ASERTAINING SORGHUM [*Sorghum bicolour* (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. Regularly consuming whole grains like sorghum is linked to a 20-30% lower risk of heart disease and diabetes, improving blood glucose control. Sorghum-based foods have a lower glycemic index, indicating potential benefits in managing postprandial blood glucose levels for diabetes prevention. *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] is 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 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. Moenchis 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].

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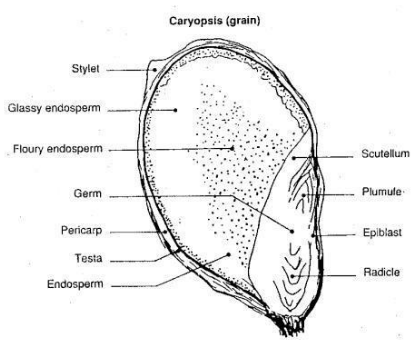

Figure 1: Structure of sorghum grain

4. Chemical composition of the grain or caryopsis

Sorghum grain which is 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 comprisesan 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) extensively reviewed a varied range of bioactive peptides in sorghum grain [23].

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 byDykes et al., 2005[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 byAwika et al., 2004 and Dykes et al., 2005 [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 byBuer et al., 2010[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 Awika, 2017 and de Morais Cardosoetal et al., 2010[33, 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 byYank et al., 2012 and Dykes et al., 2011 [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 Dykes and Rooney, 2007[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 Dykes et al., 2011;Dykes and Rooney, 2007; Dykes et al., 2009[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 Awika et al., 2004 and Xiong et al., 2019[30, 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 de Morais Cardoso et al., 2017; Girard and Awika, 2018;Awikaand Rooney, 2004; Awika et al., 2005[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 Awika et al., 2005; Dykes et al., 2005; Dykes et al., 2009; Dykes et al., 2013[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 ß-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 effectsand digestibility.

For nutritional purposes, starch is also classified into rapidly digestible starch (RDS), slowly digestible starch (SDS) and resistant starch (RS).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 Olawole et al., 2018[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. Mukai et al., 2020[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.

Kim and Park, 2012[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.

Chung et al, 2011[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 byPark et al., 2012[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 Poquette et al., 2014[83], the influence of grain sorghum on postprandial plasma glucose and insulin levels were 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 Gu, 2014[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, Lakshmi and Vimala, 1996[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 Ofosu et al., 2020[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).

Linkset al., 2016 (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 [90]. 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 Msc et al., 1993; Henry et al., 2008; Vijayan and Sumathi, 1997[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.

Prasad et al., 2015[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, Pruett, 2012[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 andalso 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. They results revealed that sorghum flour milled at particle size < 400 um resulted in the lowest GI of 32 ± 16.8. These findings should assist in development of lower GI sorghum foods.

In glucose control studies byMsc et al., 1993 [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% +/- 8 (SE), though not as elevated as the finger millet bread, which reached a GI of 104% +/- 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% +/- 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, Abdelgadir et al., 2005[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.Abdelgadir et al., 2005[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.

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