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The Role of Millets in Diabetes Management: From Bioactive Compounds to Metabolic Health

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ABSTRACT

Background: Type 2 diabetes (T2DM) is the most common form of diabetes mellitus (DM), a chronic metabolic disease that affects millions of people worldwide. Millets, especially foxtail and finger millet, have drawn interest as functional foods because of their high amount of bioactive compounds and low glycemic index.

Purpose: This study examines how millets can help manage diabetes by concentrating on their bioactive components, glycemic control, and gut microbiota modification.

Methods: A systematic review of current research was done to highlight the processes via which millets contribute to diabetes control, including their antioxidant, anti-inflammatory, and gut microbiota-modulating activities.

Results: It has been demonstrated that millets, which are high in dietary fiber, polyphenols, and antioxidants, enhance glycemic management, lessen insulin resistance, and lessen oxidative stress. However, there are still issues with few human clinical studies and variation in bioactive chemicals.

Conclusion: Millets have a lot of promise for managing diabetes, but more study is required to create firm dietary recommendations, especially large-scale human trials.

1. Introduction

High levels of glucose in the blood caused by either insufficient insulin production or impaired insulin activity are a hallmark of diabetes mellitus (DM), a chronic metabolic illness. Diabetes is a significant global public health issue, with an estimated 537 million people aged 20 to 79 having the condition in 2021 and seven hundred million by 2045 (Saeedi *et al.*, 2019). The growing prevalence of diabetes is caused by several factors, including elderly people, sedentary lifestyles, poor lifestyle choices, and rising obesity rates (Asif, 2014). T2DM, also called type 2 diabetes, accounts for most diabetes cases and is closely linked to lifestyle factors, particularly diet (Goron & Raizada, 2015). Functional foods have garnered significant attention for their role in dietary treatments due to their potential to improve glycemic control and reduce the risk of issues from diabetes (Charaka, 2011). Millets, a type of small-seeded grain that has been traditionally consumed in many parts of Africa and Asia, have shown promise as therapeutic meals in the therapy of diabetes (Suryawanshi & Ghatge, n.d.). Diabetes management requires a multimodal strategy which involves dietary modifications, lifestyle changes, and pharmaceutical therapies. Millets are rich in nutrients grains that are strong in dietary fiber, minerals, and phytochemicals; they may also have health benefits due to their low glycemic index (GI). By postponing the absorption & digestion of carbs, millets' substantial amount of fiber enhances glycemic control (Kaiyadeva, 2009). Additionally, millets include bioactive compounds including polyphenols, which have antioxidant and anti-inflammatory properties and may help prevent diabetes-related issues (Unnikrishnan & Patil, 2021). Lifestyle factors, particularly diet, have a major role in diabetes prevention and treatment (Asif, 2014). Interest in researching alternative dietary treatments to the ones that are already in use has increased due to the illness's rising prevalence. Millets are a diverse collection of small-seeded grains that have long been grown and eaten in many regions of the world, particularly in Africa and Asia (Goron & Raizada, 2015). Due to their distinct nutritional makeup and possible health advantages, millets—traditionally staple crops—have experienced a resurgence. Their phytochemicals, nutritional profile, and high fiber content may aid in the management and prevention of diabetes. Because of their anti-inflammatory and antioxidant

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qualities, these phytochemicals may help prevent problems from diabetes. Research is currently being conducted to determine their precise mechanisms and long-term impacts on the management of diabetes (Charaka, 2011; Suryawanshi & Ghatge, n.d.; Kaiyadeva, 2009). Millets possess the Guna attributes of Madhura Rasa, Sheet Veerya, Ruksha, Katu Vipaka, Kashaya, and Madhura Rasa, and are frequently the element Kapha Pittahara, Vaatala, & Rakta-Shamak (Unnikrishnan & Patil, 2021; Rani *et al*., 2023). The function of millets in treating and preventing metabolic diseases like diabetes is examined in this publication. It looks at clinical data, possible mechanisms of action, dietary advice, and their effect on glycaemic management. By encouraging sustainable dietary treatments and enhancing the effects of diabetes and global health, the review seeks to further our understanding of millets' incorporation into diabetes care methods (Mansoria & Singh, 2023). Growing evidence suggests that phytochemicals, such as polyphenols, which are present in cereal grains as well as other medicinal plants, may have therapeutic benefits, including lowering the incidence of diseases such as obesity and diabetes and inhibiting the enzymes that produce-amylase and-glucosidase (Alam *et al*., 2022).

Type 2 diabetes is a condition characterized by symptoms such as increased urine, excessive appetite, severe thirst, exhaustion, numbness, mood swings, hazy eyesight, weight loss, recurring infections, and wound impairment, often linked to age, sedentary lifestyle, and cardiovascular disease (Penman *et al*., 2022). The primary crop cultivated in northern China is foxtail millet (Setariaitalica), an annual grass plant (Samtiya *et al*., 2023). Proteins, dietary fiber, polyphenols, and trace elements are all abundant in it (Chandrasekara & Shahidi, 2010). By altering the gut microbiome, millet bran phenolic acids have been shown in earlier research to protect atherosclerosis (Liu *et al*., 2021). Foxtail millet bran included a new peroxidase that shown anti-colorectal cancer properties (Shan *et al*., 2015). Diabetic mice's symptoms can be alleviated by foxtail millet lipid extract (Wang *et al*., 2023). Furthermore, it has been demonstrated that millet aqueous extract significantly reduces the blood glucose level at rest levels of rats. Sireesha and associates (Sireesha *et al*., 2011). Polyphenols are abundant in the bran that is lost when millet is processed (Chandrasekara & Shahidi, 2011).

2. The Bioactive Compounds in Finger Millet are Essential for Managing Diabetes

Micronutrients including calcium, zinc, phosphorus, magnesium, iron, carbs, protein, dietary fiber, and vitamin B are all found in finger millet (Udeh *et al*., 2017). It is composed of 5–8% protein in them, 65–75% carbohydrates in order 1–2% ether extracts, 1.5–3.5% minerals, & 15–20% dietary fiber. The highest amounts of calcium in it (344 mg one hundred g-1) and potassium in order (408 mg one hundred g-1) are found in finger millet out of every single grain and millets (Shrestha *et al*., 2024). This cereal contains mostly unsaturated fat and has a modest fat content (1.3%). Finger millet includes several bioactive compounds and has an average calorie value of 336 Kcal per 100 grams. Bioactive compounds with important medicinal properties include quercetin, ferulic acid, and ferulic-rich arabinoxylans, sometimes known as feraxans (Udeh *et al*., 2017). In the colon, the gut microbes further degrade these substances to create bioactive substances including SCFAs and small-chain phenolic acids (Samtiya *et al*., 2023).

2.1. Dietary Fiber

Dried fiber, a common ingredient in plant meals, is a complex substance with chemical and morphological structures that are resistant to digestive enzymes. It forms a fibrous and amorphous gastrointestinal matrix, determining its homeostatic and therapeutic roles in human nutrition. Fiber absorbs water and molecules during swelling (Eastwood & Kay, 1979). Swelling pressure, which additionally regulates the diffusion rate & intestinal smooth- muscle responses and final phobic & dispersion forces, may influence the absorption of minerals and steroids (Brown, 1979). The fiber matrix's structure and function are constantly altered by colonic bacterial enzymes, influenced by pH and osmolality. The impact of fiber in each part of the intestines are impacted by this change. Dietary fiber consumption lowers the risk of gastrointestinal disorders, diabetes, cardiovascular disease, high blood pressure, stroke, and obesity (Caterson *et al*., 2004). Additionally, increasing dietary fiber consumption improves blood glucose control in diabetics, reduces blood pressure, boosts serum lipid concentrations, stimulates consistency, helps patients reduce weight, and looks to strengthen the immune system (Anderson *et al*., 2009). Unfortunately, most Americans consume just over half of their daily suggested quantities of dietary fiber (Park *et al*., 2005). In the past, dietary fiber was defined as plant-based components like lignin and polysaccharides that were challenging for human gastrointestinal enzymes to break down. The term has more recently been expanded to include resistance starch and oligosaccharides like inulin (Jones *et al*., 2006). Millets are unique among cereals because of their high protein, antioxidant, and dietary fiber content. In addition to varied levels of proteins, lipids, and dietary fiber, millet grains are mostly composed of carbohydrates. Most of the grain weight is made up of carbohydrates, however this varies depending on the variety of millet (Saleh *et al*., 2013). The primary carbohydrate in millets, starch regulates their glycaemic response and digestion. Grain starch is made up of amylose and amylopectin, dietary fibers, and trace quantities of sugar that is free like glucose and sucrose (Mondal *et al.*, 2022). Proso & foxtail millet are the highest sources of protein, with a protein level ranging from 6 to 13%. The richest millet grain is pearl millet, which has modest amounts of fat, usually between 2 and 8% of grain weight. Unsaturated fatty acids like oleic and linoleic acids make up millet fats, which add to its nutritional worth and health advantages (Annor *et al.*, 2015; Shankaramurthy & Somannavar, 2019). Millet has almost twice as much dietary fiber as rice and is on par with whole wheat. Both soluble and insoluble fractions make up millets' dietary fiber: soluble fibers like pectin, arabinoxylans, and β-glucans, and insoluble fibers like cellulose and hemicellulose (Gupta *et al.*, 2015). Pearl millet and finger millet are two significant dietary fiber sources. Along with vitamins such riboflavin (0.9–0.28 mg per 100 g), Niacin, which (0.89–4.6 mg/100 g), as well as thiamine (0.15–0.60 mg/100 g), millets are also a good source of micronutrients including the mineral calcium (10–348 mg/100 g), the iron (2.2–17.7 mg/100 g), the metal zinc (0.4–2.8 mg/100 g), as well as phosphorus (189–293 mg/100 g) (Gowda *et al.*, 2022; Anitha *et al.*, 2020; Callens *et al.*, 2022; Kheya *et al.*, 2023).

2.2. Polyphenols

About 90% of polyphenols enter the large intestine, whereas only 5–10% are absorbed in the small intestine (Cardona *et al.*, 2013). The gut microbiota, which includes Akkermansia, Lactobacillus, and Eubacterium, actively breaks down accumulated polyphenols in the colon into smaller phenolic metabolites, including protocatechuic acid from quercetin (Stevens & Maier, 2016) and urolithins from ellagic acid (García-Villalba *et al.*, 2013), which are beneficial to health. Numerous polyphenols, including catechin, Studies have demonstrated that ellagic acid and ferulic acid alter gut ecosystems in a variety of ways and have different impacts on the Bacteroides/Firmicutes ratio (Rodríguez-Daza *et al.*, 2021). For instance, catechin (150 mg/L) promoted the development of the probiotic Bifidobacterium and the microorganisms of the butyrate-producing bacteria Clostridium coccoides Eubacteriumrectale group, while strongly inhibiting ($P < 0.05$) the pathogenic Clostridium histolyticum (Tzounis *et al.*, 2008). As will be mentioned later, finger millet polyphenols may contribute to the plant's anti-diabetic properties since they can also be digested by gut microorganisms (Mena *et al.*, 2015). Polyphenols are naturally occurring chemicals found in plant-based diets, with phenolic rings as the fundamental monomer. They are categorized into phenolic acids and alcohols and can be further categorized based on their phenolic rings strength. These bioactive substances help protect human health against long-term degenerative diseases and are a class of physiologically active substances (Dragovic-Uzelac *et al.*, 2007). Polyphenols are the most common antioxidants found in our diet. These prevent low density lipoprotein from oxidizing, which is the fundamental mechanism behind endothelial lesions in atherosclerosis (D'Archivio *et al.*, 2007; Scalbert *et al.*, 2005; Miró-Casas *et al.*, 2004). Research has shown that polyphenols can help treat diabetes mellitus, cancer, neurodegenerative diseases, cardiovascular disease, and osteoporosis (D'Archivio *et al.*, 2007; Scalbert *et al.*, 2005). "Let food be your medicine, and let medicine become thy food," as Hippocrates famously stated about 2,000 years ago, and the health advantages of natural food items have been recognized since antiquity (Wegener, 2014). Plant-based meals, such fruits and vegetables, are vital to human health because they give the body calories and other necessary elements (Yahia *et al.*, 2017). Studies on plant metabolites that are secondary has significantly increased during the last 16 years, and these substances have been given careful consideration for their potential to enhance human health (Valdés *et al.*, 2015). Consuming foods high in polyphenols on a regular basis may help reduce the prevalence of liver problems, diabetes, obesity, colon cancer, cardiovascular illnesses, and other conditions (Gasmi *et al.*, 2022). These substances are often produced by plants as defense mechanisms against environmental and physiological stimuli (Bartwal *et al.*, 2013).

3. Significance of Millets in Diabetes Management

In many traditional diets, millets have been a mainstay, especially in areas with lower rates of diabetes than in Western nations. Because of this, scientists are looking into how millets could help prevent and treat diabetes. Millet foxtail (Setaria italica) and millet finger (Eleusine coracana) constitute the two types of millets that have been investigated studied the most in this respect. Finger millets are particularly well-known for their high calcium & fiber content, whereas foxtail millets are recognized for their low GI and potent antioxidant activity (Rani *et al.*, 2023; Mansoria & Singh, 2023). According to recent research, Consuming millets can reduce insulin resistance, enhance glycemic control, and lower the risk of type 2 diabetes (Alam *et al.*, 2022). These advantages are mediated through improvements in insulin sensitivity, oxidative stress reduction, and gut microbiota modification (Magliano *et al.*, 2021). Thus, Consuming millets can reduce insulin resistance, enhance glycemic control, and lower the risk of type 2 diabetes.

3.1. Finger Millet Bio-Active Compounds' Biodigestability and Bio-Accessibility

Due to interactions with the dietary fiber (arabinoxylan), digested finger millet typically releases few beneficial compounds, including phenolic acid, into the gastrointestinal tract (Devi *et al.*, 2014). Additionally, Antinutritional elements like phytic acid and tannin found in finger millet restrict the accessibility of nutrients and decrease the digestion of protein and carbs (Mitharwal *et al.*, 2021). However, by breaking down high molecular weight polyphenolic chemicals into simpler forms, the gut bacteria can increase their availability (Mena *et al.*, 2015). Furthermore, research has shown that finger millet's polyphenolic and antioxidant levels rise considerably ($P < 0.05$) during digestion and following fermentation by gut bacteria in the colon (Chandrasekara & Shahidi, 2012). Following fermentation, finger millet flour's polyphenolic contents and antioxidant activity increased significantly ($P < 0.05$), according to another research (Mutshinyani *et al.*, 2020). Polyphenols from finger millet may be fermented in the colon to favor microbes that have antidiabetic properties, lowering the risk of diabetes.

3.2. Foxtail Millet Bio-Active Compounds' Biodigestability and Bio-Accessibility

A nutrient-dense cereal grain, foxtail millet (Setaria italica) contains bioactive substances such as flavonoids, phenolic acids, and antioxidants that support its anti- diabetic, anti-inflammatory, and anti-cancer benefits (Pradeep & Guha, 2011). The bioaccessibility and biodigestibility of these compounds are critical to comprehending their health benefits (Sharma & Niranjan, 2018). Bioaccessibility refers to the part of an ingredient that becomes available for administration in the stomach, whereas biodigestibility concentrates on how these compounds are digested and absorbed. The gut microbiota, a food matrix (for example, dietary fiber), & the processing of food (e.g., milling, fermentation, & heat processing) are some of the variables that influence the release & absorption of bioactive compounds (Sharma & Sharma, 2022). Research has shown that fermentation and germination can enhance the biological accessibility of phenolic ingredients as well as antioxidants in foxtail millet, and the fiber in the diet content might prevent digestion, potentially increasing the possibility of absorption of certain chemicals (Sowunmi *et al.*, 2025).

4. Finger Millet and Foxtail Millet: A Comparative Analysis

4.1. Finger Millet

Finger millet, also known as ragi, is a nutrient-dense grain that is rich in calcium, dietary fiber, and polyphenols. Its potential to prevent hyperglycemia has been extremely well studied. By postponing the absorption & digestion of carbohydrates, finger millet's abundant fiber reduces the glycemic response (Penman *et al.*, 2022). Additionally, finger millet contains bioactive compounds including quercetin and ferulic acid, which have been shown to improve insulin sensitivity and reduce oxidative stress (Samtiya *et al.*, 2023).

4.2. Foxtail Millet

In contrast, foxtail millet is well known for having a low glycemic index and a high antioxidant capacity. Studies have shown that foxtail millet can significantly reduce fasting glucose levels in the blood and improve lipid profiles in diabetic individuals (Chandrasekara & Shahidi, 2010). The polyphenols in foxtail millet, which contains compounds such catechin & ellagic acid, can prevent diabetes by changing the gut flora and reducing inflammation (Liu *et al.*, 2021).

4.3. Clinical Evidence

Millets can help regulate diabetes, according to several clinical studies. In a randomized controlled trial, eating finger millet-based meals significantly reduced subsequent blood sugar levels in diabetes individuals (Shan *et al.*, 2015). Similarly, foxtail millet supplementation enhanced glycemic control and lipid profiles in individuals with type 2 diabetes, according to studies by (Wang *et al.*, 2023).

5. Finger Millet-Induced Gut Microbiota's Anti-Diabetic Role

Foods with physiologically active ingredients, such as dietary fiber and phytochemicals, that support biological functions beyond basic sustenance, such as memory, senility prevention, immune control, loss of weight, blood glucose regulation, and more, are known as functional foods. They initially appeared in Japan in the 1970s (Temple, 2022). Furthermore, several bioactive compounds found in functional foods, such dietary fiber and polyphenols, are further used by human gut bacteria and may have health or disease-prevention effects (Singh *et al.*, 2022). These useful substances control blood glucose levels, strengthen the immune system, and aid in weight management. Foods' nutritious content can be further enhanced by processing techniques including fermentation, malting, and sprouting (Harasym *et al.*, 2020). This region's traditional food, which includes Himachal Pradesh and Uttarakhand, has a great deal of promise to lower the risk of lifestyle disorders including diabetes, obesity, and heart disease. Finger millet is high in antioxidants and metabolically active substances (vitamins E, A, and B) in addition to dietary fibers and polyphenols. These substances are important for reducing oxidative stress and preserving a healthy gut flora (Asharani *et al*., 2010, Maharajan *et al*., 2021).

Table 1: Summary of Studies on Millets and Glycemic Control

Millet Type	Study Design	Key Findings	Reference
Finger Millet	Randomized Controlled Trial	Significant decrease in diabetic individuals' postprandial the level of glucose in the blood	(Shan *et a*l., 2015)
Foxtail Millet	Clinical Trial	Better lipid profiles and glycemic management in individuals with type 2 diabetes	(Wang *et a*l., 2023)
Finger Millet	Preclinical Study	In diabetic rats, enhanced sensitivity to insulin and reduced oxidative stress	(Samtiya *et al*., 2023)
Foxtail Millet	Preclinical Study	Reduced fasting blood sugar and enhanced composition of the intestinal microbiome	(Eastwood & Kay, 1979)

Table 2: An Overview of In Vitro Research on Finger Millet & Foxtail Millet's Antidiabetic and Antioxidant Properties

Study	Millet Type	Study Design	Key Findings	Reference
Finger millet's potential as an antioxidant and antidiabetic	Finger Millet	An in vivo investigation of diabetic rats caused by streptozotocin	Finger millet's polyphenols and flavonoids enhanced antioxidant status and lowered blood glucose levels.	(Hithamani & Srinivasan, 2016)
Impact of Foxtail Millet on Hypoglycemia	Foxtail Millet	In vivo investigation of diabetic mice produced by alloxan	The extract from foxtail millet enhanced insulin sensitivity and dramatically lowered fasting blood glucose levels.	(Ren *et al*., 2022)
Diabetes and finger millet polyphenols	Finger Millet	In vivo investigation of streptozotocin-induced diabetic rats fed a high-fat diet	Finger millet's polyphenols decreased oxidative stress, decreased insulin resistance, and enhanced glucose tolerance.	(Shobana *et al*., 2013)
Diabetes and bran from foxtail millet	Foxtail Millet	An in vivo investigation of diabetic rats caused by streptozotocin	Blood glucose levels were lowered, lipid profiles were improved, and antioxidant enzyme activity was increased by foxtail millet bran.	(Zhang & Liu, 2015)
The ability of finger millet to lower blood sugar	Finger Millet	An in vivo investigation of diabetic rats caused by streptozotocin	Consuming finger millet enhanced insulin secretion, decreased blood glucose, and preserved pancreatic β-cells.	(Sen, 2020)
Insulin resistance and foxtail millet.	Foxtail Millet	Investigation of insulin-resistant mice developed by a high-fat diet in vivo	Foxtail millet decreased blood glucose, decreased inflammation, and enhanced insulin sensitivity.	(Wang *et al*., 2023)
Oxidative stress and finger millet in diabetes	Finger Millet	An in vivo investigation of diabetic rats caused by streptozotocin	Finger millet enhanced glycemic management and decreased oxidative stress indicators (SOD, MDA).	(Tripathi *et al*., 2016)
Nephropathy caused by diabetes and foxtail millet	Foxtail Millet	An in vivo investigation of diabetic rats caused by streptozotocin	In diabetic nephropathy, foxtail millet enhanced antioxidant status, decreased blood glucose, and reduced kidney damage.	(Liu *et al*., 2023)
Lipid metabolism & finger millet	Finger Millet	An in vivo investigation of diabetic rats caused by streptozotocin	Finger millet decreased blood glucose levels and enhanced the lipid profile (higher HDL, lower LDL).	(Shobana *et al*., 2018)
Gut microbiota and foxtail millet	Foxtail Millet	In vivo investigation of diabetic mice generated by a high-fat diet	Foxtail millet decreased inflammation, enhanced glucose tolerance, and altered gut microbiome.	(Wang *et al*., 2023)

Study	Millet Type	Study Design	Key Findings	Reference
Pancreatic β-cells and finger millet	Finger Millet	An in vivo investigation of diabetic rats caused by streptozotocin	Finger millet enhanced insulin output while safeguarding pancreatic β-cells against oxidative harm.	(Sen, 2020)
Complications of diabetes with foxtail millet	Foxtail Millet	An in vivo investigation of diabetic rats caused by streptozotocin	Foxtail mill*et al*leviated diabetes complications and decreased advanced glycation end products (AGEs).	(Wang *et al.*, 2022)
The metabolism of glucose and finger millet	Finger Millet	An in vivo investigation of diabetic rats caused by streptozotocin	Finger millet increased insulin signaling and GLUT4 translocation, which enhanced glucose metabolism.	(Lu & Chen, 2022)
Foxtail millet and the control of hepatic glucose	Foxtail Millet	In vivo investigation of diabetic mice generated by a high-fat diet	Foxtail millet decreased insulin resistance and enhanced hepatic glucose control.	(Ren *et al.*, 2018)
Diabetes and diabetic neuropathy in finger millet	Finger Millet	An in vivo investigation of diabetic rats caused by streptozotocin	Finger millet improved diabetic neuropathy by lowering inflammation and oxidative stress.	(Kaur *et al.*, 2024)
Millet foxtail and diabetic retinopathy	Foxtail Millet	An in vivo investigation of diabetic rats caused by streptozotocin	In diabetic retinopathy, foxtail millet decreased oxidative stress and retinal damage.	(Krueger *et al.*, 2022)
Insulin signaling and finger millet	Finger Millet	An in vivo investigation of diabetic rats caused by streptozotocin	Finger millet decreased hyperglycemia and enhanced insulin signaling pathways.	(Kumar *et al.*, 2021)
Foxtail millet and the healing of diabetic wounds	Foxtail Millet	An in vivo investigation of diabetic rats caused by streptozotocin	Foxtail millet decreased oxidative stress and inflammation, which hastened the healing of wounds.	(Sharif *et al.*, 2024)
Diabetes-related cardiomyopathy and finger millet	Finger Millet	An in vivo investigation of diabetic rats caused by streptozotocin	In diabetic cardiomyopathy, finger millet enhanced heart function and decreased cardiac oxidative stress.	(Qaisar, n.d.)
Diabetes-related liver damage and foxtail millet	Foxtail Millet	An in vivo investigation of diabetic rats caused by streptozotocin	Foxtail millet decreased blood glucose, enhanced lipid profiles, and reduced liver damage.	(Ren *et al.*, 2021)

5.1. Microbiological Control of Oxidative Stress and Inflammation

Many microbial communities are found in the human digestive system, and they are essential to preserving health. Unbalanced gut flora can also worsen certain behaviours that lead to a series of metabolic disorders, and vice versa. Numerous illnesses, including as obesity, diabetes type II, heart disease, and autoimmune diseases, have markedly changed microbiome composition and activity (Miele *et al.*, 2015; Haghikia *et al.*, 2015). Furthermore, Chronic kidney dysfunction (CKD) patients' gut microbiota, differs both quantitatively and qualitatively from that of healthy persons, which contributes to uremic syndrome and problems associated with CKD (Khiabani *et al.*, 2023). In a range of physiological & pathological situations, fatty acids with short chains, or SCFAs, are versatile molecules that contribute to cell communication (Haase *et al.*, 2018). Several pieces of evidence suggest that the gut microbiota's production of SCFAs is altered in conditions such as inflammation of the bowel, obesity, diabetes, both type 1, type 2, autism, depressive disorders, colon cancer, and renal diseases (Schönfeld & Wojtczak, 2016; Li *et al.*, 2017). SCFAs mainly function as inhibitors of histone deacetylase (HDACs) or by triggering the activation of free fatty acid receptors (FFARs), which belong to the family of olfactory receptors (Olfr) and orphan G-protein-coupled receptors (GPCRs). Fatty acids with different carbon chains are bound by G-protein-coupled transmembrane receptors called FFARs. Additionally, the Olfr78 receptor is bound by butyrate, propionate, and acetate (Kimura *et al.*, 2019; Marinissen & Gutkind, 2001). SCFAs have several metabolic and signaling characteristics in addition to their structural and metabolic functions. They can in fact operate locally following gut microbial fermentation (Table 3) (Brown *et al.*, 2003; Hong *et al.*, 2005; Thangaraju *et al.*, 2009). Additionally, ferulic acid raises butyrogenic Faecalibacterium levels (Song *et al.*, 2020). The most prevalent butyrate maker, Faecalibacterium, has a reputation for reducing inflammation in the gut by blocking NF-κB activation and IL-8 production (Lenoir *et al*., 2020). Furthermore, by maintaining the strength of the barrier to the intestinal tract and lowering endotoxemia, butyrate generated by Faecalibacterium reduces the risk of developing diabetes (Carlsson *et al*., 2013). Oxidative stress results from an imbalance between the formation of reactive oxygen species, which are gases (ROS) and the antioxidant capacity of cells (Dayem *et al*., 2010; Newsholme *et al*., 2016). The development of Crohn's disease (CD) and colitis with ulceration (UC), two types of inflammatory bowel disease, or IBD, are significantly influenced by prolonged oxidative stress (Muro *et al*., 2024). Oxidative stress also seems to have a harmful function in chronic inflammatory disorders, according to recent data (Piechota-Polanczyk & Fichna, 2014). In Nrf2 knockout mice, suppression of NF-E2 related factor-2 (Nrf2) promoted inflammation and reduced the anti-oxidative stress pathway (Cheung *et al*., 2014). Patients with IBD have reduced antioxidant defense capability and elevated ROS in their intestinal mucosae (Wilson *et al*., 2010). Dihydroresveratrol (DH-RES), a metabolite of resveratrol, is produced by gut microbiota fermentation in the cecum, colon, and rectum. Its concentration is significantly more than that of resveratrol. As a result, this metabolite could also support pharmacological action in the large intestine of humans (Walle *et al*., 2004). Additionally, Numerous investigations have assessed how resveratrol affects the diversity and makeup of the gut microbiota, demonstrating that it inhibits the growth of Enterococcus faecalis, increases the ratios of Bacteroidetes to Firmicutes, and increases the populations of Lactobacillus and Bifidobacterium (Zhao *et al*., 2017; Qiao *et al*., 2014). The human colon produces butyrate, propionate, and acetate in an approximate 3:1:1 ratio. SCFAs may bind to various receptors once they are created, and they are made by a variety of bacteria. Table 3 lists the receptors against which each SCFA has a robust affinity along with their intestinal & non-intestinal expression (Brown *et al*., 2003; Hong *et al*., 2005; Thangaraju *et al*., 2009).

Table 3: Receptors against which each SCFA has a Robust Affinity along with their Intestinal & Non-Intestinal Expression

SCFAs	Producers	Binding	Intestinal Expression	Non-Intestinal Expression
Acetate	Muciniphila Akkermansia, Ruminococcus species, Prevotella species, Bifidobacterium species, Bacterioides species, Hydrogenotrophic Blautia, Streptococcus species and Clostridium species.	GPR43 Olfr78	Colonic, intestinal epithelium, small colonic propria lamina cells and tiny intestine leukocytes	Heart, skeletal muscle, adipocytes, polymorphonuclear cells, Spleen Olfr78
Propionate	Phascolarctobacterium succinatutens, Bacterioides species, Veilonella species, Dialister species, Elesdenii Megasphera, Coprococcus catus Obeum Ruminococcus, Salmonella species, Inulinivorous roseburia	GPR43 GPR41 Olfr78	Gut enteroendocrine cells are found in the crypts and lower part of the villi, as well as the colonic intestinal epithelium that lies in the small pancreas and colonic propria lamina cells (mast cells)	Afferent periportal system, peripheral nerve system, bone marrow, spleen, lymph nodes, adipose tissue, and mononuclear peripheral blood cells
Butyrate	Coprococcus eutacus, Coprococcus viene, Anaerostipes species, Coprococcus catus Eubacterium rectale Roseburia species, Eubacterium hallii, and Faecalibacterium prausnitzii.	GPR109A GPR41 GPR43	Dendritic cells, neutrophils, monocytes, macrophages, and the apical membrane of the colonic/small intestinal epithelium	White & brown adipocytes, epidermal Langerhans cells, and retinal pigment epithelium

5.2. Mechanisms of Action: Gut Microbiota and Oxidative Stress

The gut bacteria have a major impact on how dietary items, including millets, are metabolized. It has been shown that gut bacteria that break down dietary fiber and polyphenols create short-chain fatty acids (SCFAs), such as acetate, propionate, and butyrate, enhance insulin sensitivity and lower inflammation (Sireesha *et al.*, 2011). The following are the molecular mechanisms:

- Insulin Sensitivity and SCFAs: SCFAs bind to receptors associated with G-proteins (GPCRs), that are expressed in the pancreas and adipose tissue, and include GPR41 and GPR43. In peripheral tissues, activation of these receptors promotes glucose absorption and increases insulin secretion (Chandrasekara & Shahidi, 2011).
- Decrease in Oxidative Stress: Gut bacteria break down the polyphenols in millets into smaller phenolic compounds, which are strong antioxidants. By increasing the levels of antioxidant enzymes such as superoxide dismutase, or SOD, and glutathione peroxidase (GPx), scavenging reactive oxygen species (ROS), these substances lessen oxidative stress (Udeh *et al.*, 2017).
- Anti-inflammatory Effects: SCFAs and phenolic metabolites also suppress nuclear factor-kappa B, a key regulator of inflammation. Cytokines that promote inflammation, such as TNF-α and IL-6, which are linked to insulin resistance and the advancement of diabetes, are produced less often as a result (Kajla *et al.*, n.d.).

6. Impact of Millet-Induced Gut-Microbiota Possible Anti-Diabetic

For about 10,000 years, millet has been used as fodder and for human sustenance. It belongs to the Poaceae family. In hot, dry areas, it thrives as small-seeded grasses (Tripathi *et al.*, 2021). The Food and Agriculture Organization of the United Nations (FAO) (Garibaldi, 2012), states that while Asia and Africa are the primary producers, China, India, and Niger are the three countries with the greatest yields. The millet that is grown includes foxtail millet (FM), proso millet, pearl millet, finger millet, and others. Millet is higher in a number of macronutrients, minerals (iron, zinc, phosphorus, calcium, & potassium), and vitamins than rice and wheat (Saini *et al.*, 2021). The digestibility of the grains is influenced by the quantity of amylase and protease inhibitors (Yin *et al.*, 2018). Millet naturally possesses several significant qualities, including low glycaemic index, hypolipidemic, and antioxidant properties (Sharma & Niranjan, 2018).

Table 4: Several Millet Varieties and Possible Characteristics

Millet Type	Features	References
Foxtail millet	Anti-diabetic qualities, decreases cholesterol, and reduces the risk of colon cancer. Reduces the harm that ethanol causes to the liver.	(Yang *et al.*, 2020; Ren *et al.*, 2016)
Pearl millet	Celiac illness is prevented by the gluten-free property. Shigella-induced pathogenicity is inhibited, strengthening the immune system.	(Akinola *et al.*, 2017; Ganguly *et al.*, 2019)
Finger millet	Accelerates the healing process and reduces soft damaged tissue. Reduces the risk of heart disease by lowering plasma triglycerides.	(Sarita & Singh, 2016)
Kodo millet	Reduce the incidence of diabetes and the glycaemic index while also having antioxidant properties.	(Srilekha *et al.*, 2019)
Proso millet	Gluten-free qualities can avoid celiac disease. Foods with a low glycaemic index (GI) lower the risk of type 2 diabetes.	(Tyl *et al.*, 2018; Das *et al.*, 2019)
Little millet	The presence of polyphenols aids in the prevention of certain disorders of metabolism.	(Srilekha *et al.*, 2019, Almaski *et al.*, 2017)
Barnyard millet	Dead cell damage lowers the risk of cancer of the colon. Reduces the symptoms of diabetes by blocking the glycation and glycoxidation of proteins.	(Ramadoss & Sivalingam, 2020; Anis & Sreerama, 2020)

Figure 1: Global Millet Production (million tons) (Bartley, 2020)

7. The Millets' Methods for Assisting in the Treatment of Diabetes Mellitus

Through several methods, millets help regulate diabetes. Their low glycaemic index (GI) helps control blood sugar levels by delaying the ingestion and digestion of carbohydrates. The high fiber content of millets also helps to reduce blood sugar spikes. Additionally, millets are a great supplier of phytochemicals such phenolics and flavonoids, which lower blood sugar and enhance insulin sensitivity, as well as antioxidants. Further supporting their efficacy in controlling diabetes is their nutritional content, which includes vital vitamins and minerals, as well as their function in weight management (Vidhyalakshmi & Meera, 2024; Jacob *et al.*, 2024).

Table 5: Pathways through which Millets Act in the Treatment of Diabetes Mellitus

Pathway	Mechanism	References
Low GI, or Glycaemic Index	Millets' low GI aids in improved blood sugar regulation by delaying the breaking down and absorption of carbs.	(Vidhyalakshmi & Meera, 2024)
Elevated Fiber Levels	Millets' substantial amount of fiber reduces blood sugar rises by delaying the consumption of glucose.	(Vidhyalakshmi & Meera, 2024)
Properties of Antioxidants	Antioxidant substances included in millets assist lower cellular stress, which is advantageous for diabetes management.	(Jacob *et al.*, 2024)
Plant-based Chemicals	It has been demonstrated that the phytochemicals found in millets, such as flavonoids and phenolics, increase insulin sensitivity and lower blood sugar levels.	(Jacob *et al.*, 2024)
Value of Nutrition	The vital minerals and vitamins included in millets support general health and aid in the management of diabetes.	(Jacob *et al.*, 2024)
Controlling Weight	Due to millets' high fiber content and low calorie content, they aid in managing your weight, which is essential for controlling diabetes.	(Jacob *et al.*, 2024)

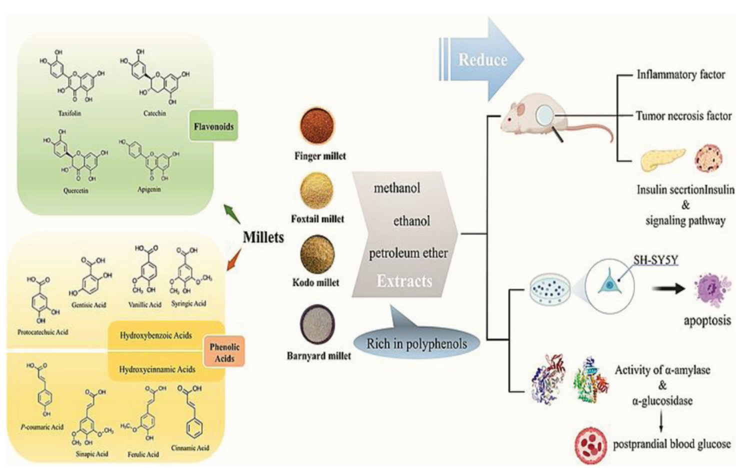

Figure 2: Millets' Polyphenols and their Impact on Variables Linked to Diabetes

Flavonoids and phenolic acids make up most millet's polyphenols. It was discovered that millet polyphenol extracts impacted the insulin signal pathway, postprandial blood glucose-related enzyme activities, Its anti-inflammatory and antioxidant factors derived from an analysis of in vitro and in vivo research on millet polyphenols' effects on diabetes (Wang *et al.*, 2022).

8. Limitations and Conflicting on Finger Millets and Foxtail Millets in the Role of Controlling Diabetes Mellitus

- **Bioactive Compound Variability:** Depending on the kind, growing environment, and processing techniques, the number of bioactive substances (such as polyphenols, flavonoids, and dietary fiber) in finger millet and foxtail millet might vary greatly. Their antidiabetic effects may vary because of this heterogeneity (Mikulajova *et al.*, 2017).
- **Restricted Human Research:** In vivo research (animal models) provides most of the data for finger millet and foxtail millet's antidiabetic benefits. Large-scale, well planned human clinical studies are needed to validate these results (Pradeep & Guha, 2011).
- **Differing Glycemic Control Results:** While some studies show that consuming millet increases insulin sensitivity and dramatically decreases blood glucose levels, other studies show little to no change. This disparity might result from variations in the study's design, dose, and intervention's length (Wang *et al.*, 2021).
- **Interaction with Additional Dietary Elements:** Other dietary elements including lipids, proteins, and carbs may have an impact on millets' antidiabetic properties. For instance, the positive benefits of millets on glycemic management may be lessened by a high-fat diet (Maurya *et al.*, 2023).
- Milling, heating, and fermentation are examples of processing techniques that can change the bioaccessibility and bioavailability of bioactive components in millet. Their antidiabetic potential may be diminished by overprocessing (Zhang *et al.*, 2021).
- **Variability in the Gut Microbiota:** The metabolism of millets' bioactive components depends heavily on the gut microbiota. Individual variations in the gut microbiota's composition, however, may result in varying outcomes in terms of their antidiabetic benefits (Tsubokawa *et al.*, 2022).
- **Possible Side consequences:** Compounds in finger millet might interfere with thyroid function, causing goitrogenic consequences if consumed in excess. Those who suffer from thyroid problems should be concerned about this (Chandra *et al.*, 2016).
- **Lack of Standardization:** To obtain antidiabetic benefits, millets cannot be consumed in a standardized dosage or form (such as whole grain, flour, or extract). It is challenging to compare research and get firm results because of this lack of uniformity (Pradeep & Guha, 2011).

9. Conclusion

In 2021, 537 million individuals worldwide suffered from Type 2 diabetes (DM), a long-term metabolic condition characterized by elevated blood glucose levels. By 2045, that number is expected to rise to 700 million. The most prevalent kind of diabetes is diabetes with type 2 mellitus (T2DM), which is strongly linked to lifestyle variables. Millets, such foxtail millet (Setaria italica) and finger millet (Eleusine coracana), have drawn interest as functional foods because of their high dietary fiber content, low glycemic index (GI), and nutritional richness, polyphenols, and antioxidants. These bioactive compounds offer anti-inflammatory, antioxidant, and glycemic control benefits, helping to reduce insulin resistance and modulate gut microbiota. There are still issues, nevertheless, such the variation in bioactive substances, the paucity of human clinical studies, and how processing affects bioaccessibility. Risks such as goitrogenic consequences might potentially result from consuming too much millet. To firmly establish millet-based dietary guidelines for diabetes treatment, more research is essential, including extensive human trials.

10. Future Prospective

Millets have a lot of potential for managing diabetes because of their excellent nutritional profile & bioactive components. They are perfect for controlling blood sugar levels because of their low glycemic index and high dietary fiber content. By increasing the bioavailability of the beneficial chemicals in millets, advanced food processing methods like fermentation & malting can improve metabolic health and help control diabetes. This may result in the creation of nutraceuticals and prebiotic formulations for the treatment and prevention of diabetes. Additionally, millets might be utilized to make ready-to-eat snacks and other sustainable, diabetic-friendly food products. To optimize their influence on diabetes management and diet, more study is required.

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Authorship Contribution

Bipin Singh: conceived and designed the manuscript, analyzed the data, and contributed to the writing and editing of the manuscript; Mohd. Sayam, Md. Shamim Ahmad: collected and organized data, contributed to the literature review, and assisted in drafting the manuscript; Vishal Kajla: contributed to the writing, figure conceptualization, and drafting of the manuscript; Shalu Kashyap: critically reviewed the manuscript, provided intellectual input, and assisted in finalizing the content; Ajay Bilandi: performed final approval of the version to be published and ensured the accuracy of the content.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Declaration

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