

ASERTAINING SORGHUM [*Sorghum bicolor* (L.) Moench] AS AN ANTIDIABETIC PLANT

ABSTRACT

Sorghum, an ancient grain crop with origins in Egypt, holds significant dietary benefits for diabetes. As the fifth most consumed grain globally, it serves as a staple in cereal production and is utilized in various forms, including food, animal feed, and bio-available fuel. Being gluten-free, sorghum is a common ingredient in gluten-free flour blends. The grain's dietary advantages stem from its rich composition of fibre, tannins, phenols, antioxidants, phytochemicals, proteins, vitamins, minerals, and its low-glycemic status. Regular consumption of whole grains, like sorghum, has been linked to a 20-30% reduction in heart disease and diabetes risk, improving blood glucose control. Sorghum-based foods exhibit lower glycemic index and load compared to other cereals, suggesting potential benefits in managing postprandial blood glucose levels for diabetes prevention. Human studies show that sorghum muffin consumption leads to a significant reduction in plasma glucose and insulin levels. Cooking methods, recipes, and functional drinks made from sorghum bran also influence starch digestibility, impacting carbohydrate metabolism and the overall anti-diabetic effects of sorghum. *In vitro* studies reveal that decorticated sorghum grains contain substantial flavonoids, making them promising candidates for preventing and treating diabetes and obesity. Anti-diabetic experiments involving oral administration of sorghum grain extract demonstrate a noticeable reduction in blood glucose concentration by inhibiting hepatic gluconeogenesis. Additionally, sorghum extract improves insulin sensitivity through peroxisome proliferator-activated receptor gamma (PPAR- γ). Fermented sorghum diets show effectiveness against hyperglycemia and inhibit glucose utilization in the liver. Polyphenol-containing sorghum extract affects plasma lipid metabolism and chronic inflammation by upregulating AMP-activated protein kinase (AMPK) and acetyl-CoA carboxylase. Studies report that sorghum's anti-diabetic effects are comparable to pharmaceuticals like glibenclamide and acarbose. Integrating sorghum into the regular diet emerges as a contemporary strategy for preventing obesity and diabetes, promoting overall human health. Ongoing research focuses on tannin-rich sorghum genotypes to identify their potential anti-diabetic effects.

Keywords: Sorghum, Diabetes, Phenols, Tannins, Flavanoids, Glycemic index.

1. Introduction

Sorghum [*Sorghum bicolor*(L.) Moench], the major cereal crops of the semi-arid tropics and is the fifth most important crop of the world after wheat, rice, maize and pearl millet. It is the staple food in arid and semi-arid parts of the world, due to its drought tolerance property. It is commonly known as Jowar and known to be originated and domesticated in Africa about 5000–8000 years ago [1]. Indian subcontinent is the secondary origin of this most important cereal with high diversity and is distributed throughout India.

Sorghum has several uses. It is used primarily as food for human consumption. It is used for the preparation of various food items like roti, porridge, syrup, alcoholic beverages, malted beverages, flaked cereal, sorghum pops and tortillas. Flour from white sorghum is being used for its mild flavor in exploring many applications such as cookies, cakes, brownies, bread, pizza dough, pastas, pancakes, waffles and more. It is also used as fodder for livestock and also for extraction of ethanol as biofuel, starch, adhesives and paper. Its stalks being utilized for fencing, firewood or for making brooms. The fibre can be used commercially to make wallboards and biodegradable packaging material [2] and even solvents or dye can be extracted from the plant.

Sorghum is an often-cross pollinated crop; diploid ($2n = 2x = 20$) with a genome of about 25% the size of maize or sugarcane. It is a C_4 plant with higher photosynthetic efficiency and higher abiotic stress tolerance. It's small genome (730 Mbp) makes sorghum an attractive model for functional genomics of C_4 grasses.

Sorghum is cultivated in India in an area of about 5624.42 thousand hectares and production was 4567.90 thousand tonnes with productivity of 812 kg/ha during 2016-17. Among Indian states, Maharashtra stands first in area and production followed by Karnataka. Sorghum is grown both during rainy (*kharif*) and post rainy (*rabi*) seasons. Post rainy sorghum is primarily used as food owing to its good grain quality and also serves as a main source of stover, especially during dry seasons.

Sorghum can act as an important grain to cope up with food security, nutritional security at lower cost [3]. It is an important source of minerals, vitamins, proteins, antioxidants and energy. The absence of gluten makes the crop very special and safe for people with celiac disease [4].

2. Plant structure

Sorghum bicolor L. Moench is an ancient, cereal grain crop that belongs to the grass family Poaceae. The plant consists of roots, a stalk, leaves of various shape and sizes, and a panicle, or seed head. The grains are called kernels or caryopsis may vary in size and shape, but are usually spherical to tear drop shaped and range from 4-8 mm in diameter. Glumes cover the caryopsis. Colour of the caryopsis varies between several shades of white, yellow, bronze, brown, black, pink, purple and reddish.

3. Structure of the grain or caryopsis

As it is a cereal grain, the average caryopsis consists of three main components: 6% pericarp, 10% germ, and 84% endosperm. The thick pericarp is then further divided into three layers: epicarp, mesocarp and endocarp (Figure 1). The testa layer resides under the pericarp and may be absent, partially present, or fully present depending on genetic control. The aleurone layer is a single layer of cells surrounding the endosperm. The endosperm contains both vitreous (corneous) and opaque (floury) endosperm [5]. The germ contains the embryonic axis and the scutellum[5, 6].

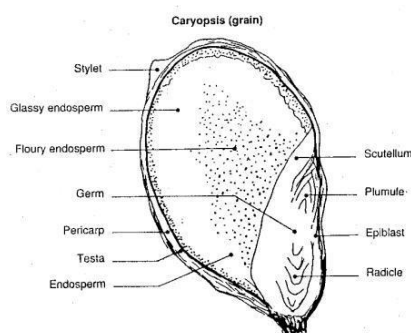


Figure 1: Structure of sorghum grain

4. Chemical composition of the grain or caryopsis

Sorghum grain, abundant in macronutrients, micronutrients, and antioxidants, exhibits varied composition influenced by factors like variety and environmental conditions. Starch predominates as the main constituent, accompanied by protein, lipids, non-starch polysaccharides, and phytochemicals like phenolic compounds, phytosterols, and policosanols. Sorghum grain is a source of dietary fibre, featuring resistant starch and various micronutrients such as vitamins and minerals, along with oil bodies and waxes. The kernel coat is particularly rich in polyphenolic compounds, flavonoids, anthocyanins, and anthocyanidins, contributing to the diverse colours of the grain [7].

Sorghum whole grain's proximate nutritional composition comprises an energy density of 1377 kJ/100g dry weight, with total carbohydrates at 74.6g, fat at 3.3g, and protein at 11.3g/100g dry weight[8].

4.1. Starch

Sorghum grain is a major starch source, comprising approximately 71% of the dry whole grain weight [9]. Most of the starch is in the endosperm, with a smaller portion in the

pericarp's mesocarp layer. The two starch polymers present are highly branched amylopectin (70-80%) and linear amylose (20-30%) [10]. There are a few varieties of waxy sorghum that will contain almost entirely amylopectin [5]. In normal (nonwaxy) grain sorghum, starch content ranges from 60% to 75% of the total starch, with 14% to 31% of the starch being amylose. Special grain sorghums including waxy sorghum and high amylose sorghum, contains extremely high amylopectin and amylose content, respectively. The amylose content in waxy sorghum can be as low as 0 - 5%, while high amylose sorghum may contain up to 70% amylose.

Non-Starch Polysaccharides (NSP) constitute the main dietary fiber component in sorghum grain, located in pericarp and endosperm cell walls. Composition varies among cultivars, comprising 2-7% of the total grain weight [11,12]. Sorghum NSPs consist of cellulose and non-cellulosic elements, including arabinose, xylose, mannose, galactose, glucose, and uronic acid monomers [13,14]. Key non-cellulosic polysaccharides in sorghum are predominantly water-insoluble glucuronoarabinoxylans (GAX) and β -glucans [15]. However, sorghum's natural β -glucans are relatively lower compared to barley and oats [16,17]. Abundant in sorghum, glucuronoarabinoxylans (GAX) are extensively substituted with glucuronic acid residues, acetyl, and feruloyl compounds. Additionally, sorghum contains non-carbohydrate cell-wall components, such as lignins, constituting up to 20% of the total cell wall content by dry weight [18].

4.2. Proteins

Sorghum grain, comprising approximately 6-18% protein, ranks as the second-largest component after starch [19]. The proteins in sorghum fall into categories including albumins, globulins, kafirins (prolamin), cross-linked kafirins, and glutelins [20]. Kafirins, constituting 50-70% of the total protein content, stand out as the predominant protein in sorghum [21]. While lysine is the limiting amino acid, certain sorghum varieties do exhibit higher lysine levels. Sorghum kafirins display poor digestibility, attributed to cross-linking, particularly when subjected to moist cooking, leading to protease resistance [22]. Lin *et al.* (2013) [23] extensively reviewed a varied range of bioactive peptides in sorghum grain.

4.3. Lipids

Sorghum grain comprises approximately 3-4% lipids, mainly neutral triglycerides, with a higher concentration of unsaturated fatty acids, predominantly located in the germ [24]. Key fatty acids include 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%) [9, 25]. Certain sorghum varieties contain uncommon saturated fatty acids, namely octanedioic (C8:0) and azelaic acid (C9:0) [25]. Sorghum also includes policosanols, a blend of long-chained primary alcohols.

Sorghum wax, found on the grain kernel's surface, is mainly composed of docosanol (C22), tetracosanol (C24), hexacosanol (C26), octacosanol (C28), triacontanol (C30), and dotriacontanol (C32) (Irmak *et al.*, 2006). The prevalent policosanols in sorghum are C28 and C30 [26]. Sorghum's lipid profile, rich in monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA), particularly with elevated PUFA levels compared to MUFA, has generated interest as a potential source of edible oil [25]. This lipid composition is advantageous for mechanisms that can reduce lipid levels in humans, potentially lowering risk factors associated with heart disease.

4.4. Phytochemicals

Except for white sorghums, most sorghum varieties are rich in phytochemicals, particularly phenolic compounds, known for their potent antioxidant activity and associated health benefits [27, 28, 29]. Remarkably, the bran of certain sorghum grain varieties is reported to possess the highest antioxidant activity among cereal crop fractions, surpassing many fruits and vegetables. Certain sorghum bran varieties demonstrate markedly superior antioxidant activity, reaching up to two orders of magnitude higher than oat bran and wheat cereal, and one order of magnitude surpassing rice bran. Antioxidant levels vary depending on the specific sorghum variety [27].

4.5. Phenolic compounds

Certain sorghum grain varieties stand out among cereal grains for their rich and diverse phenolic compounds, surpassing others in both abundance and variety [30]. The highest levels of these compounds are found in varieties with pigmented testa and thick pericarps, as highlighted in research by [31]. Phenolic compounds in sorghum grains, primarily found in the bran, particularly the testa and pericarp, can be classified into three main groups: 1) phenolic acids (hydrobenzoic 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. These compounds display robust antioxidant activity by effectively scavenging free radicals [30].

4.6. Flavonoids

Flavonoids, the primary phenolic compounds in sorghum, are predominantly present in the sorghum bran. The types and concentrations of these flavonoids are associated with pericarp colour, thickness, and the presence of pigmented testa, as documented by [30, 31]. Essential in plants, these compounds form the abundant and diverse phenolics in sorghum. Flavonoids, defined by the fundamental flavan skeleton, are classified by the presence of a C2–C3 double bond and substituent groups on the C ring, as outlined by [32]. Sorghum exhibits a variety of flavonoids, such as anthocyanins (3-deoxyanthocyanidins), flavones, flavanones, flavan-3-ols, flavan-4-ols, flavonols, and dihydroflavonols, as documented by [33] and [34]. Notably, the prevalent flavonoids in sorghum include 3-deoxyanthocyanidins, flavones, and flavanones.

4.6.1. **Flavones:** Flavones, prominent yellow-coloured flavonoids found in a variety of foods like fruits, vegetables, legumes, and cereal grains, have a content range of approximately 20 to 390 µg/g in sorghum grain—a relatively lower concentration compared to other flavonoids [35]. Certain flavonoids, like luteolin, are naturally present as glycosides, while others, such as apigenin, predominantly exist in aglycone forms, as highlighted by [36, 37]. Prevalent O-glycosides in sorghum display high instability in acidic conditions, rapidly undergoing hydrolysis of glycosidic bonds and forming aglycones. The prevailing flavones in sorghum are the aglycone forms of luteolin and apigenin, known for their vulnerability to acidic conditions [37, 38]. Luteolin and apigenin commonly appear as the primary flavones in sorghum, as reported by [39]. Commonly found in sorghum, O-glycosides exhibit superior bioaccessibility compared to C-glycosides, readily undergoing hydrolysis in the acidic stomach environment. This enhanced bioavailability, even at low concentrations, contributes to the greater abundance of sorghum flavones compared to other cereals [37]. Notably, sorghum varieties with red and yellow pericarp are well-known for their elevated flavone levels, as documented by [38-40].

4.6.2. **Flavanones:** Flavanones, mainly exemplified by naringenin and its derivatives, are commonly found in diverse food plants, playing essential roles in flavonoid

biosynthesis. However, their presence in cereal grains is typically rare, with sorghum being a notable exception. Some sorghum varieties stand out for having the highest flavanone levels among food plants, a departure from the general scarcity of flavanones in cereals [33,41]. Sorghum's flavanone content ranges from 0 to 2,000 µg/g, with white sorghum displaying the lowest levels and yellow pericarp sorghum showing the highest concentrations [37, 38,42]. Sorghum's major flavanones include naringenin and eriodictyol glycosides, with their aglycones and O-methylated derivatives being relatively scarce [36, 37, 43]. Like flavones, the predominant O-glycosides of flavanones are sensitive to low pH, facilitating easy hydrolysis and increased bioavailability[37].

- 4.6.3. **3-Deoxyanthocyanidins:** Sorghum's distinctive flavonoid composition includes a unique feature—its anthocyanin content. Sorghum's anthocyanins fall into the uncommon category of 3-deoxyanthocyanidins, characterized by C-3-deoxylated analogs. The primary 3-deoxyanthocyanidins in sorghum are apigeninidin and luteolinidin aglycones, as identified in studies by [30] and [44]. 3-Deoxyanthocyanidins, among the most prevalent flavonoids in sorghum, can range from 200 to 4,500 µg/g in specific sorghum varieties. Comprising potentially 80% of the total flavonoids in sorghum grain, these anthocyanins exhibit particularly high accumulation in the bran layer—four to five times more than in the whole grain. Sorghum varieties with a red pericarp genotype (R Y) are recognized for their notable richness in 3-deoxyanthocyanidins, as indicated by studies conducted by [34, 35, 27,28]. Among red pericarp sorghum genotypes, the bran of black sorghum (genotypically red but phenotypically black) stands out with the highest levels of 3-deoxyanthocyanidins, ranging from 1,790 to 6,120 µg/g. This concentration is at least twice as high as those observed in the bran of red (both genotypically and phenotypically red) and brown sorghum (red genotype with pigmented testa), as reported by [28, 31, 40, 45]. Apart from contributing vibrant colours to plants, 3-deoxyanthocyanidins demonstrate potent antioxidant and antimicrobial properties, positioning sorghum as a primary dietary source for these beneficial compounds in human nutrition [44]. Sorghum holds a prominent status as a key dietary provider of 3-deoxyanthocyanidins in human diets.

4.7. Condensed tannins

Sorghum polyphenols, particularly tannins, specifically in the form of condensed tannins or proanthocyanidins, have undergone extensive study. Distinctive to sorghum, its tannins are condensed, showcasing a noteworthy molecular weight and a substantial degree of polymerization (DP), a trait uncommon among major cereals [46]. Comprising primarily of oligomers or polymers of flavan-3-ol and flavan-3,4-diol, sorghum condensed tannins are linked predominantly through B-type linkages, with an average degree of polymerization (DP) around 20. Sorghum's tannins stand out from those in other cereal grains, typically having a DP ranging from 3 to 10 [35, 47]. Despite containing low molecular weight forms like monomers (mainly catechin) and dimers (mainly procyanidin B1), sorghum grain has these components in relatively small quantities [48]. Sorghum varieties exhibit significant tannin content variations, leading to classification into three types based on genotype, tannin concentration, and extractability. Type I sorghums have negligible or very low tannin levels (0 to 1.8 mg CAE/g) due to recessive B1 and/or B2 genes and the absence of pigmented testa. Type II sorghums, with dominant B1 and B2 genes but a homozygous recessive S gene, show moderate tannin levels (6.4 to 15.5 mg CAE/g), primarily located in testa vesicles and extractable with acidified methanol. Type III sorghums, characterized by dominant B1, B2, and S genes, possess elevated tannin levels (11 to 50.2 mg CAE/g), mainly in testa cell walls and the pericarp, extractable by methanol or acidified methanol [47, 49, 50]. Sorghum varieties with pigmented testa typically exhibit elevated condensed tannin content, with type III sorghums demonstrating some of the highest concentrations—surpassing those in other tannin-containing cereals by more than 10 times [35, 45].

4.8. Vitamins and minerals

Sorghum is recognized as a rich source of vitamins B and E, particularly with yellow pigmented sorghum providing β -carotene, a precursor converted into vitamin A in the body [6]. Additionally, sorghum is acknowledged for its nutritional value, serving as a good source of over 20 minerals. The average gelatinization temperature of isolated sorghum starch falls within the range of 75.3 to 78.4°C.

4.9. Functional Starch

Starch represents the major source of available carbohydrate in the human diet. There are two structures of starch defined by its linkage. Amylose is the starch molecule specified by highly linear structure linked by alpha 1→4 linkage, while amylopectin have more alpha 1→6 linkages, which make it highly branched and easily hydrolysed. The ratios of amylose

and amylopectin vary largely in starches from different sources, which generate diverse starch structure, physiological effects and digestibility.

For nutritional purposes, starch is also classified into rapidly digestible starch (RDS), slowly digestible starch (SDS) and resistant starch (RS) (Berry, 1986). RDS is the starch fraction that is converted to glucose by enzymes in 20 min. RDS is mainly amorphous starch in food cooked in high moist conditions, such as baked potato and bread. The category of SDS includes enzyme inaccessible starch and raw starch that is fully hydrolysed *in vitro* during prolonged incubation (20–120 min). SDS may include both amorphous and crystalline starch that cannot be digested immediately in small intestine for its granule sizes or retrogradation. Resistant starch is the starch fraction that is not hydrolysed after 120 min incubation with α -amylase and pullulanase and calculated by subtracting SDS and RDS from the total starch content. SDS and RS fractions are usually considered as functional starch. The low digestibility of SDS and RS can attribute to granule size, amylose ratio, processing conditions. Resistant starch family is further categorized into five different types by their resistant mechanisms [51, 52].

RS was widely reported for its health benefits in blood glucose control and diabetes' prevention. Since RS is not digestible within small intestine, food rich in RS can prevent a sudden rise of postprandial blood glucose and insulin. Human study demonstrated that the RS intake could significantly reduce postprandial plasma glucose, insulin and satiety hormones including gastric inhibitory polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) [53].

SDS has been noted for its medium to low glycemic index (GI) [54]. Foods rich in SDS were reported for a significantly lower glycemic load when compared with foods high in RDS with a higher GI [54, 55]. Significant reduction was observed in blood glucose, insulin after the consumption of SDS than consumption of RDS in a few studies [54, 56]. According to Mayer's theory [57], low blood glucose could trigger feeding manner and high blood glucose could trigger satiety. Based on this theory, the consumption of food rich in SDS can maintain a prolonged glucose and insulin response, which may increase satiety. Though studies on the direct relation of SDS and satiety are limited, the significant findings of SDS on glycaemic control make it an important study focus on diabetes prevention.

Grain sorghum contains higher content of resistant starch (RS), which affects its digestibility. Raw grain sorghum contains 40 – 65% of RS, while the RS content of cooked sorghum ranges from 05-20%, correlated to their cultivars. Grain sorghum usually has the lowest starch digestibility among all cereals. Factors affecting sorghum starch digestibility may include starch-protein matrix, amylose content, presence of tannins, endosperm texture

(vitreous or floury), and cooking conditions. Most of the starch exists in granule form embedded within a protein matrix. Some sorghum cultivars contain high level of tannin, which may decrease the activity of α -amylase and thus reduce the digestibility of starch in whole sorghum products. Tannin is a polyphenolic compound unique in sorghum among all cereals. Condensed tannin isolated from sorghum grain has showed to inhibit α -amylase activity and hence, reduce starch digestibility [58]. Starch-protein interaction also exerts a strong influence in sorghum's starch digestibility. Grain sorghum has a protein range of 07 to 15%. Among the varieties of proteins, a prolamin (alcohol soluble protein) - kafirins comprise about 50-70% of the proteins [59, 60, 61]. The kafirins, mainly in endosperm, wrap the starch granules and greatly inhibit water penetration and enzymatic digestion. The presence of kafirins significantly decreases the digestibility of sorghum starch[62, 63].

Experimental evidences for Sorghum on diabetes control

Diabetes mellitus (DM) is a metabolic disorder leading to elevated blood glucose levels due to inadequate insulin action or secretion. Type 1 DM, also known as juvenile diabetes, is characterized by a complete absence of insulin, attributed to the autoimmune destruction of pancreatic beta cells [64]. DM impacts carbohydrate, lipid, and protein metabolism by modifying enzymatic activities in essential pathways such as gluconeogenesis, glycolysis, lipolysis, and the pentose phosphate pathway [65]. Insulin, a pivotal regulator facilitating glucose uptake through glucose transporters, is central to cellular processes. Glucose absorption stimulates hepatic glucokinase (GK), initiating the activation of phosphofructokinase-1 (PFK-1), the key enzyme regulating glycolysis. This activation facilitates the swift conversion of glucose into pyruvate. In the absence of sufficient insulin, prolonged elevated blood glucose levels promote lipid peroxidation, increasing the generation of reactive oxygen species (ROS). Consequently, this leads to damage to macromolecular components and compromises the antioxidant defense system [66].

The increasing prevalence of diabetes mellitus (DM) has prompted exploration of natural remedies and dietary interventions as safer alternatives for managing the disease, given the potential side effects associated with various antidiabetic medications[67]. *Sorghum bicolor*, a grain consumed by both animals and humans, is known for its rich phytochemical content with reported properties of lowering glucose and cholesterol levels. Processing methods like flour production, fermentation, and malting contribute to the creation of processed sorghum foods for human consumption [68]. Fermenting foods offers numerous health benefits, enhancing flavour, texture, nutritional value, and extending shelf life [69].

"Ogi" or "oka-baba," a prevalent fermented cereal, is a staple derived from sorghum, millet, maize, or guinea corn (*Sorghum spacers*), contributing to improved bioavailability of nutrients and carbohydrate digestibility. Widely consumed by individuals of all ages, it serves as a popular weaning food for children [48, 69]. Both unfermented sorghum grains [48, 70] and their fermented counterparts have been studied for their phytochemical composition. Caffeic acid, a key phytochemical in fermented sorghum, shows promise in diabetes treatment. The traditional utilization of fermented sorghum is credited to its antioxidant and antibacterial properties, specifically in addressing diarrhoea [71]. The analysis of "ogi" extract has revealed notable bioactive compounds like quercetin, caffeic acid, hesperidin, and rosmarinic acid. Understanding how the sorghum diet imparts its hypoglycemic properties can aid in addressing diabetes challenges. With the escalating costs of antidiabetic drugs, there is an increasing demand for alternative approaches, including nutritional strategies, to prevent the disease, especially in developing countries.

In a study by [72], alloxan-induced diabetic rats were used to investigate the protective and modulatory effects of a sorghum diet on genes related to antioxidant and glycolytic enzymes. Rats were randomly divided into six groups. The control group received a normal diet, while the remaining groups were pretreated with daily doses of 12.5%, 25%, 50%, 75%, and 100% sorghum diets for 8 weeks before alloxan administration (100 mg/kg BW). Evaluating sorghum diets' effects on alloxan-induced diabetic rats, they assessed blood glucose levels, liver function indices, oxidative stress markers, and the gene expressions of glycolytic enzymes and enzymatic antioxidants. Sorghum diet pre-treatment normalized blood glucose levels both before and after alloxan administration. Moreover, the sorghum-treated groups showed a marked decrease in liver dysfunction indices and oxidative damage markers compared to the control. The diets significantly reduced the relative expression of genes linked to superoxide dismutase, glutathione peroxidase, glucokinase, phosphofructokinase, and hexokinase in comparison to the control group. The research concluded that pre-administering a fermented sorghum diet provided substantial protection against hyperglycemia, suppressing glucose utilization through glycolysis in the livers of alloxan-induced diabetic rats. Consequently, consuming a sorghum diet may function as a beneficial food in managing diabetes mellitus, providing protection against hyperglycemia and oxidative damage.

Chronic hyperglycemia poses a high-risk factor for progressive chronic liver diseases, including abnormal lipid metabolism. AMP-activated protein kinase (AMPK) activation has a beneficial impact on dyslipidemia, and various plant-derived polyphenols are implicated in

this activation. [73] conducted a study using streptozotocin-induced diabetic rats receiving oral doses of 0, 50, or 250 mg/kg of sorghum extract over a 4-week period. The study examined blood chemistry, total and phosphorylated protein levels of AMPK and ACC, sterol regulatory element-binding protein-1c (SREBP-1c) mRNA and protein levels, as well as macrophage infiltration in the livers. They noted elevated plasma glucose and triacylglycerol levels in untreated diabetic rats, with significantly lower levels observed in diabetic rats treated with 250 mg/kg of sorghum extract (SE). The phosphorylation levels of AMPK and ACC were notably increased in the 250 mg/kg SE-treated diabetic rats compared to untreated rats. The findings suggest that SE treatment may influence plasma lipid metabolism and chronic inflammation by upregulating the phosphorylation of AMPK and ACC in the livers of diabetic rats.

[74] conducted a six-week study to assess the effects of oral administration of sorghum extract (SE) on hepatic gluconeogenesis and muscle glucose uptake in streptozotocin-induced diabetic rats. The Male Wistar rats were categorized into five groups (n=5 per group): normal control (NC), rats with streptozotocin-induced diabetes mellitus (DM), diabetic rats administered 0.4 g/kg body weight of SE (DM-SE 0.4) and 0.6 g/kg body weight of SE (DM-SE 0.6), and diabetic rats administered 0.7 mg/kg body weight of glibenclamide (DM-G). They observed that the administration of sorghum extract (SE) and glibenclamide (G) reduced concentrations of triglycerides, total and LDL-cholesterol, and glucose in non-diabetic rats. Moreover, the administration of 0.4 and 0.6 g/kg SE and 0.7 mg/kg glibenclamide significantly reduced the expression of phosphoenolpyruvate carboxykinase and the phosphor-p38/p38 ratio. They also noted an increase in the phosphor adenosine monophosphate-activated protein kinase (AMPK)/AMPK ratio. However, only the administration of G significantly increased glucose transporter 4 translocation and the phosphor-Akt/Akt ratio. Their conclusion suggested that the hypoglycemic effect of SE was linked to hepatic gluconeogenesis rather than the glucose uptake of skeletal muscle, with the effect resembling that of anti-diabetic medication.

[75] conducted an assessment of the antidiabetic effects of phenolic extracts derived from three Korean sorghum varieties (Hwanggeumchal sorghum, Chal sorghum, and Heuin sorghum) in both normal and streptozotocin-induced diabetic rats. Their findings highlighted the notable hypoglycemic activity of Hwanggeumchal sorghum phenolic extracts in streptozotocin-induced diabetic rats over a 14-day period. Additionally, significant reductions were observed in serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine,

aspartate aminotransferase, and alanine aminotransferase activities in diabetic rats, while serum insulin content increased, particularly at doses of 100 and 250 mg/kg over the 14-day duration. They also compared the efficacy of Hwanggeumchal sorghum phenolic extracts with glibenclamide (600 µg/kg), a recognized antidiabetic drug. The antidiabetic effects of Hwanggeumchal sorghum phenolic extracts were found to be similarly effective to those observed with glibenclamide. In their analysis, 29 phenolic components were detected in Korean sorghum. The correlation between antidiabetic effects and phenolic components in Hwanggeumchal sorghum phenolic extracts was notably higher compared to Chal sorghum and Heuin sorghum phenolic extracts.

Several studies have highlighted the crucial role of adipocytokines, such as tumor necrosis factor- α (TNF- α) and adiponectin, secreted by adipocytes in maintaining normal metabolic homeostasis and influencing the development of type 2 diabetes and dyslipidemia [76-78]. Thiazolidinedione agonists, which activate peroxisome proliferator-activated receptor- γ (PPAR- γ) and are commonly used in managing type 2 diabetes, have been shown to enhance endogenous insulin sensitivity by inducing adiponectin gene expression [79-81]. TNF- α levels are significantly elevated in obese individuals and those with diabetes mellitus, as noted in studies[76]. Importantly, TNF- α plays a direct role in reducing adiponectin levels in adipocytes[79]. The quest for novel compounds to treat type 2 diabetes has led to the exploration of plants as a potentially rich and untapped source, presenting an alternative avenue for therapeutic research.

In a study by [82], the antidiabetic effects of sorghum extract (SE) were investigated in mice on a high-fat (HF) diet. Administering either 0.5% or 1% SE orally for 6 weeks to mice on an HF diet resulted in a significant reduction in perirenal fat content, total and low-density lipoprotein cholesterol, triglycerides, glucose, and serum insulin levels compared to the HF group. Notably, the area under the curve for glucose was also significantly lower in the SE groups. The expression of peroxisome proliferator-activated receptor-gamma (PPAR- γ) and adiponectin was significantly higher, while tumor necrosis factor- α expression was lower in the 1% SE and 0.5% SE groups compared to the HF group. The findings suggest that the hypoglycemic effects of SE may be associated with the regulation of PPAR- γ -mediated metabolism in the studied mouse model.

In a study by [83], the influence of grain sorghum on postprandial plasma glucose and insulin levels was investigated in 10 healthy men. The study involved a comparison between

a whole-wheat flour muffin (control) and a grain sorghum muffin, both with 50 g of total starch. The findings indicated a notable reduction in mean glucose responses, particularly between 45–120 minutes post-consumption, and a decrease in mean insulin responses at 15–90 minutes compared to the control group. These results suggest that grain sorghum could serve as a beneficial functional ingredient for managing glucose and insulin levels in healthy individuals.

In a study by [84], the effects of sorghum starch on postprandial blood glucose and insulin levels in prediabetic men were examined. Fifteen male subjects with prediabetes consumed muffins made from grain sorghum and wheat (control), each containing 50 g of total starch, on two separate mornings with a one-week washout period. Plasma samples were collected at various time points (-15, 0, 15, 30, 45, 60, 75, 90, 120, and 180 minutes) after each treatment. The grain sorghum muffin exhibited a higher functional starch content (combined SDS and RS) compared to the control muffin. These findings imply that sorghum starch could positively influence postprandial blood glucose and insulin levels in individuals with prediabetes. The study demonstrated noteworthy decreases in postprandial blood glucose and insulin responses, especially during the 45–120 minute intervals when prediabetic men consumed grain sorghum muffins. The mean incremental area under the curve (iAUC) for glucose experienced a substantial 35.0% decrease, dropping from 5457.5 ± 645.4 to 3550.0 ± 428.9 mg (~3 h) dL⁻¹. Likewise, the mean iAUC of insulin saw a significant 36.7% reduction, declining from 7254.6 ± 1228.9 to 4589.3 ± 737.2 mU (~3 h) L⁻¹. The outcomes led to the conclusion that grain sorghum shows promise in effectively regulating blood glucose and insulin levels in individuals with prediabetes, potentially aiding in the prevention of type 2 diabetes.

In a similar study, [85] discovered that the consumption of whole grain sorghum meals led to notably lower glycemic responses in six subjects diagnosed with Type 2 diabetes mellitus, as opposed to dehulled sorghum and control meals prepared with wheat and rice. The variations in glycemic response were partly attributed to differences in fibre content. The whole grain sorghum treatment meals had a fibre content ranging from 2.2 g to 4.8 g, whereas the dehulled sorghum treatment meals had a lower fibre content, ranging from 1.8 g to 2.7 g. Varied cooking methods employed in the treatment meal recipes, including pan-frying, boiling, and fermented-steaming, could have influenced starch digestibility, thereby affecting carbohydrate metabolism.

The processing of cereal grains typically involves decortication, a method that separates the pericarp and germ from the endosperm, eliminating coarse, unpleasant, and anti-

nutritional factors. In a study by [86], eight new genotypes of brown sorghum grain underwent decortication, and their antioxidant, antidiabetic, and anti-obesity activities were assessed *in vitro*. The soluble fractions were analysed using DPPH and ABTS radical scavenging assays, along with evaluations for digestive enzymes and advanced glycation end-products (AGEs) formation inhibition. The study revealed that flavonoids, particularly flavones, were the predominant compounds in these extracts. This suggests that decorticated sorghum grains contain substantial amounts of flavonoids, making them promising candidates for preventing and treating diabetes and obesity.

Functional foods, particularly plant-based nutraceuticals, have emerged as potential contributors to diabetes treatment. Plant extracts, a longstanding tradition, are known for their ability to inhibit starch-hydrolysing enzymes, thereby reducing carbohydrate digestion [87]. Natural medicinal products, offering fewer reported side effects compared to conventional pharmaceuticals and being more cost-effective, are increasingly regarded as viable alternatives in diabetes management [88]. Utilizing nutraceuticals derived from locally grown plants holds significant promise, especially in regions where drug-based therapies face challenges within weaker healthcare systems. An example is condensed tannins isolated from sorghum (sorghum condensed tannins or SCT), which exhibit potent inhibition of both α -amylase and α -glucosidase *in vitro*. Notably, SCT demonstrates superior efficacy against α -glucosidase compared to acarbose, a conventional diabetes treatment α -glucosidase inhibitor, and does so at a much lower concentration [89]. Encapsulating SCT preparations in microparticles crafted from kafirin, known as sorghum prolamin protein (SCT-KEMS), proved effective in preserving inhibitory activity against both α -amylase and α -glucosidase during simulated gastrointestinal digestion. This suggests that SCT-KEMS has potential as a nutraceutical to mitigate hyperglycemia by impeding carbohydrate-hydrolysing enzymes in the small intestine. *In vitro* analyses have further demonstrated the resilience of sorghum condensed tannins (SCT) during simulated gastric digestion and their ability to inhibit digestive amylases when encapsulated within sorghum kafirin protein microparticles (SCT-KEMS).

[90] (Unpublished) explored the potential of SCT-KEMS as an anti-hyperglycemic nutraceutical agent through *in vivo* investigations using oral starch tolerance tests on healthy rats. Results revealed that SCT-KEMS effectively prevented a blood glucose spike, reducing the maximum blood glucose level by an average of 11.8% compared to the water control—a similar reduction as observed with the acarbose standard. Notably, neither SCT-KEMS nor acarbose led to an elevation in serum insulin levels. The study suggests that SCT-KEMS

holds promise as an effective nutraceutical for hyperglycemia management. This potential efficacy is attributed to the strong affinity of SCT for proline-rich kafirin and the slow digestibility of kafirin, which masks SCT bitterness and enables targeted delivery to the small intestine, inhibiting carbohydrate hydrolysis and reducing the glycaemic response.

Consuming foods with a low glycemic index (GI) and, consequently, a low glycemic load (GL) has a protective role against diabetes. The GI reflects the glycemic response to carbohydrates in various foods, while the GL is the product of a food's GI and its carbohydrate content, serving as a comprehensive indicator of the glucose response and insulin demand induced by food servings [91]. In India, there is a high prevalence of glucose intolerance, with diabetes rates increasing in both urban and rural areas [92]. Therefore, reducing postprandial blood glucose is a crucial aspect of diabetes prevention and management. Dietary factors, particularly the quantity and type of carbohydrates (CHO), significantly influence insulin secretion and postprandial blood glucose levels [93]. Indian diets are primarily carbohydrate-rich (>80%), with a focus on cereals, notably rice and wheat. Traditional recipes like roti, paratha, puri, and upma are commonly prepared. Rice, consumed as boiled rice or in various dishes like khichidi, biriyani, pulav, and idli, has a significant presence. The glycemic index (GI) of several cereals consumed in India is well-documented in studies such as [94, 95, 96]. Sorghum has garnered increased attention for its health benefits, being rich in energy, complex carbohydrates, protein, and essential micronutrients such as B vitamins (excluding B12), calcium, phosphorus, iron, zinc, and magnesium [97]. Despite these nutritional advantages, concerns arise regarding the bioavailability of these nutrients due to sorghum's high content of antinutrients like phytate, polyphenols, and oxalate. Processing techniques like village-based milling, soaking, fermentation, and malting have been identified as means to improve nutrient bioavailability in sorghum [98]. Various health-promoting products, including flour, staple foods, and beverages, have been derived from sorghum grains. With a growing health consciousness among the general public, the Indian market has witnessed the introduction of sorghum-based ready-to-eat/cook foods like multigrain flour, pasta, vermicelli, and biscuits.

[99] assessed the glycemic index (GI) and glycemic load (GL) of various sorghum foods, comparing them with wheat/rice-based counterparts. Sorghum-based foods like coarse semolina upma ($P < 0.05$), fine semolina upma ($P < 0.01$), flakes poha ($P < 0.01$), and pasta ($P < 0.01$) demonstrated significantly lower GI values compared to their respective controls (wheat/rice-based foods). Sorghum-based foods consistently exhibited significantly lower glycemic load (GL) values ($P < 0.01$) compared to their respective controls (wheat/rice-based

foods). Therefore, incorporating low-glycemic index (GI) and low-GL sorghum-based foods into the diet may contribute to reducing postprandial blood glucose levels in individuals with diabetes.

Similarly, [100] determined and compared the GI of sorghum muffins with muffins made from commonly consumed grains in the United States. They studied the effect of particle size and damaged starch on GI and also GI values were determined for muffins made from white sorghum, corn, brown rice, whole wheat, and all-purpose flours. Weighed portions of muffin containing 20g of available carbohydrates were eaten on separate occasions by eight healthy volunteers (ages 18-40) after an overnight fast (10 hours) to determine GI. Each muffin was administered twice. They were taken two capillary blood samples at 0 (fasting), 30, 45, 60, 90 and 120 minutes after consumption and averaged. Their results revealed that sorghum flour milled at particle size < 400 μm resulted in the lowest GI of 32 ± 16.8 . These findings should assist in development of lower GI sorghum foods.

In glucose control studies by [94], the glycemic index (GI) of six traditional Indian meals, including one centered on sorghum, was evaluated. The test meals were ingested in two forms: as baked bread made from sorghum, finger millet, or pearl millet flours, and as pressure-cooked meals using kodo millet, either alone or with the inclusion of whole mung beans or mung bean dal. In the preparation of these test meals, fats were notably excluded. The study involved 36 subjects diagnosed with Type 2 diabetes mellitus, evaluating glucose responses at one and two hours after consuming test foods containing 50 g of available carbohydrates. The results were then compared to a 50 g glucose load. The sorghum bread exhibited a relatively high mean glycemic index (GI) of $77\% \pm 8$ (SE), though not as elevated as the finger millet bread, which reached a GI of $104\% \pm 13$ (SE), equivalent to the glucose load. Conversely, the pearl millet bread exhibited the lowest glycemic index (GI) among the six test meals, registering at $55\% \pm 13$ (SE). No notable differences were noted in blood glucose levels at the 1-hour and 2-hour intervals when comparing each test food to the corresponding response to the 50 g glucose load. This study highlights that the digestibility of sorghum in the baked bread format may not be as gradual as suggested by *in-vitro* studies.

In a related study, [101] examined the impacts of six traditional Sudanese carbohydrate-rich meals, incorporating flours from wheat, sorghum, millet, and maize, on glucose and insulin responses. The research employed a randomized crossover design with 10 subjects diagnosed with Type 2 diabetes mellitus, including 6 males and 4 females. [101] found that among the traditional Sudanese carbohydrate-rich meals investigated, millet

porridge exhibited the most favourable (lowest) post-prandial glucose and insulin responses. Followed by millet porridge, wheat pancakes, sorghum porridge, and sorghum flatbread showed lower post-prandial glucose and insulin responses. In contrast, maize porridge led to higher glucose and insulin responses, as evidenced by mean incremental area under the curves (AUCs). Comprehending these findings necessitates attention to factors such as preparation method, duration, milling degree, and the nature of starch and fibre content. The observed variations highlight the significance of these aspects in result interpretation.

5. Conclusion

Sorghum, rich in phytochemicals, provides numerous health benefits. Experimental evidence supports its hypoglycemic effects, suggesting that incorporating sorghum into the diet or as a functional food can aid in controlling diabetes mellitus. Sorghum is important as an anti-diabetic agent lies in its holistic approach, addressing multiple aspects of diabetes prevention and management. Its nutrient-rich composition, low glycemic index, and various mechanisms of action make sorghum a valuable addition to dietary strategies for individuals with diabetes. Ongoing research continues to explore and validate its potential in the field of diabetes prevention and treatment.

Reference

1. De Candolle AP. Origin of cultivated plants, Hafner publishing company, New York. 1884.
2. Delsereone, LM. Sorghum Journal of Agriculture Food Information. 2007;8(1):9-14.
3. Jacob AA, Fidelis AE, Salaudeen KO, Queen KR. Sorghum: Most under-utilized grain of the semi-arid Africa. Scholarly Journal of Agricultural Science. 2013;3(4):147-53.
4. Stefoska-Needham A, Beck EJ, Johnson SK, Tapsell LC. Sorghum: an underutilized cereal whole grain with the potential to assist in the prevention of chronic disease. Food Reviews International. 2015 Oct 2;31(4):401-37.

5. Delcour, J.A. and Hosney, C. Principles of cereal science and technology. American Association of Cereal Chemists (AACC); 1994. 270.
6. Food and Agriculture Organization (FAO) of the United Nations. Sorghum and millets in human nutrition. Rome: David Lubin Memorial Library Cataloguing. 1995.
7. Gu-AyebeafoOkrah S. Screening of six local sorghum varieties for their malting and brewing qualities (Doctoral dissertation). 2008.
8. USDA National Nutrient Database for Standard Reference. USDA National Nutrient Database for Standard Reference, Release 27. 2014.
9. Serna-Saldivar S. Structure and chemistry of sorghum and millets. Sorghum and millets: chemistry and technology. 1995:69-124.
10. Dicko MH, Gruppen H, Traoré AS, Voragen AG, Van Berkel WJ. Sorghum grain as human food in Africa: relevance of content of starch and amylase activities. African journal of biotechnology. 2006;5(5):384-95.
11. Knudsen KB, Munck L. Dietary fibre contents and compositions of sorghum and sorghum-based foods. Journal of cereal science. 1985 Apr 1;3(2):153-64.
12. Verbruggen MA, Beldman G, Voragen AG, Hollemans M. Water-unextractable cell wall material from sorghum: isolation and characterization. Journal of Cereal Science. 1993 Jan 1;17(1):71-82.
13. Taylor JR, Emmambux MN. Developments in our understanding of sorghum polysaccharides and their health benefits. Cereal chemistry. 2010 Jul;87(4):263-71.
14. Knudsen KE, Kirleis AW, Eggum BO, Munck L. Carbohydrate composition and nutritional quality for rats of sorghum to prepared from decorticated white and whole grain red flour. The Journal of Nutrition. 1988 May 1;118(5):588-97.
15. Verbruggen MA, Beldman G, Voragen AG. The selective extraction of glucuronoarabinoxylans from sorghum endosperm cell walls using barium and potassium hydroxide solutions. Journal of Cereal Science. 1995 May 1;21(3):271-82.
16. Niba LL, Hoffman J. Resistant starch and β -glucan levels in grain sorghum (*Sorghum bicolor* M.) are influenced by soaking and autoclaving. Food Chemistry. 2003 May 1;81(1):113-8.
17. Henry RJ. Pentosan and (1 \rightarrow 3),(1 \rightarrow 4)- β -glucan concentrations in endosperm and wholegrain of wheat, barley, oats and rye. Journal of Cereal Science. 1987 Nov 1;6(3):253-8.
18. Hatfield RD, Wilson JR, Mertens DR. Composition of cell walls isolated from cell types of grain sorghum stems. Journal of the Science of Food and Agriculture. 1999 May 1;79(6):891-9.
19. Taylor JR, Anyango JO. Sorghum flour and flour products: production, nutritional quality, and fortification. In Flour and breads and their fortification in health and disease prevention 2011 Jan 1 (pp. 127-139). Academic Press.
20. De Mesa- Stonestreet NJ, Alavi S, Bean SR. Sorghum proteins: the concentration, isolation, modification, and food applications of kafirins. Journal of food science. 2010 Jun;75(5):R90-104.
21. Belton PS, Delgadillo I, Halford NG, Shewry PR. Kafirin structure and functionality. Journal of cereal science. 2006 Nov 1;44(3):272-86.

22. Duodu KG, Taylor JR, Belton PS, Hamaker BR. Factors affecting sorghum protein digestibility. *Journal of cereal science*. 2003 Sep 1;38(2):117-31.
23. Lin P, Wong JH, Ng TB, Ho VS, Xia L. A sorghum xylanase inhibitor-like protein with highly potent antifungal, antitumor and HIV-1 reverse transcriptase inhibitory activities. *Food chemistry*. 2013 Dec 1;141(3):2916-22.
24. Glew RH, VanderJagt DJ, Lockett C, Grivetti LE, Smith GC, Pastuszyn A, Millson M. Amino acid, fatty acid, and mineral composition of 24 indigenous plants of Burkina Faso. *Journal of food composition and analysis*. 1997 Sep 1;10(3):205-17.
25. Mehmood S, Orhan I, Ahsan Z, Aslan S, Gulfrac M. Fatty acid composition of seed oil of different Sorghum bicolor varieties. *Food chemistry*. 2008 Aug 15;109(4):855-9.
26. Avato P, Bianchi G, Murelli C. Aliphatic and cyclic lipid components of sorghum plant organs. *Phytochemistry*. 1990 Jan 1;29(4):1073-8.
27. Awika JM, Rooney LW. Sorghum phytochemicals and their potential impact on human health. *Phytochemistry*. 2004 May 1;65(9):1199-221.
28. Awika JM, Rooney LW, Waniska RD. Anthocyanins from black sorghum and their antioxidant properties. *Food Chemistry*. 2005 Mar 1;90(1-2):293-301.
29. Rooney LW, Awika JM. Overview of Products and Health Benefits of Specialty Sorghums1. *Cereal Foods World*. 2005 May 1;50(3):109.
30. Awika JM, Rooney LW, Waniska RD. Properties of 3-deoxyanthocyanins from sorghum. *Journal of agricultural and food chemistry*. 2004 Jul 14;52(14):4388-94.
31. Dykes L, Rooney LW, Waniska RD, Rooney WL. Phenolic compounds and antioxidant activity of sorghum grains of varying genotypes. *Journal of Agricultural and Food Chemistry*. 2005 Aug 24;53(17):6813-8.
32. Buer CS, Imin N, Djordjevic MA. Flavonoids: new roles for old molecules. *Journal of integrative plant biology*. 2010 Jan;52(1):98-111.
33. Awika JM. Sorghum: Its unique nutritional and health-promoting attributes. In *Gluten-free ancient grains 2017* Jan 1 (pp. 21-54). Woodhead publishing.
34. de Moraes Cardoso L, Pinheiro SS, Martino HS, Pinheiro-Sant'Ana HM. Sorghum (*Sorghum bicolor* L.): Nutrients, bioactive compounds, and potential impact on human health. *Critical reviews in food science and nutrition*. 2017 Jan 22;57(2):372-90.
35. Girard AL, Awika JM. Sorghum polyphenols and other bioactive components as functional and health promoting food ingredients. *Journal of Cereal Science*. 2018 Nov 1;84:112-24.
36. Yang L, Allred KF, Geera B, Allred CD, Awika JM. Sorghum phenolics demonstrate estrogenic action and induce apoptosis in nonmalignant colonocytes. *Nutrition and cancer*. 2012 Apr 1;64(3):419-27.
37. Yang L, Allred KF, Dykes L, Allred CD, Awika JM. Enhanced action of apigenin and naringenin combination on estrogen receptor activation in non-malignant colonocytes: Implications on sorghum-derived phytoestrogens. *Food & function*. 2015;6(3):749-55.
38. Dykes L, Peterson GC, Rooney WL, Rooney LW. Flavonoid composition of lemon-yellow sorghum genotypes. *Food Chemistry*. 2011 Sep 1;128(1):173-9.

39. Dykes L, Rooney LW. Phenolic compounds in cereal grains and their health benefits. *Cereal foods world*. 2007 Jun;52(3):105-11.
40. Dykes L, Seitz LM, Rooney WL, Rooney LW. Flavonoid composition of red sorghum genotypes. *Food Chemistry*. 2009 Sep 1;116(1):313-7.
41. Koes RE, Quattrocchio F, Mol JN. The flavonoid biosynthetic pathway in plants: function and evolution. *BioEssays*. 1994 Feb;16(2):123-32.
42. Bhagwat S, Haytowitz DB, Holden JM. USDA database for the flavonoid content of selected foods, release 3. US Department of Agriculture: Beltsville, MD, USA. 2011 Sep 27;159.
43. Gujer R, Magnolato D, Self R. Glucosylated flavonoids and other phenolic compounds from sorghum. *Phytochemistry*. 1986 May 22;25(6):1431-6.
44. Xiong Y, Zhang P, Warner RD, Fang Z. 3- Deoxyanthocyanidin colorant: Nature, health, synthesis, and food applications. *Comprehensive Reviews in Food Science and Food Safety*. 2019 Sep;18(5):1533-49.
45. Dykes L, Rooney WL, Rooney LW. Evaluation of phenolics and antioxidant activity of black sorghum hybrids. *Journal of Cereal Science*. 2013 Sep 1;58(2):278-83.
46. Wu Y, Li X, Xiang W, Zhu C, Lin Z, Wu Y, Li J, Pandravada S, Ridder DD, Bai G, Wang ML. Presence of tannins in sorghum grains is conditioned by different natural alleles of Tannin1. *Proceedings of the National Academy of Sciences*. 2012 Jun 26;109(26):10281-6.
47. Dykes L, Rooney LW. Sorghum and millet phenols and antioxidants. *Journal of cereal science*. 2006 Nov 1;44(3):236-51.
48. Awika JM, Rooney LW. Sorghum phytochemicals and their potential impact on human health. *Phytochemistry*. 2004 May 1;65(9):1199-221.
49. Earp CF, McDonough CM, Rooney LW. Microscopy of pericarp development in the caryopsis of *Sorghum bicolor* (L.) Moench. *Journal of Cereal Science*. 2004 Jan 1;39(1):21-7.
50. Rooney LW, Murty DS, Mertin JV. *Proceedings of the International Symposium on Sorghum Grain Quality*. 1982.
51. Englyst HN, Kingman SM, Cummings JH. Classification and measurement of nutritionally important starch fractions. *European journal of clinical nutrition*. 1992 Oct 1;46:S33-50.
52. Sajilata MG, Singhal RS, Kulkarni PR. Resistant starch—a review. *Comprehensive reviews in food science and food safety*. 2006 Jan;5(1):1-7.
53. Raben A, Tagliabue A, Christensen NJ, Madsen J, Holst JJ, Astrup A. Resistant starch: the effect on postprandial glycemia, hormonal response, and satiety. *The American journal of clinical nutrition*. 1994 Oct 1;60(4):544-51.
54. Ells LJ, Seal CJ, Kettlitz B, Bal W, Mathers JC. Postprandial glycaemic, lipaemic and haemostatic responses to ingestion of rapidly and slowly digested starches in healthy young women. *British Journal of Nutrition*. 2005 Dec;94(6):948-55.
55. Englyst KN, Vinoy S, Englyst HN, Lang V. Glycaemic index of cereal products explained by their content of rapidly and slowly available glucose. *British Journal of Nutrition*. 2003 Mar;89(3):329-39.

56. Seal CJ, Daly ME, Thomas LC, Bal W, Birkett AM, Jeffcoat R, Mathers JC. Postprandial carbohydrate metabolism in healthy subjects and those with type 2 diabetes fed starches with slow and rapid hydrolysis rates determined in vitro. *British Journal of Nutrition*. 2003 Nov;90(5):853-64.
57. Mayer J. Glucostatic mechanism of regulation of food intake. *Obesity Research*. 1996 Sep;4(5):493-6.
58. Davis AB, Hoseney RC. Grain sorghum condensed tannins. I. Isolation, estimation, and selective adsorption by starch. *Cereal Chem*. 1979 Jan 1;56(4):310-4.
59. Hamaker BR, Mohamed AA, Habben JE, Huang CP, Larkins BA. Efficient procedure for extracting maize and sorghum kernel proteins reveals higher prolamin contents than the conventional method. *Cereal chemistry*. 1995;72.
60. Oria MP, Hamaker BR, Shull JM. Resistance of Sorghum. alpha-, beta-, and gamma.-Kafirins to Pepsin Digestion. *Journal of Agricultural and Food Chemistry*. 1995 Aug;43(8):2148-53.
61. Duodu KG, Taylor JR, Belton PS, Hamaker BR. Factors affecting sorghum protein digestibility. *Journal of cereal science*. 2003 Sep 1;38(2):117-31.
62. Axtell JD, Kirleis AW, Hassen MM, D'Croz Mason NA, Mertz ET, Munck L. Digestibility of sorghum proteins. *Proceedings of the National Academy of Sciences*. 1981 Mar;78(3):1333-5.
63. Taylor J, Taylor JR. Alleviation of the adverse effect of cooking on sorghum protein digestibility through fermentation in traditional African porridges. *International journal of food science & technology*. 2002 Feb;37(2):129-37.
64. Craig ME, Hattersley A, Donaghue KC. Definition, epidemiology and classification of diabetes in children and adolescents. *Pediatr diabetes*. 2009 Sep 1;10(Suppl 12):3-12.
65. Punitha IR, Rajendran K, Shirwaikar A, Shirwaikar A. Alcoholic stem extract of *Cosciniumfenestratum* regulates carbohydrate metabolism and improves antioxidant status in streptozotocin–nicotinamide induced diabetic rats. *Evidence-Based Complementary and Alternative Medicine*. 2005 Sep;2:375-81.
66. Maritim AC, Sanders A, Watkins Iii JB. Diabetes, oxidative stress, and antioxidants: a review. *Journal of biochemical and molecular toxicology*. 2003;17(1):24-38.
67. Nayak BS, Marshall JR, Isitor G, Adogwa A. Hypoglycemic and hepatoprotective activity of fermented fruit juice of *Morindacitrifolia* (Noni) in diabetic rats. *Evidence-Based Complementary and Alternative Medicine*. 2010;2011.
68. Chhikara N, Abdulahi B, Munezero C, Kaur R, Singh G, Panghal A. Exploring the nutritional and phytochemical potential of sorghum in food processing for food security. *Nutrition & Food Science*. 2018 Oct 24;49(2):318-32.
69. Iwuoha CI, Eke OS. Nigerian indigenous fermented foods: their traditional process operation, inherent problems, improvements and current status. *Food Research International*. 1996 Jun 1;29(5-6):527-40.
70. Kim J, Hyun TK, Kim M. Anti-oxidative activities of sorghum, foxtail millet and proso millet extracts. *African Journal of Biotechnology*. 2010;9(18):2683-90.

71. Adebolu TT, Olodun AO, Ihunweze BC. Evaluation of ogi liquor from different grains for antibacterial activities against some common diarrhoeal bacteria in Southwest Nigeria. *African Journal of Biotechnology*. 2007;6(9).
72. Olawole TD, Okundigie MI, Rotimi SO, Okwumabua O, Afolabi IS. Preadministration of fermented sorghum diet provides protection against hyperglycemia-induced oxidative stress and suppressed glucose utilization in alloxan-induced diabetic rats. *Frontiers in nutrition*. 2018 Mar 12;5:16.
73. Mukai Y, Kataoka S, Sato S. Sorghum (*Sorghum bicolor*) extract affects plasma lipid metabolism and hepatic macrophage infiltration in diabetic rats. *Current Nutrition & Food Science*. 2020 Jun 1;16(5):824-32.
74. Kim J, Park Y. Anti-diabetic effect of sorghum extract on hepatic gluconeogenesis of streptozotocin-induced diabetic rats. *Nutrition & metabolism*. 2012 Dec;9:1-7.
75. Chung IM, Kim EH, Yeo MA, Kim SJ, Seo MC, Moon HI. Antidiabetic effects of three Korean sorghum phenolic extracts in normal and streptozotocin-induced diabetic rats. *Food Research International*. 2011 Jan 1;44(1):127-32.
76. Hotamisligil GS. The role of TNF α and TNF receptors in obesity and insulin resistance. *Journal of internal medicine*. 1999 Jun;245(6):621-5.
77. Yamauchi T, Kamon J, Waki H, Terauchi Y, Kubota N, Hara K, Mori Y, Ide T, Murakami K, Tsuboyama-Kasaoka N, Ezaki O. The fat-derived hormone adiponectin reverses insulin resistance associated with both lipodystrophy and obesity. *Nature medicine*. 2001 Aug;7(8):941-6.
78. Maeda N, Takahashi M, Funahashi T, Kihara S, Nishizawa H, Kishida K, Nagaretani H, Matsuda M, Komuro R, Ouchi N, Kuriyama H. PPAR γ ligands increase expression and plasma concentrations of adiponectin, an adipose-derived protein. *Diabetes*. 2001 Sep 1;50(9):2094-9.
79. Lehmann JM, Moore LB, Smith-Oliver TA, Wilkison WO, Willson TM, Kliewer SA. An Antidiabetic Thiazolidinedione Is a High Affinity Ligand for Peroxisome Proliferator-activated Receptor γ (PPAR γ)*. *Journal of Biological Chemistry*. 1995 Jun 2;270(22):12953-6.
80. Bouskila M, Pajvani UB, Scherer PE. Adiponectin: a relevant player in PPAR γ -agonist-mediated improvements in hepatic insulin sensitivity?. *International journal of obesity*. 2005 Mar;29(1):S17-23.
81. Spranger, J., Kroke, A., Mohlig, M., Bergmann, M.M., Ristow, M., Boeing, H. And Pfeiffer, A.F., 2003, Adiponectin and protection against type 2 diabetes mellitus. *Lancet*, 361:226-8.
82. Park JH, Lee SH, Chung IM, Park Y. Sorghum extract exerts an anti-diabetic effect by improving insulin sensitivity via PPAR- γ in mice fed a high-fat diet. *Nutrition research and practice*. 2012 Aug;6(4):322-7.
83. Poquette NM, Gu X, Lee SO. Grain sorghum muffin reduces glucose and insulin responses in men. *Food & function*. 2014;5(5):894-9.
84. Gu X. Effects of grain sorghum muffin on blood glucose and insulin responses in prediabetic men. University of Arkansas; 2014.
85. Lakshmi KB, Vimala V. Hypoglycemic effect of selected sorghum recipes. *Nutrition research*. 1996 Oct 1;16(10):1651-8.

86. Ofosu FK, Elahi F, Daliri EB, Yeon SJ, Ham HJ, Kim JH, Han SI, Oh DH. Flavonoids in decorticated sorghum grains exert antioxidant, antidiabetic and antiobesity activities. *Molecules*. 2020 Jun 20;25(12):2854.
87. Etxeberria U, de la Garza AL, Campión J, Martínez JA, Milagro FI. Antidiabetic effects of natural plant extracts via inhibition of carbohydrate hydrolysis enzymes with emphasis on pancreatic alpha amylase. *Expert opinion on therapeutic targets*. 2012 Mar 1;16(3):269-97.
88. Tundis R, Loizzo MR, Menichini F. Natural products as α -amylase and α -glucosidase inhibitors and their hypoglycaemic potential in the treatment of diabetes: an update. *Mini reviews in medicinal chemistry*. 2010 Apr 1;10(4):315-31.
89. Links MR, Taylor J, Kruger MC, Taylor JR. Sorghum condensed tannins encapsulated in kafirin microparticles as a nutraceutical for inhibition of amylases during digestion to attenuate hyperglycaemia. *Journal of functional foods*. 2015 Jan 1;12:55-63.
90. Links MR, Taylor J, Kruger MC, Naidoo V, Taylor JR. Kafirin microparticle encapsulated sorghum condensed tannins exhibit potential as an anti-hyperglycaemic agent in a small animal model. *Journal of Functional Foods*. 2016 Jan 1;20:394-9.
91. Salmerón J, Ascherio A, Rimm EB, Colditz GA, Spiegelman D, Jenkins DJ, Stampfer MJ, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes care*. 1997 Apr 1;20(4):545-50.
92. Abate N, Chandalia M. The impact of ethnicity on type 2 diabetes. *Journal of Diabetes and its Complications*. 2003 Jan 1;17(1):39-58.
93. Radhika G, Sumathi C, Ganesan A, Sudha V, Henry CJ, Mohan V. Glycaemic index of Indian flatbreads (rotis) prepared using whole wheat flour and 'atta mix'-added whole wheat flour. *British journal of nutrition*. 2010 Jun;103(11):1642-7.
94. Msc UM, Fien BM, Msc SD, Msc IM. Glycaemic index of some commonly consumed foods in western India. *Asia Pacific J Clin Nutr*. 1993;2:111-4.
95. Henry CJ, Lightowler HJ, Newens K, Sudha V, Radhika G, Sathya RM, Mohan V. Glycaemic index of common foods tested in the UK and India. *British journal of nutrition*. 2008 Apr;99(4):840-5.
96. Vijayan L, Sumathi S. Glycaemic response to selected Kerala breakfast items in people with diabetes. *Asia Pacific Journal of Clinical Nutrition*. 1997;6:80-3.
97. Gopalan C, Rama Sastri BV, Balasubramanian SC. *Nutritive value of Indian foods*. (No Title). 1971.
98. Gibson RS, Perlas L, Hotz C. Improving the bioavailability of nutrients in plant foods at the household level. *Proceedings of the Nutrition Society*. 2006 May;65(2):160-8.
99. Prasad MP, Rao BD, Kalpana K, Rao MV, Patil JV. Glycaemic index and glycaemic load of sorghum products. *Journal of the Science of Food and Agriculture*. 2015 Jun;95(8):1626-30.
100. Pruett A. A comparison of the glycemic index of sorghum and other commonly consumed grains (Doctoral dissertation, Kansas State University). 2012.
101. Abdelgadir M, Abbas M, Järvi 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. *Diabetic medicine*. 2005 Feb;22(2):213-7.