autoclaving. Food Chem. **2003**, *81*(1), 113-118.
16. Glew, R.H.; Vanderjagt, D.J.; Lockett, C., et al. Amino Acid, Fatty Acid, and Mineral Composition of 24 Indigenous Plants of Burkina Faso. J Food Compost Anal. **1997**, *10*(3), 205-217.
17. Avato, P.; Bianchi, G.; Murelli, C. Aliphatic and cyclic lipid components of Sorghum plant organs. Phytochemistry. **1990**, *29*(4), 1073-1078.
18. Ciacci, C.; Maiuri, L.; Caporaso, N., et al. Celiac disease: *in vitro* and *in vivo* safety and palatability of wheat-free sorghum food products. Clin Nutr. **2007**, *26*(6), 799-805.
19. Kayitesi, E.; Duodu, K.G.; Minnaar, A.; de Kock, H.L. Sensory quality of marama/sorghum composite porridges. J Sci Food Agric. **2010**, *90*(12), 2124-2132.
20. Amegovu, A.K.; Ogwok, P.; Ochola, S.; Yiga, P.; Musalima, J.H.; Mutenyo, E. Formulation of sorghum-peanut blend using linear programming for treatment of moderate acute malnutrition in Uganda. J Food Chem Nutr. **2013**, *01*(02), 67-77.

21. da Silva, L.S.; Taylor, J.; Taylor, J.R. Transgenic sorghum with altered kafirin synthesis: kafirin solubility, polymerization, and protein digestion. J Agric Food Chem. **2011**, *59*(17), 9265-9270.
22. World Health Organisation. *Global status report on noncommunicable diseases 2010.* Geneva April 2011.
23. Dicko, M.H.; Gruppen, H.; Traoré, A.S.; Voragen, A.G.J.; van Berkel, W.J.H. Review: Sorghum Grain as Human Food in Africa: Relevance of Starch Content and Amylase Activities. Afr J Biotechnol. **2006**, *Vol. 5*(5), 384-395.
24. Taylor, J.R.N.; Emmambux, M.N. REVIEW: Developments in Our Understanding of Sorghum Polysaccharides and Their Health Benefits. Cereal Chem. **2010**, *87*(4), 263-271.
25. USDA National Nutrient Database for Standard Reference, R. USDA National Nutrient Database for Standard Reference, Release 27. 2014; http://ndb.nal.usda.gov/ndb/foods/show/6477. Accessed Jan 8, 2015.
26. Serna-Saldivar, S.; Rooney, L.W. Structure and chemistry of sorghum and millets. In: Dendy DAV, ed. *Sorghum and Millets Chemistry and Technology*. St Paul, MN: American Association of Cereal Chemists; 1995:69-124.
27. Duodu, K.G.; Taylor, J.R.N.; Belton, P.S.; Hamaker, B.R. Factors affecting sorghum protein digestibility. J Cereal Sci. **2003**, *38*(2), 117-131.
28. Badi, S.; Pedersen, B.; Monowar, L.; Eggum, B.O. The nutritive value of new and traditional sorghum and millet foods from Sudan. Plant Food Hum Nutr. **1990**, *40*(1), 5-19.
29. Gopalan, C.; Srikantia, S.G. Leucine and Pellagra. Lancet. **1960**, *275*(7131), 954-957.
30. Nakagawa, I.; Ohguri, S.; Sasaki, A.; Kajimoto, M.; Sasaki, M.; Takahashi, A. Effects of Excess Intake of Leucine and Valine Deficiency on Tryptophan and Niacin Metabolites in Humans. J Nutr. **1975**, *105*(10), 1241-1252.
31. Nakagawa, I., Sasaki, A. Effect of an excess intake of leucine, with and without additions of vitamin B6 and/or niacin, on tryptophan and niacin metabolism in rats. J Nutr Sci and Vitaminol. **1977**, *23* (6), 535-548.
32. Cook, N.E.; Carpenter, K.J. Leucine Excess and Niacin Status in Rats. J Nutr. **1987**, *117*(3), 519-526.
33. Hegedüs, M.; Pedersen, B.; Eggum, B.O. The influence of milling on the nutritive value of flour from cereal grains. 7. Vitamins and tryptophan. Qualitas Plantarum **1985**, *35*(2), 175-180.
34. Khalil, J.K.; Sawaya, W.N.; Safi, W.J.; Al-Mohammad, H.M. Chemical composition and nutritional quality of sorghum flour and bread. Qualitas Plantarum. **1984**, *34*(2), 141-150.
35. Hurrell, R.F.; Reddy, M.B.; Juillerat, M.-A.; Cook, J.D. Degradation of phytic acid in cereal porridges improves iron absorption by human subjects. Am J Clin Nutr. **2003**, *77*, 1213-1219.
36. Mohammed, N.A.; Ahmed, I.A.M.; Babiker, E.E. Nutritional evaluation of sorghum flour (Sorghum bicolor L. Moench) during processing of injera. World Acad Sci Eng Technol. **2011**, *75*, 72-76.
37. Daiber, K.H. Enzyme inhibition by polyphenols of sorghum grain malt. J Sci Food Agric. **1975**, *26*(9), 1399-1411.
38. Beta, T.; Rooney, L.W.; Marovatsangaa, L.T.; Taylor, J.R.N. Effect of Chemical Treatments on Polyphenols and Malt Quality in Sorghum. J Cereal Sci. **2000**, *31*(3), 295-302.
39. Barros, F.; Awika, J.M.; Rooney, L.W. Interaction of tannins and other sorghum phenolic compounds with starch and effects on in vitro starch digestibility. J Agric Food Chem. **2012**, *60*(46), 11609-11617.
40. Lemlioglu-Austin, D.; Turner, N.D.; McDonough, C.M.; Rooney, L.W. Effects of sorghum [Sorghum bicolor (L.) Moench] crude extracts on starch digestibility, Estimated Glycemic Index (EGI), and Resistant Starch (Rs) contents of porridges. Molecules. **2012**, *17*(9), 11124-11138.

41. Hargrove, J.L.; Greenspan, P.; Hartle, D.K.; Dowd, C. Inhibition of Aromatase and a-Amylase by Flavonoids and Proanthocyanidins from Sorghum bicolor Bran Extracts. J Med Food. **2011**, *14*(7/8), 799-807.
42. Kim, J.-S.; Hyun, T.K.; Kim, M.-J. The inhibitory effects of ethanol extracts from sorghum, foxtail millet and proso millet on α-glucosidase and α-amylase activities. Food Chem. **2011**, *124*(4), 1647-1651.
43. Akingbala, J.O.; Gomez, M.H.; Rooney, L.W.; Sweat, V.E. Thermal properties of sorghum starch. Starch - Stärke. **1988**, *40*, 375-378.
44. Parada, J.; Aguilera, J.M. Review: starch matrices and the glycemic response. Food Sci Technol Int. **2011**, *17*(3), 187-204.
45. Licata, R.; Chu, J.; Wang, S., et al. Determination of formulation and processing factors affecting slowly digestible starch, protein digestibility and antioxidant capacity of extruded sorghum-maize composite flour. Int J Food Sci Technol. **2014**, *49*(5), 1408-1419.
46. Yousif, A.; Nhepera, D.; Johnson, S. Influence of sorghum flour addition on flat bread in vitro starch digestibility, antioxidant capacity and consumer acceptability. Food Chem. **2012**, *134*(2), 880-887.
47. Sajilata, M.G.; Singhal, R.S.; Kulkarni, P.R. Resistant starch - a review. Compr Rev Food Sci Food Saf. **2006**, *5* (1), 1-17.
48. Ferguson, L.R.; Tasman-Jones, C.; Englyst, H.; Harris, P.J. Comparative effects of three resistant starch preparations on transit time and short-chain fatty acid production in rats. Nutr Cancer. **2000**, *36*(2), 230-237.
49. Flint, H.J.; Scott, K.P.; Duncan, S.H.; Louis, P.; Forano, E. Microbial degradation of complex carbohydrates in the gut. Gut Microbes. **2012**, *4*(3).
50. Martínez, I.; Kim, J.; Duffy, P.R.; Schlegel, V.L.; Walter, J. Resistant starches types 2 and 4 have differential effects on the composition of the fecal microbiota in human subjects. PLoS One. **2010**, *5*(11), e15046.
51. Topping, D.L. Soluble fiber polysaccharides: Effects on plasma cholesterol and colonic fermentation. Nutr Rev. **1991**, *49*(7), 195-203.
52. Warrand, J. Healthy Polysaccharides The Next Chapter in Food Products. Food Technol Biotechnol. **2006**, *44*(3), 355–370.
53. Verbruggen, M.A.; Beldman, G.; Voragen, A.G.J.; Hollemans, M. Water-unextractable Cell Wall Material from Sorghum: Isolation and Characterization. J Cereal Sci. **1993**, *17*(1), 71-82.
54. Bach Knudsen, K.E.; Kirleis, A.W.; Eggum, B.O.; Munck, L. Carbohydrate composition and quality for rats of sorghum to prepared from decorticated white and whole grain red flour. J Nutr. **1988**, *118* (5), 588-597.
55. Verbruggen, M.A.; Beldman, G.; Voragen, A.G.J. The Selective Extraction of Glucuronoarabinoxylans from Sorghum Endosperm Cell Walls using Barium and Potassium Hydroxide Solutions. J Cereal Sci. **1995**, *21*(3), 271-282.
56. Henry, R.J. Pentosan and (1 → 3),(1 → 4)- *β* -Glucan concentrations in endosperm and wholegrain of wheat, barley, oats and rye. J Cereal Sci. **1987**, *6*(3), 253–258.
57. Hatfield, R.D.; Wilson, J.R.; Mertens, D.R. Composition of cell walls isolated from cell types of grain sorghum stems. J Sci Food Agric. **1999**, *79*(6), 891-899.
58. Maclean Jr, W.C.; Lopez De Romana, G.; Gastanaduy, A.; Graham, G.G. The Effect of Decortication and Extrusion on the Digestibility of Sorghum by Preschool Children. J Nutr. **1983**, 2071-2077.
59. Taylor, J.R.N.; Anyango, J.O. Sorghum Flour and Flour Products: Production, Nutritional Quality, and Fortification. In: Preedy V, Watson R, Patel V, eds. *Flour and Breads and their Fortification in Health and Disease Prevention*. Oxford: Academic Press; 2011:127-139.

60. de Mesa-Stonestreet, N.J.; Alavi, S.; Bean, S.R. Sorghum proteins: the concentration, isolation, modification, and food applications of kafirins. J Food Sci. **2010**, *75*(5), R90-R104.
61. Belton, P.S.; Delgadillo, I.; Halford, N.G.; Shewry, P.R. Kafirin structure and functionality. J Cereal Sci. **2006**, *44*(3), 272-286.
62. Taylor, J.R.N.; Schussler, L. The protein compositions of the different anatomical parts of sorghum grain. J Cereal Sci. **1986**, *4*(4), 361-369.
63. Hager, A.-S.; Wolter, A.; Czerny, M., et al. Investigation of product quality, sensory profile and ultrastructure of breads made from a range of commercial gluten-free flours compared to their wheat counterparts. Eur Food Res Technol. **2012**, *235*(2), 333-344.
64. Axtell, J.D.; Kirleis, A.W.; Hassen, M.M.; D'Cros Mason, N.; Mertz, E.T.; Munck, L. Digestibility of sorghum proteins. Proc Nat Acad Sci. **1981**, *78*(3), 1333-1335.
65. Cherney, D.J.R. In vitro ruminal fiber digestion as influenced by phenolic-carbohydrate complexes released from sorghum cell walls Anim Feed Sci Tech. **1992**, *39*(1-2), 79-93.
66. Taylor, J.; Taylor, J.R.N. Alleviation of the adverse effect of cooking on sorghum protein digestibility through fermentation in traditional African porridges. Int J Food Sci Technol. **2002**, *37*, 129-137.
67. Cornu, A.; Delpeuch, F. Effect of fiber in sorghum on nitrogen digestibility. Am J Clin Nutr. **1981**, *34*, 2454-2459.
68. Llopart, E.E.; Drago, S.R.; De Greef, D.M.; Torres, R.L.; Gonza´lez, R.J. Effects of extrusion conditions on physical and nutritional properties of extruded whole grain red sorghum (sorghum spp). Int J Food Sci Nutr. **2014**, *65*(1), 34–41.
69. Lin, P.; Wong, J.H.; Ng, T.B.; Ho, V.S.; Xia, L. A sorghum xylanase inhibitor-like protein with highly potent antifungal, antitumor and HIV-1 reverse transcriptase inhibitory activities. Food Chem. **2013**, *141*(3), 2916-2922.
70. Strumeyer, D.H.; Malin, M.J. Identification of the amylase inhibitor from seeds of Leoti sorghum. Biochimica et biophysica acta. **1969**, *184*(3), 643-645.
71. Kumar, P.M.; Virupaksha, T.K.; Vithayathil, P.J. Sorghum proteinase inhibitors: Purification and some biochemical properties Int J Peptide Protein Res. **1978**, *12* (4), 185-196.
72. Dicko, M.H.; Gruppen, H.; Hilhorst, R.; Voragen, A.G.; van Berkel, W.J. Biochemical characterization of the major sorghum grain peroxidase. The FEBS journal. **2006**, *273*(10), 2293-2307.
73. Camargo Filho, I.; Cortez, D.A.G.; Ueda-Nakamura, T.; Nakamura, C.V.; Dias Filho, B.P. Antiviral activity and mode of action of a peptide isolated from Sorghum bicolor. Phytomedicine. **2008**, *15*(3), 202-208.
74. Cavazos, A.; Gonzalez de Mejia, E. Identification of Bioactive Peptides from Cereal Storage Proteins and Their Potential Role in Prevention of Chronic Diseases. Compr Rev Food Sci Food Saf. **2013**, *12*(4), 364-380.
75. Mehmood, S.; Orhan, I.; Ahsan, Z.; Aslan, S.; Gulfraz, M. Fatty acid composition of seed oil of different Sorghum bicolor varieties. Food Chem. **2008**, *109*(4), 855-859.
76. Adeyeye, A., Ajewole, K. Chemical composition and fatty acid profiles of cereals in Nigeria. Food Chem. **1992**, *44*(1), 41-44.
77. Carr, T.; Weller, C.; Schlegel, V.; Cuppett, S.; Guderian Jr, D.; Johnson, K. Grain sorghum lipid extraction reduces cholesterol absorption and plasma non-HDL cholesterol concentrations in hamsters. Nutrition. **2005**, *135*(9), 2236-2240.
78. Lee, B.H.; Carr, T.P.; Weller, C.L.; Cuppett, S.; Dweikat, I.M.; Schlegel, V. Grain sorghum whole kernel oil lowers plasma and liver cholesterol in male hamsters with minimal wax involvement. J Funct Foods. **2014**, *7*, 709-718.
79. Irmak, S.; Dunford, N.T.; Milligan, J. Policosanol contents of beeswax, sugar cane and wheat extracts. Food Chem. **2006**, *95*(2), 312-318.

80. Gouni-Berthold, I.; Berthold, H.K. Policosanol: Clinical pharmacology and therapeutic significance of a new lipid-lowering agent. A Heart J. **2002**, *143*(2), 356-365.
81. Martinez, I.; Wallace, G.; Zhang, C., et al. Diet-induced metabolic improvements in a hamster model of hypercholesterolemia are strongly linked to alterations of the gut microbiota. Appl Environ Microbiol. **2009**, *75*(12), 4175-4184.
82. Macfarlane, S.; Macfarlane, G.T.; Cummings, J.H. Review article: prebiotics in the gastrointestinal tract. Alimentary pharmacology & therapeutics. **2006**, *24*(5), 701-714.
83. Wong, J.M.W.; De Souza, R.; Kendall, C.W.C.; Emam, A.; Jenkins, D.J.A. Colonic Health: Fermentation and Short Chain Fatty Acids. J Clin Gastroenterol. **2006**, *40*(3), 235-243.
84. Broekaert, W.F.; Courtin, C.M.; Verbeke, K.; Van de Wiele, T.; Verstraete, W.; Delcour, J.A. Prebiotic and other health-related effects of cereal-derived arabinoxylans, arabinoxylan-oligosaccharides, and xylooligosaccharides. Crit Rev Food Sci Nutr. **2011**, *51*(2), 178-194.
85. Zbasnik, R.; Carr, T.; Weller, C., et al. Anti proliferation Properties of Grain Sorghum Dry Distiller's Grain Lipids in Caco-2 Cells. J Agr Food Chem. **2009**, *57*(21), 10435-10441.
86. Awika, J.M.; Rooney, L.W.; Waniska, R.D. Anthocyanins from black sorghum and their antioxidant properties. Food Chem. **2005**, *90*(1-2), 293-301.
87. Rooney, L.W.; Awika, J.M. Overview of Products and Health Benefits of Specialty Sorghums. Cereal Food World. **2005**, *50*(3), 109.
88. Awika, J.M.; Rooney, L.W.; Waniska, R.D. Properties of 3-Deoxyanthocyanins from Sorghum. J Agric Food Chem. **2004**, *52*, 4388-4394.
89. Dykes, L.; Rooney, L.W.; Waniska, R.D.; Rooney, W.L. Phenolic Compounds and Antioxidant Activity of Sorghum Grains of Varying Genotypes. J Agric Food Chem. **2005**, *53*, 6813-6818.
90. Towo, E.; Matuschek, E.; Svanberg, U. Fermentation and enzyme treatment of tannin sorghum gruels: effects on phenolic compounds, phytate and in vitro accessible iron. Food Chem. **2006**, *94*(3), 369-376.
91. Dlamini, N.R.; Taylor, J.R.N.; Rooney, L.W. The effect of sorghum type and processing on the antioxidant properties of African sorghum-based foods. Food Chem. **2007**, *105*(4), 1412-1419.
92. N'Dri, D.; Mazzeo, T.; Zaupa, M.; Ferracane, R.; Fogliano, V.; Pellegrini, N. Effect of cooking on the total antioxidant capacity and phenolic profile of some whole-meal African cereals. J Sci Food Agric. **2012**, *93*, 29-30.
93. Kayodé, A.P.P.; Hounhouigan, J.D.; Nout, M.J.R. Impact of brewing process operations on phytate, phenolic compounds and in vitro solubility of iron and zinc in opaque sorghum beer. LWT - Food Sci Technol. **2007**, *40*(5), 834-841.
94. Wu, L.; Huang, Z.H.; Qin, P.Y.; Ren, G.X. Effects of processing on phytochemical profiles and biological activities for production of sorghum tea. Food Res Int. **2013**, *53*(2), 678-685.
95. Adom, K.K.; Liu, R.H. Antioxidant Activity of Grains. J Agric Food Chem. **2002**, *50*, 6182-6187.
96. Hsu, C.L.; Yen, G.C. Phenolic compounds: evidence for inhibitory effects against obesity and their underlying molecular signaling mechanisms. Molecular nutrition & food research. **2008**, *52*(1), 53-61.
97. Montonen, J.; Knekt, P.; Jarvinen, R.; Reunanen, A. Dietary antioxidant intake and risk of type 2 diabetes. Diabetes Care. **2004**, *27*, 362-366.
98. Farrar, J.L.; Hartle, D.K.; Hargrove, J.L.; Greenspan, P. A novel nutraceutical property of select sorghum (Sorghum bicolor) brans: inhibition of protein glycation. Phytotherapy research : PTR. **2008**, *22*(8), 1052-1056.
99. Dykes, L.; Rooney, L.W. Sorghum and millet phenols and antioxidants. J Cereal Sci. **2006**, *44*(3), 236-251.

100. Dykes, L.; Seitz, L.M.; Rooney, W.L.; Rooney, L.W. Flavonoid composition of red sorghum genotypes. Food Chem. **2009**, *116*(1), 313-317.
101. Dykes, L.; Peterson, G.C.; Rooney, W.L.; Rooney, L.W. Flavonoid composition of lemon-yellow sorghum genotypes. Food Chem. **2011**, *128*(1), 173-179.
102. Carbonneau, M.A.; Cisse, M.; Mora-Soumille, N., et al. Antioxidant properties of 3-deoxyanthocyanidins and polyphenolic extracts from Cote d'Ivoire's red and white sorghums assessed by ORAC and in vitro LDL oxidisability tests. Food Chem. **2014**, *145*, 701-709.
103. Devi, P.S.; Kumar, M.; Mohandas, S. In Vitro Antiproliferative Effects of Anthocyanin Extracted From Red Sorghum (Sorghum Bicolor) Bran On Human Larynx Carcinoma Cell Line. Int J Pharm Pharm Sci. **2012**, *4*(4), 532-536.
104. Awika, J.M.; Yang, L.Y.; Browning, J.D.; Faraj, A. Comparative antioxidant, antiproliferative and phase II enzyme inducing potential of sorghum (Sorghum bicolor) varieties. LWT - Food Sci Technol. **2009**, *42*(6), 1041-1046.
105. Yang, L.Y.; Browning, J.D.; Awika, J.M. Sorghum 3-Deoxyanthocyanins Possess Strong Phase II Enzyme Inducer Activity and Cancer Cell Growth Inhibition Properties. J Agr Food Chem. **2009**, *57*(5), 1797-1804.
106. Yang, L.; Allred, K.F.; Geera, B.; Allred, C.D.; Awika, J.M. Sorghum phenolics demonstrate estrogenic action and induce apoptosis in nonmalignant colonocytes. Nutr Cancer. **2012**, *64*(3), 419-427.
107. Suganyadevi, P.; Saravanakumar, K.M.; Mohandas, S. 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 **2013**, *92*(6-7), 379-382.
108. Hwang, J.M.; Choi, K.C.; Bang, S.J., et al. Anti-oxidant and anti-inflammatory properties of methanol extracts from various crops. Food Sci Biotechnol. **2013**, *22*(1), 265-272.
109. Earp, C.F.; McDonough, C.M.; Awika, J.; Rooney, L.W. Testa development in the caryopsis of Sorghum bicolor (L.) Moench. J Cereal Sci. **2004**, *39*(2), 303-311.
110. Gu, L.; House, S.E.; Rooney, L.W.; Prior, R.L. Sorghum Extrusion Increases Bioavailability of Catechins in Weanling Pigs. J Agric Food Chem. **2008**, *56*, 1283–1288.
111. Chung, I.-M.; Kim, E.-H.; Yeo, M.-A.; Kim, S.-J.; Seo, M.C.; Moon, H.-I. Antidiabetic effects of three Korean sorghum phenolic extracts in normal and streptozotocin-induced diabetic rats. Food Res Int. **2011**, *44*(1), 127-132.
112. Haslam, E. Protein-polyphenol interactions. International Congress and Symposium Series - Royal Society of Medicine. **2000**, (226), 25.
113. Emmambux, N.M.; Taylor, J.R.N. Sorghum kafirin interaction with various phenolic compounds. J Sci Food Agric. **2003**, *83*(5), 402-407.
114. Hagerman, A.E.; Butler, L.G. The specificity of proanthocyanidin-protein interactions. J Agric Food Chem. **1980**, *28*(5), 947-952.
115. Naczk, M.; Shahidi, F. Nutritional implications of canola condensed tannins. Antinutirents and Chemicals in Food: ACS Symposium Series. **1997**, *662*, 186-208.
116. Lizardo, R.; Peiniau, J.; Aumaitre, A. Effect of sorghum on performance, digestibility of dietary components and activities of pancreatic and intestinal enzymes in the weaned piglet. Anim Feed Sci Tech. **1995**, *56*(56), 67-82.
117. Al-Mamary, M.; Al-Habori, M.; Al-Aghbari, A.; Al-Obeidi, A. In vivo effects of dietary sorghum tannins on rabbit digestive enzymes and mineral absorption. Nutr Res. **2001**, *21*, 1393-1401.
118. King, D.; Fan, M.Z.; Ejeta, G.; Asem, E.K.; Adeola, O. The effects of tannins on nutrient utilisation in the White Pekin duck. Br Poult Sci. **2000**, *41*(5), 630-639.
119. Sarni-Manchado, P.; Cheynier, V.; Moutounet, M. Interactions of Grape Seed Tannins with Salivary Proteins. J Agric Food Chem. **1999**, *47*, 42-47.

120. Muriu, J.I.; Njoka-Njiru, E.N.; Tuitoek, J.K.; Nanua, J.N. Evaluation of sorghum (Sorghum bicolor) as replacement for maize in the diet of growing rabbits (Oryctolagus cuniculus). Asian-Aust J Anim Sci. **2002**, *15*, 565-569.
121. Bralley, E.; Greenspan, P.; Hargrove, J.L.; Hartle, D.K. Inhibition of hyaluronidase activity by select sorghum brans. J Med Food. **2008**, *11*(2), 307-312.
122. Burdette, A.; Garner, P.L.; Mayer, E.P.; Hargrove, J.L.; Hartle, D.K.; Greenspan, P. Anti-inflammatory activity of select sorghum (Sorghum bicolor) brans. J Med Food. **2010**, *13*(4), 879-887.
123. Grimmer, H.R.; Parbhoo, V.; McGarth, R.M. Antimutagenicity of polyphenol-rich fractions from Sorghum bicolor grain. J Agr Food Chem. **1992**, *59*, 251-256.
124. Gomez-Cordoves, C.; Bartolome, B.; Vieira, W.; Virador, V.M. Effects of Wine Phenolics and Sorghum Tannins on Tyrosinase Activity and Growth of Melanoma Cells. J Agric Food Chem. **2001**, *49*, 1620-1624.
125. Deosthale, Y.G., Gopalan, C. The effect of molybdenum levels in sorghum (Sorghum vulgare Pers.) on uric acid and copper excretion in man. Br J Nutr. **1974**, *31*, 351-355.
126. Krishnaswamy, K.; Rao, B.; Raghuram, T.C.; Srikantia, S.G. Effect of vitamin B6 on leucine induced changes in human subjects. Am J Clin Nutr. **1976**, *29*, 177-181.
127. Obizoba, I.C.; Ezekwe, M.O.; Akaigwe, B.N. Utilization of sorghum, wheat, and navy beans by human adults: protein metabolism. Nutr Rep Int. **1979**, *20*(3), 291-301
128. Wang, R.S.; Kies, C. Niacin status of humans as affected by eating decorticated and whole-ground sorghum (Sorghum gramineae) grain, ready-to-eat breakfast cereals. Plant Food Hum Nutr. **1991**;41(4):355-369.
129. Schmid, M.A.; Salomeyesudas, B.; Satheesh, P.; Hanley, J.; Kuhnlein, H.V. Intervention with traditional food as a major source of energy, protein, iron, vitamin C and vitamin A for rural Dalit mothers and young children in Andhra Pradesh, South India. Asia Pac J Clin Nutr. **2007**;16(1):84-93.
130. Derman, D.P.; Bothwell, T.H.; Torrance, J.D., et al. Iron absorption from maize (Zea mays) and sorghum (Sorghum vulgare) beer. Brit J Nut. **1980**, *43*, 271-279.
131. Radhakrishnan, M.R.; Sivaprasad, J. Tannin Content of Sorghum Varieties and Their Role in Iron Bioavailability. J Agric Food Chem. **1980**, *28*, 55-57.
132. Gillooly, M.; Bothwell, T.H.; Charlton, R.W., et al. Factors affecting the absorption of iron from cereals. Brit J Nut. **1984**, *51*, 37-46.
133. Haidar, J.; Nekatibeb, H.; Urga, K. Iron deficiency anaemia in pregnant and lactating mothers in rural Ethiopia. East Afr Med J. **1999**, *76* (11), 618-622.
134. Suhasini, G.E.; Krishna, D.R. Influence of unrefined sorghum or maize on serum lipids. Anc Sci Life. **1991**, *1&2*, 26-27.
135. Mani, U.V.; Prabhu, B.M.; Damle, S.S.; Mani, I. Glycaemic index of some commonly consumed foods in western India. Asia Pac J Clin Nutr. **1993**, *2*, 111-114.
136. Lakshmi, K.B.; Vimala, V. Hypoglycemic effect of selected sorghum recipes. Nutr Res. **1996**, *16*(10), 1651-1658.
137. Abdelgadir, M.; Abbas, M.; Jarvi, A.; Elbagir, M.; Eltom, M.; Berne, C. Glycaemic and insulin responses of six traditional Sudanese carbohydrate-rich meals in subjects with Type 2 diabetes mellitus. Diabet Med. **2005**, *22*(2), 213-217.
138. Poquette, N.M.; Gu, X.; Lee, S.O. Grain sorghum muffin reduces glucose and insulin responses in men. Food & function. **2014**, *5*(5), 894-899.
139. Khan, I.; Yousif, A.M.; Johnson, S.K.; Gamlath, S. Acute effect of sorghum flour-containing pasta on plasma total polyphenols, antioxidant capacity and oxidative stress markers in healthy subjects: A randomised controlled trial. Clin Nutr. **2014**, *In Press*.
140. Fedail, S.S.; Badi, S.M.; Musa, R.M. The effects of sorghum and wheat bran on the colonic functions of healthy Sudanese subjects. Am J Clin Nutr **1984**, *40*, 776-779.

141. Cornu, A.; Delpeuch, F. Effects of Dietary Fiber Intake on the Digestibility of Lipids in an African Sorghum-Consuming Population. Ann Nutr Metab. **1986**, *30*, 227-232.
142. Kurien, P.P.; Narayanarao, M.; Kurien, M.; Swaminathan, M.; Subrahmanyan, V. The metabolism of nitrogen, calcium and phosphorus in undernourished children. The effect of partial or complete replacement of rice in poor vegetarian diets by kaffir corn (Sorghum vulgare). Brit J Nut. **1960**, *14*, 339.
143. Nicol, B.M.; Phillips, P.G. The utilization of proteins and amino acids in diets based on cassava (Manihot utilissima), rice or sorghum (Sorghum sativa) by young Nigerian men of low income. Brit J Nutr. **1978**;39(2):271-287.
144. Maclean Jr, W.C.; Lopez De Romana, G.; Placko, R.P.; Graham, G.G. Protein Quality and Digestibility of Sorghum in Preschool Children: Balance Studies and Plasma Free Amino Acids. J Nutr. **1981**, 1928-1936.
145. Dibari, F.; Bahwere, P.; Huerga, H., et al. Development of a cross-over randomized trial method to determine the acceptability and safety of novel ready-to-use therapeutic foods. Nutrition. **2013**;29(1):107-112.
146. Bisimwa, G.; Owino, V.O.; Bahwere, P., et al. Randomized controlled trial of the effectiveness of a soybean-maize-sorghum-based ready-to-use complementary food paste on infant growth in South Kivu, Democratic Republic of Congo. Am J Clin Nutr. **2012**, *95*(5), 1157-1164.
147. Mustafa, S.A.; Karrar, Z.E.; Suliman, J.I. Cereal-based oral rehydration solutions in Sudanese children with diarrhoea: a comparative clinical trial of rice-based and sorghum-based oral rehydration solutions. Ann Trop Paediatr. **1995**;15(4):313-319.
148. Molla, A.M.; Molla, A.; Nath, S.K.; Khatun, M. Food-based oral rehydration salt solution for acute childhood diarrhoea. Lancet. **1989**;2(8660):429-431.
149. Pelleboer, R.A.; Felius, A.; Goje, B.S.; Gelderen, H.H. Sorghum-based oral rehydration solution in the treatment of acute diarrhoea. Trop Geogr Med. **1990**;42(1):63-68.
150. Vazquez-Araujo, L.; Chambers, E.; Cherdchu, P. Consumer input for developing human food products made with sorghum grain. J Food Sci. **2012**, *77*(10), S384-389.
151. Muhihi, A.; Gimbi, D.; Njelekela, M., et al. Consumption and acceptability of whole grain staples for lowering markers of diabetes risk among overweight and obese Tanzanian adults. Global Health. **2013**, *9*.
152. Motswagole, B.S.; Mongwaketse, T.C.; Mokotedi, M., et al. The efficacy of micronutrient-fortified sorghum meal in improving the immune status of HIV-positive adults. Ann of Nutr Metab. **2013**;62(4):323-330.
153. Ayuba, G.I.; Jensen, G.S.; Benson, K.F.; Okubena, A.M.; Okubena, O. Clinical Efficacy of a West African Sorghum bicolor-Based Traditional Herbal Preparation Jobelyn Shows Increased Hemoglobin and CD4+ T-Lymphocyte Counts in HIV-Positive Patients. J Altern Complement Med. **2014**, *20*(1), 53-56.
154. Featherstone, W.R. Influence of tannins on the utilization of sorghum grain by rats and chicks. Nutr Rep Int. **1975**, *11*(6), 491.
155. Cousins, B.W.; Tanksley Jr., T.D.; Knabe, D.A.; Zebrowska, T. Nutrient digestibility and performance of pigs fed sorghums varying in tannin concentration. J Anim Sci. **1981**, *53*(6), 1524-1537.
156. Liu, S.; Willett, W.C.; Manson, J.E.; Hu, F.B.; Rosner, B.; Colditz, G. Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle-aged women. Am J Clin Nutr. **2003**, *78*, 920-927.
157. Lairon, D.; Arnault, N.; Bertrais, S., et al. Dietary fiber intake and risk factors for cardiovascular disease in French adults. Am J Clin Nutr. **2005**, *82*, 1185–1194.
158. Flint, H.J. The impact of nutrition on the human microbiome. Nutr Rev. **2012**, *70 Suppl 1*, S10-13.

159. Shen, R.L.; Zhang, W.L.; Dong, J.L.; Ren, G.X.; Chen, M. Sorghum resistant starch reduces adiposity in high-fat diet-induced overweight and obese rats via mechanisms involving adipokines and intestinal flora. Food Agric Immunol. **2014**, *In Press*.
160. Appleton, D.J.; Rand, J.S.; Priest, J.; Sunvold, G.D.; Vickers, J.R. Dietary carbohydrate source affects glucose concentrations, insulin secretion, and food intake in overweight cats. Nutr Res. **2004**, *24*(6), 447-467.
161. Kim, J.; Park, Y. Anti-diabetic effect of sorghum extract on hepatic gluconeogenesis of streptozotocin-induced diabetic rats. Nutr Metab. **2012**, *9*(106), 1-7.
162. Park, J.H.; Lee, S.H.; Chung, I.M.; Park, Y. Sorghum extract exerts an anti-diabetic effect by improving insulin sensitivity via PPAR-gamma in mice fed a high-fat diet. Nutr Res Pract. **2012**, *6*(4), 322-327.
163. Cervantes-Pahm, S.K.; Liu, Y.; Stein, H.H. Comparative digestibility of energy and nutrients and fermentability of dietary fiber in eight cereal grains fed to pigs. J Sci Food Agric. **2014**, *94*(5), 841-849.
164. Dixit, A.A.; Azar, K.M.; Gardner, C.D.; Palaniappan, L.P. Incorporation of whole, ancient grains into a modern Asian Indian diet to reduce the burden of chronic disease. Nutr Rev. **2011**, *69*(8), 479-488.
165. Chung, I.M.; Yeo, M.A.; Kim, S.J.; Kim, M.J.; Park, D.S.; Moon, H.I. Antilipidemic activity of organic solvent extract from Sorghum bicolor on rats with diet-induced obesity. Hum ExpToxicol. **2011**, *30*(11), 1865-1868.
166. Cho, S.H.; Ha, T.Y. In vitro and in vivo effects of prosomillet and sorghum on cholesterol metabolism. Food Sci Biotechnol. **2003**, *12*(5), 485-490.
167. Hoi, J.T.; Weller, C.L.; Schlegel, V.L.; Cuppett, S.L.; Lee, J.-Y.; Carr, T.P. Sorghum distillers dried grain lipid extract increases cholesterol excretion and decreases plasma and liver cholesterol concentration in hamsters. J Funct Foods. **2009**, *1*(4), 381-386.
168. Klopfenstein, C.F.; Varriano-Marston, E.; Hoseney, R.C. Cholesterol-lowering effect of sorghum diet in guinea pigs. Nutr Rep Int. **1981**, *24*, 621–626.
169. Lee, S.H.; Chung, I.M.; Cha, Y.S.; Park, Y. Millet consumption decreased serum concentration of triglyceride and C-reactive protein but not oxidative status in hyperlipidemic rats. Nutr Res. **2010**, *30*(4), 290-296.
170. Lee, S.M.; Pan, B.S. Effect of dietary sorghum distillery residue on hematological characteristics of cultured grey mullet (Mugil Cephalus) - An animal model for prescreening antioxidant and blood thinning activities. J Biotechnol. **2003**, *27*, 1-18.
171. Loefler, I.J.P. Sorghum in oesophageal cancer. Lancet. **1985**, *2* (8454), 562.
172. Van Rensburg, S.J. Epidemiologic and dietary evidence for a specific nutritional predisposition to esophageal cancer. J Natl Cancer Inst. **1981**, *67*(2), 243-251.
173. Chen, F.; Cole, P.; Mi, Z.; Xing, L.Y. Corn and wheat-flour consumption and mortality from esophageal cancer in Shanxi, China. Int J Cancer. **1993**, *53*(6), 902-906.
174. Isaacson, C. 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 Hypothoses. **2005**, *64*(3), 658-660.
175. Park, J.H.; Darvin, P.; Lim, E.J., et al. Hwanggeumchal sorghum induces cell cycle arrest, and suppresses tumor growth and metastasis through Jak2/STAT pathways in breast cancer xenografts. PLoS One. **2012**, *7*(7), e40531.
176. Wu, L.; Huang, Z.; Qin, P., et al. Chemical characterization of a procyanidin-rich extract from sorghum bran and its effect on oxidative stress and tumor inhibition in vivo. J Agric Food Chem. **2011**, *59*(16), 8609-8615.
177. Beck, E.J.; Tosh, S.M.; Batterham, M.J.; Tapsell, L.C.; Huang, X.F. Oat beta-glucan increases postprandial cholecystokinin levels, decreases insulin response and extends

subjective satiety in overweight subjects. Molecular nutrition & food research. **2009**, *53*(10), 1343-1351.
178. Hall, R.S.; Baxter, A.L.; Fryirs, C.; Johnson, S.K. Liking of health-functional foods containing lupin kernel fibre following repeated consumption in a dietary intervention setting. Appetite. **2010**, *55*(2), 232-237.
179. National Health and Medical Research Council. *Final guidance general level health claims Sept 2013*. Canberra: NHMRC; 2013.
180. Sacks, F.M.; Bray, G.A.; Carey, V.J., et al. Comparison of Weight-Loss Diets with Different Compositions of Fat, Protein, and Carbohydrates. New Engl J Med. **2009**, *360*(9), 859-873.
181. Kamath, V.G.; Chandrashekar, A.; Rajini, P.S. Antiradical properties of sorghum (Sorghum bicolor L. Moench) flour extracts. J Cereal Sci. **2004**, *40*(3), 283-288.
182. Oboh, G.; Akomolafe, T.L.; Adetuyi, A.O. Inhibition of Cyclophosphamide-Induced Oxidative Stress in Brain by Dietary Inclusion of Red Dye Extracts from Sorghum (Sorghum bicolor) Stem. J Med Food. **2010**, *13*(5), 1075-1080.
183. Moraes, E.A.; Natal, D.I.G.; Queiroz, V.A.V., et al. Sorghum genotype may reduce low-grade inflammatory response and oxidative stress and maintains jejunum morphology of rats fed a hyperlipidic diet. Food Res Int. **2012**, *49*(1), 553-559.
184. Ajiboye, T.O.; Komolafe, Y.O.; Oloyede, H.O.B., et al. Diethylnitrosamine-induced redox imbalance in rat microsomes: Protective role of polyphenolicrich extract from Sorghum bicolor grains. J Basic and Clin Physiol Pharmacol. **2013**, *24*(1), 41-49.
185. He, J.; Giusti, M.M. Anthocyanins: natural colorants with health-promoting properties. Ann Rev Food Sci Technol. **2010**, *1*, 163-187.