Proceedings of the Indian National Science Academy (2026) 92:52–62
https://doi.org/10.1007/s43538-025-00402-5

REVIEW ARTICLE

Exploring the nutraceutical potential of foxtail millet: a minor millet with a major impact on nutrition security

Pooja Shukla[1] · Pooja R. Aggarwal[1] · Pooja Choudhary[2] · Mehanathan Muthamilarasan[1]

Received: 17 August 2024 / Accepted: 14 February 2025 / Published online: 23 February 2025

Abstract
Foxtail millet (*Setaria italica* L.) is an important small millet grown in the arid and semi-arid regions of the world for food and forage purposes. India is the second top-most producer of foxtail millet in Asia after China in terms of area and production. Being a C_4 crop, foxtail millet has excellent photosynthetic efficiency and produces a high yield even in minimal nutrient-containing soil and low precipitation. Foxtail millet also has high water use efficiency and exhibits remarkable tolerance against abiotic stresses. Owing to these properties and their genetic relatedness to the C_4 grasses, foxtail millet serves as a model for studying C_4 photosynthetic and biofuel traits. However, the nutritional potential of this crop is often overlooked. The nutrient content of foxtail millet is far superior to major cereals as the grains are rich in protein, carbohydrates, fats, vitamins and minerals, and diverse health-promoting bioactive compounds. This nutritional superiority has the potential to significantly impact human health and well-being, offering a promising solution to nutritional deficiencies and related health issues. However, a comprehensive investigation of foxtail millet for its nutraceutical properties is lacking due to the scarcity of concrete molecular evidence. This underscores the need for further research in this area. The present review highlights the potential of foxtail millet as a nutri-cereal and discusses various molecular studies performed on it to harness its nutraceutical properties, emphasizing the importance of ongoing and future research in this field.

Keywords Foxtail millet · C4 crop · Nutri-cereal · Therapeutics · Bioactive compounds · Nutrition security

Introduction

Adequate nutrition is a fundamental requirement for the healthy growth and development of any living organism. In humans, a healthy diet plays a significant role in preparing the body against various diseases and health conditions such as anaemia, irregular blood pressure (BP), hypertension, and obesity. The effects of poor nutrition can be observed as the physical, physiological, mental, psychological, and emotional symptoms, including the first few physiological symptoms such as childhood stunting, anaemia, and low birth weight. According to a recent WHO report, the estimated number of children showing stunting symptoms under the age of 5 years was 149.2 million globally, while about 45.4 million children were underweight due to poor nutrition (https://www.who.int/health-topics/nutrition). Considering the importance of nutrition for human health, it is imperative to precisely investigate the effect of food components in growth and development as well as in managing several diseases/health conditions. Nutraceuticals, substances derived from food products, have captured the interest of researchers for a long time. Stephen De Felice coined the term "Nutraceutical', which broadly involves food that provides therapeutic/medicinal effects in addition to nutrition (Parulekar et al. 2019). Although the potential of other crops to be developed as nutraceutical and industrial resources has been realized through a plethora of studies, the exploration of millets in this regard, especially foxtail millet, is still in its infancy. One of the oldest cultivated crops, foxtail millet was first domesticated about 8000 years ago in northern China. Later, it was cultivated in India, Afghanistan, Korea, Georgia, Central Asia, Japan, and other parts of the world.

Pooja Shukla and Pooja R. Aggarwal authors contributed equally.

✉ Mehanathan Muthamilarasan
muthu@uohyd.ac.in

[1] The Millet Lab, Department of Plant Sciences, School of Life Sciences, University of Hyderabad, Hyderabad, Telangana 500046, India

[2] Department of Biotechnology, Jaypee Institute of Information Technology, Noida, Uttar Pradesh 201309, India

It is regarded as the major small millet and identified as the sixth-highest grain-yielding crop in terms of worldwide production (Saleh et al. 2013). The gross yield of the foxtail millet crop contributes to human consumption and animal and poultry feeding, in addition to hay and silage production. Foxtail millet germinates and initiates the flowering within a short duration of 5–8 weeks, with a single main inflorescence producing hundreds of seeds, which mature within 15 weeks of germination (Doust et al. 2009). Morphologically, similar to the other cereal grains, foxtail millet grain also has husk and bran, constituting about 13.5% (w/w) and 1.5–2% (w/w) of the grain, respectively. Due to its efficient water use, stability in arid and semi-arid conditions, and short cycle, the crop is regarded as a C_4 model crop for genetic and genomic studies (Lata et al. 2013).

Foxtail millet is considered nutritionally superior to major cereal crops as their grains are naturally enriched with micro as well as macronutrients, bioactive compounds, proteins and dietary fiber (Muthamilarasan and Prasad 2015). Foxtail millet grains contain high levels of linoleic and stearic acids, which aid in maintaining a healthy lipid profile (Gowda et al. 2022). Additionally, the considerably higher resistant starch content, which acts as dietary fiber, helps to impart its therapeutic effects (Ren et al. 2016; Guo et al. 2023). Considering the nutritional and therapeutic significance of foxtail millet, it is regarded as one of the 'Nutri-cereals' (Karpagapandi et al. 2023; Kalsi and Bhasin 2023; Ingle et al. 2023). Foxtail millet possesses vast nutritional diversity among different cultivars. Seventy-five foxtail millet germplasm lines showed large variation in their nutritional content. GS1000 was found as the highest energy-providing germplasm (Kamatar et al. 2015). Brunda et al. (2015) investigated the nutrition profile of 78 foxtail millet accessions highlighting the vast genetic diversity in terms of nutritional aspects, encompassing protein, crude fiber, total minerals, total iron, zinc, manganese, and copper contents (Brunda et al. 2015). Given the nutritional and nutraceutical properties of foxtail millet, it is important to comprehensively analyze these traits to efficiently harness the therapeutic potential of millets. The current review aims to highlight the nutraceutical benefits of foxtail millet, by enumerating the reports depicting its therapeutic properties and the studied effects on the human body.

Nutraceutical properties of foxtail millet bran and bran-derived bioactive components

Bran is the outer layer of the cereal grain consisting of the pericarp, testa, aleuronic layer, germ, and a part of starchy endosperm. Of these, the aleuronic layer is rich in total phosphorus, phytate phosphorus, protein, fat, and niacin. Earlier, cereal bran was considered a waste by-product and discarded during milling and primary processing. Later on, the advancement in processing technologies unlocked the nutritional potential of cereal bran (Luithui et al. 2019). In addition to imparting sensory attributes such as texture, gelling, emulsifying, thickening, and stabilizing related properties, bran is rich in macronutrients and micro-nutrients. It is also abundant in antioxidants, essential fatty acids (palmitic, oleic, and linoleic acids), vitamins (especially B and E), phytosterols, bioactive compounds, and prebiotics (Patel 2012; Kouhestani and Azizkhani 2024). Numerous studies have been performed in the past to analyze the nutritional profile of foxtail millet bran (Fig. 1; Table 1).

Foxtail millet bran consists of insoluble and soluble dietary fiber (IDF and SDF), which have significantly different functional attributes. Foxtail millet SDFs are rich

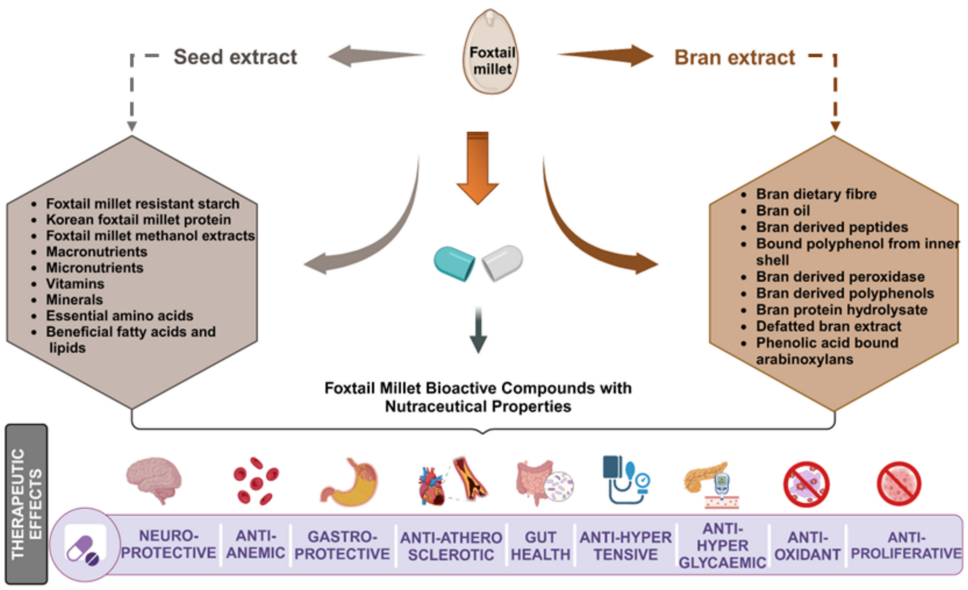

Fig. 1 The key components of foxtail millet grain (present in seed extract and bran extract) provide important bioactive compounds that hold the nutraceutical potential to impart therapeutic effects to the human body against major health issues and chronic diseases. The illustration is created with BioRender

Table 1 Bioactive compounds identified from foxtail millet and their therapeutic effects

Plant part	Bioactive compound	Therapeutic effect	References
Bran	Bran derived peroxidase (FMBP)	Anti-atherosclerosis activity	Liu et al. (2020a, b)
	Bio-active peptides	Anti-atherosclerosis activity	Shan et al. (2022)
	Bound polyphenol from inner shell (BPIS)	Anti-cancer activity	Shi et al. (2015)
	Ferulic acid and p-coumaric acid	Anti-cancer activity	Cui et al. (2022)
	Bound polyphenol (BPIS), ferulic acid (FA), and p-coumaric acid (p-CA)	Anti-cancer activity; increased chemotherapy sensitivity towards oxaliplatin drug	Zhang et al. (2020)
	Bioactive peptides with sequences such as VLER, WVGK, VVRP, VLLF, VALVR, LFGK and FGPK	Anti-hypertensive activity; Anti-inflammatory activity	He et al. (2022)
	Protein hydrolysate	Anti-NAFLD effect; Hepato-protective activity; Hypolipidaemic activity	Shan et al. (2023)
	Hydroxycinnamic acid bound arabinoxylans; phenolic compounds (caffeic, p-coumaric, and ferulic acid)	Antioxidant activity	Bijalwan et al. (2016)
	Novel 35 kDa protein (FMBP)	Anti-proliferative activity	Shan et al. (2014)
	Bound polyphenol from inner shell (BPIS)	Anti-proliferative activity	Shi et al. (2019)
	Dietary fibre	Cholesterol binding/absorption activity	Zhu et al. (2019)
Bran oil	Linoleic acid and oleic acid	Antioxidant and hepato-protective effect	Pang et al. (2014)
Bran wine	Phenolic compounds (vanillic acid, syringic acid, p-coumaric acid, and ferulic acid)	Antioxidant activity	Guo et al. (2018)
Defatted bran extract	Phenolic content	Antioxidant activity	Amadou et al. (2011)
Dry seeds	Novel 26.9 kDa antifungal peptide	Antifungal activity	Xu et al. (2011)
Fermented and germinated whole-grain	–	Diabetic kidney disease amelioration	Liu et al. (2022a, b)
Fermented meal	Derived peptides	Trypsin resistant; antimicrobial and antioxidant activity	Amadou et al. (2013)
Foxtail millet flour	–	Gastroprotective effect against ulceration	Lin et al. (2020)
Grain polyphenols	Polyphenols	Anti-inflammatory; Cytoprotective; Neuroprotective activity	Li et al. (2020)
	Phenolic acid-bound arabinoxylans	Immunostimulatory activity	Srinivasan et al. (2020)
Husk	Phenolic compounds	Acetylcholinesterase and α-glucosidase inhibitory activities	Wang et al. (2023)
Inner shell	Bound polyphenols of Inner Shell (BPIS); ferulic acid and p-coumaric acid	Anti-proliferative activity	Zhang et al. (2023)
Whole grain (Korean)	Grain protein	Improved insulin sensitivity and cholesterol metabolism	Choi et al. (2005)
Red foxtail millet seeds	Methanol extracts	Neuroprotective activity	Nakajima et al. (2023)
Seeds	Phytochemical rich fractions	Anti-cancer activity	Kuruburu et al. (2022)

– Data not available

in total phenolic and flavonoid content and possess strong antioxidant activity. It also contains α-amylase inhibition and sodium cholate adsorption abilities as compared to IDFs (Dong et al. 2019). High dietary fiber content, concentrated especially in the bran, plays an important role in the formation of antioxidant dietary fiber (ADF) (Shahidi and Chandrasekara 2017). Foxtail millet dietary fiber can be efficiently used as a food additive based on its physiochemical properties (Zhu et al. 2018). Xylanase treatment changes the composition and microstructure of dietary fiber derived from foxtail millet bran and increases the cholesterol binding/absorption capacity (Zhu et al. 2019).

Foxtail millet bran oil is polyunsaturated and monounsaturated fatty acids, while stearic acid (6.3%) and palmitic acid (6.4%) were found as the major saturated fatty acids (Liang et al. 2010). Liang et al. (2010) showed dilinoleoylmonoolein and trilinoleate as the major triacylglycerols, while Ji et al. (2019) reported trilinolein (LLL) and oleodilinolein (OLL) as the main triacylglycerols. Pang et al. (2014) revealed that foxtail millet bran oil imparts antioxidant and hepato-protective effects that attenuate ethanol-induced hepatic injury via antagonizing the increase in MDA, SOD, triglycerides, aspartate aminotransferase, and alanine aminotransferase.

Millet bran and bran-derived peptides are shown to have immense therapeutic potential (Fig. 1; Table 1). A novel 26.9 kDa peptide in foxtail millet seeds was found to exhibit high antifungal activity against different fungal species (Xu et al. 2011). Shan et al. (2014) isolated a 35 kDa protein, FMBP from foxtail millet bran showing high homology with peroxidase. FMBP inhibited colon cancer cell progression in vivo via G1 phase arrest and induced caspase-dependent apoptosis (Shan et al. 2014). Millet bran-derived bioactive peptides mitigated inflammation in hypertensive rats and lipopolysaccharide-induced RAW264.7 cells, in vivo and in vitro, respectively (He et al. 2022). Millet bran protein hydrolysate was shown to exert an anti-NAFLD effect and alleviate hepatic steatosis and hepatic vacuolar degeneration leading to reduced accumulation of lipids via inducing PPARγ (peroxisome proliferator-activated receptor γ). Consequently, the reduced expression of fatty acid uptake-related genes, such as *FABP1*, *FABP2*, *FABP4*, *CPT-1α*, and *CD36* was observed (Shan et al. 2023).

Bound polyphenol from the inner shell (BPIS) derived from foxtail millet bran also holds immense therapeutic significance. Shi et al. (2015) revealed that BIPS show anti-colon cancer activity by inducing apoptosis and inhibiting the growth of cancer cells. Further, BPIS was shown to act as a glycolysis inhibitor by upregulating the expression of miR-149 and targeting the 3′-UTR of c-myc, thereby blocking the aerobic glycolysis mediated by PKM2 and exhibiting anti-proliferative activity (Shi et al. 2019). Zhang et al. (2020) studied the anticancer activity of BPIS from foxtail millet bran, rich in ferulic acid (FA) and *p*-coumaric acid (*p*-CA), on colorectal cancer cells. Interestingly, upon supplementation with foxtail millet BPIS, the colorectal cancer cells showed increased chemotherapy sensitivity towards oxaliplatin, a common CRC chemotherapy drug towards which the patients easily develop resistance. Further, the multi-omics-based analysis indicated the remodeling of NEU3-mediated ganglioside GM3 catabolism through inhibition of NEU3 expression, increased levels of GM3, and reduced Gb3 and P-gp levels, eventually leading to impairment of multidrug resistance protein 1 (*MDR1*) expression (Zhang et al. 2020). Ferulic acid and *p*-coumaric acid in foxtail millet bran were shown to suppress the growth of colorectal cancer by inhibiting aerobic glycolysis via the lncRNA 495810/PKM2 axis (Cui et al. 2022). Foxtail millet BPIS is also reported to inhibit breast cancer by triggering ferulic acid and p-coumaric acid-induced autophagy. The expression of *PCYT1A*, a key enzyme for glycerophospholipid synthesis, was increased leading to glycerophospholipids accumulation in breast cancer cells, thereby triggering autophagy (Zhang et al. 2023).

Ethanolic extract of foxtail millet bran displayed significant antioxidant activity, which was positively correlated with its phenolic content (Amadou et al. 2011). Hydroxycinnamic acid-bound arabinoxylans from the bran of Indian foxtail millet variety, CO-Te-7, contained three major phenolics (caffeic, *p*-coumaric, and ferulic acids), showing antioxidant potential (Bijalwan et al. 2016). HPLC identified major phenolic compounds such as ferulic acid, vanillic acid, *p*-coumaric acid, and syringic acid in foxtail millet bran wine imparting effective antioxidant activity (Guo et al. 2018). Foxtail millet bran-derived peroxidase (FMBP) treatment reduced lipid phagocytosis effectively, repressed lipid uptake by downregulating CD36 expression, and inhibited STAT3 expression, thus preventing atherosclerosis (Liu et al. 2020a, b). Interestingly, a novel Bowman-Birk type trypsin inhibitor derived from foxtail millet bran was found to exhibit anti-atherosclerosis activity, which was evident by reduced atherosclerotic plaque and reduced inflammatory cytokines. Additionally, 16S rRNA sequencing unraveled the remodeling of gut microbiota and enrichment of *Firmicutes* and *Lactobacillus* (Shan et al. 2022). Foxtail millet polyphenols were reported to exert neuroprotective and cytoprotective effects in SH-SY5Y cells under oxidative stress by increasing the expression and activities of antioxidant enzymes such as GPX, CAT, and SOD (Li et al. 2020). In addition to alleviating neural inflammation, these polyphenols significantly lowered the expression of AD-related genes such as *APP*, *TAU*, *PS1*, *BACE1*, and *IDE* (Li et al. 2020).

The presence of phytochemicals in bran imparts a characteristic color. Purple brans are rich in anthocyanins, whereas orange and light brown bran contain carotenoids and phenolics, respectively. The presence of such compounds is significantly associated with their potential to act as a functional food for human health (Gonçalves et al. 2021; Mozos et al. 2021; Oteiza et al. 2023; Matsumura et al. 2023; Bohn et al. 2023; Bayazid and Lim 2024; Sharma et al. 2024). The phytochemical-rich fraction from foxtail millet seeds exhibited anti-cancer activity on breast cancer cells through increased fragmentation of DNA and cell arrest at the G2/M stage, leading to the accumulation of cells at the sub-G1 phase (Kuruburu et al. 2022). Considering the importance of bran color in influencing the adaptability of a food product, these attributes should be promoted in the future based on their nutritional properties. Given the above, the research on bran and bran-derived bioactive components of foxtail millet is projected to progress significantly, driven by growing interest in functional foods and sustainable agriculture. Studies should focus on isolation and characterization of bioactive compounds, such as phenolics, flavonoids, and dietary fibers, found in foxtail millet bran, as these compounds have potential health benefits, including antioxidant, anti-inflammatory, and anti-diabetic properties. Also, studies are imperative to understand how these compounds work at molecular level, to gain mechanistic insights in to the mode of action for the development of nutraceuticals and functional food products.

Nutraceuticals attributes of foxtail millet grain phenolic compounds

Millet grain phenolic components possess nutraceutical and therapeutic effects (Fig. 1; Table 1), substantially evident by studies summarizing their bioactivities (Shahidi and Chandrasekara 2013). Grain phenolic compounds are broadly classified into tannins, flavonoids, and phenolic acids, which can be further categorized into hydroxyphenylpropanoic acids, hydroxycinnamic acids, hydroxybenzoic acids, and hydroxyphenylacetic acid. In addition to imparting antioxidant, anti-inflammatory, and antiviral effects, millet phenols have been demonstrated to possess anti-mutagenic, anti-oestrogenic, and platelet aggregation inhibitory activity (Shahidi and Chandrasekar 2013). Foxtail millet contains total phenolic content (TPC) ranging between 0.4–1.83 mg/g, total flavonoid content (TFC) ranging between 0.02–0.79 mg/g, proanthocyanidin between 0.14–1.2 mg/g of millet flours. Additionally, phytic acid (PA) was estimated to be 5.4 mg/g for the PS-4 variety, while the highest PA content (9.9 mg/g) was estimated in SIA-3126 (Devisetti et al. 2014).

Chandrasekara and Shahidi (2011) reported that whole millet phenolic extract was able to significantly inhibit cell proliferation in vitro. Owing to the presence of hydroxycinnamic acids (p-coumaric and ferulic acids), the soluble and bound phenolic extracts of millets showed effective free radicals and ROS scavenging activities (Chandrasekara and Shahidi 2011). In a subsequent study, dehulling and cooking of the grains led to the release of phenolics bound to insoluble grain fiber into more bioaccessible phenolic compounds upon colonic fermentation, thereby imparting antioxidant activity (Chandrasekara and Shahidi 2012a, b). Zhang and Liu (2015) reported the antioxidant and anti-proliferative activity of Jingu28 and Jingu34 varieties of foxtail millet, correlating with their respective phenolic and carotenoid contents. The phenolic acid-bound arabinoxylans from millets were examined using gas chromatography, mass spectroscopy, and HPLC. These compounds exhibited immunostimulatory activity due to the release of ROS, NO, and cytokines (Srinivasan et al. 2020). Comparative transcriptome analysis revealed that the supplementation of fermented and germinated foxtail millet helped in preventing diabetic kidney disease by inhibiting inflammation and immunity-related signaling pathways. In addition, cecal microbiota analysis using 16s rRNA sequencing revealed *Firmicutes* as the most abundant taxa, followed by *Bacteroidetes*, while the *Proteobacteria* were found to decrease significantly (Liu et al. 2022a, b). The phenolic compounds from foxtail millet husk were extracted using deep eutectic solvents (DESs) coupled with ultrasonic-assisted extraction (UAE). Further, UPLC/MS was used to identify 12 phenolic compounds showing α-glucosidase and acetylcholinesterase inhibitory activities (Wang et al. 2023). In this direction, studies should focus on identifying, quantifying, and understanding the health benefits of phenolic compounds of foxtail millet. Advanced analytical techniques, including mass spectrometry and chromatography, should be deployed to identify, isolate, and characterize the phenolic compounds having health benefits. Exploring the bioavailability and metabolism of these phenolic compounds in the human body, investigating their antioxidant, anti-inflammatory, and anti-cancer properties, are imperative. At the same time, studying the synergistic effects of phenolics with other bioactive compounds in foxtail millet is also important to enhance the health benefits of this millet.

Importance of foxtail millet to battle chronic diseases

Various studies have elucidated the potential of foxtail millet in managing/preventing chronic diseases, highlighting its nutraceutical significance (Fig. 1; Table 1). The role of nutrition and nutrients in preventing chronic diseases like obesity, cardiovascular diseases, and cancer has been extensively studied (Byers 2002; Ojo 2019). With a major part of the adult population of India suffering from osteoporosis, calcium and iron deficiency remains widely spread in the country (Saini et al. 2021). Millet consumption can alleviate anaemia due to its rich iron content as compared to other cereals (Anitha et al. 2021a, b). Additionally, a foxtail millet-based diet shows a gastroprotective effect against ulceration. This effect was observed by an increase in non-protein sulfhydryl levels and a decrease in ulcer index and thiobarbituric acid reactive substances in stressed rats (Lin et al. 2020). A range of nutraceutical effects imparted by foxtail millet is described in the subsequent sections.

Hypolipidemic and anti-hypertensive effect

Foxtail millet has been studied for its commendable therapeutic role in dyslipidemia by increasing high-density lipoproteins (HDL) levels, reducing low-density lipoprotein (LDL), and providing hypolipidemic effects upon consumption (Table 1). Korean foxtail millet protein supplementation to genetically type 2 diabetic KK-A^y mice led to increased HDL-cholesterol and adiponectin, exhibiting the potential to prevent obesity-related disorders, through improved insulin sensitivity and cholesterol metabolism (Choi et al. 2005). Foxtail millet diet supplementation in comparison to Atorvastatin showed a better hypolipidemic effect, with an evident increase in HDL-C and total cholesterol, triglycerides, and

LDL (Onteddu et al. 2023). Foxtail millet consumption also helps to manage increased BP, hypertension, and chronic artery disease. In another study, intervention with a whole grain diet (100 g/d for 16 weeks) led to a diastolic blood pressure decline of 5.8 mmHg (Kirwan et al. 2016). Hou et al. (2018) reported as the first clinical confirmation that foxtail millet consumption for 12 weeks helps to significantly decrease systolic and diastolic BP. Additionally, an increase in the total protein, minerals, and fiber contents > 10% was also suggested to have a beneficial impact on maintaining blood pressure (Hou et al. 2018). The supplementation of other nutritional components and their interactions may also contribute to these therapeutic benefits. A significant reduction in BP in hypertensive rats was observed with the help of foxtail millet protein hydrolysates (Chen et al. 2017). Moreover, it was suggested that different varieties of millet exhibited differential levels of lipid oxidation inhibition. Millet extract (concentration 0.05 mg/ml) showed LD inhibition between 1–41% (Chandrasekara and Shahidi 2012a, b). Godos et al. (2017) mentioned that foods rich in phenolic acids may reduce the risk of hypertension.

The RAAS (renin–angiotensin–aldosterone system), a key physiological regulator of BP, exhibited a downward trend following a 12-week foxtail millet diet (Hou et al. 2018). Chen et al. (2017) suggested that the possible mechanism underlying the antihypertensive effect of whole foxtail millet is via inhibiting the activity of serum ACE and decreasing the Ang II levels in mild hypertensive subjects. A meta-analysis study conducted by Anitha et al. (2021a, b) showed that the 21 days to 4-month millet-based diet leads to a reduction in TC, triacylglycerol, VLDL-C, and LDL-C levels, along with a decrease in diastolic/systolic BP, and body mass index (BMI), with a significant increase in HDL-C. Altogether, this evidence highlights that the consumption of millet might alleviate hyperlipidemia and hypertension. Also, improved HDL-C, known as good cholesterol, may help reduce the risk of atherosclerotic cardiovascular diseases.

Anti-hyperglycaemic effect

Foxtail millet is a low glycaemic index (GI) food as compared to other major cereals, suitable food for patients with type 2 diabetes. Millets are rich in slowly digestible starch (SDS) and resistant starch (RS) (Liu et al. 2020b). These types of starch play a significant role in managing diabetes, particularly type 2 diabetes, by controlling meal-associated hyperglycemia (Lehmann and Robin 2007). Regular consumption of foxtail millet can be beneficial for diabetic patients due to the abundance of several minerals and specific amino acids such as leucine that are shown to be an important factor in muscle loss prevention and improved glycaemic index (Manders et al. 2006; Norton et al. 2012). Moreover, resistant starch improves insulin sensitivity, without significantly affecting the body weight, muscle or liver fat storage, or visceral depots (Johnston et al. 2010). Type 2 diabetic subjects fed with foxtail millet biscuits showed a significant reduction in serum glucose, cholesterol, LDL, and GHb, while increased serum HDL was observed (Thathola et al. 2011). Sireesha et al. (2011) demonstrated the effect of foxtail millet seed aqueous extract on streptozotocin-induced diabetic rats. The study revealed a significant decrease of 70% in blood glucose levels, evidencing the anti-hyperglycaemic and anti-lipidemic properties of millets. Millet phenolics might play a role in partially terminating the activity of α-glucosidase and amylase during the enzymatic hydrolysis of complex carbohydrates. Delayed glucose absorption further helps in controlling the levels of postprandial blood glucose (Sireesha et al. 2011). Incorporation of a foxtail millet-based diet in type 2 diabetic patients prevented hyperinsulinemia and showed reduced levels of HbA1c, fasting glucose, insulin concentrations, and improved lipid profile (Jali et al. 2012). Ren et al. (2018) reported that the foxtail millet consumption for 12 weeks shows an anti-hyperglycaemic effect by reducing the fasting blood glucose levels and increasing the serum leptin (Ren et al. 2018). Type 2 diabetic mice when fed with prolamin from cooked foxtail millet showed improved diabetes-related gut-microbiota dysbiosis and modulated serum metabolomics profile as increased serotonin levels may stimulate insulin secretion, leading to a hypoglycaemic effect (Fu et al. 2020).

Singh et al. (2020) studied the coronary risk factors among diabetes mellitus patients and suggested that 12 weeks of a foxtail millet-based diet showed a decrease in the fasting blood glucose, along with VLDL, triglycerides, and total cholesterol (Singh et al. 2020). Foxtail millet whole grain supplementation to high-fat diet/streptozotocin (HFD/STZ)-induced diabetic rats resulted in decreased fasting blood glucose level and improved insulin resistance, in addition to an improved *Bifidobacterium* abundance and butyrate concentration (Ren et al. 2022). In a previous study, oral administration of foxtail millet seed aqueous extract (SAE) was shown to reduce the HbA1c levels, thereby imparting antihyperglycemic and hypolipidemic effects in STZ diabetic rats (Sireesha et al. 2011). These results were consistent with the study performed by Singh et al. (2022) using seed aqueous extracts of six foxtail millet genotypes.

Anti-proliferative activity

Birt et al. (2013) showed that SCFAs, generated after the fermentation of foxtail millet-derived resistant starch, stabilize colonic cell proliferation. Shan et al. (2014) observed that FMBP, with peroxidase activity, exhibits anti-colon-cancer effects by inhibiting cell proliferation. Zhang and Liu (2015)

suggested that foxtail millet possesses significant anti-proliferative activity due to the presence of phytochemicals which might aid in preventing cancer (Zhang and Liu 2015). BPIS from foxtail millet was shown to reverse the multidrug resistance of colorectal cancer cells in human HCT-8/Fu cell lines in clinical trials (Lu et al. 2018). The anticancer potential of BPIS in cancer was further confirmed by Yang et al. (2020). The suppression of colorectal cancer in mice has also been demonstrated by supplementation of a foxtail millet-rich diet (Zhang et al. 2020). A foxtail millet-based diet may lead to reduced levels of interleukin-6, tumor necrosis factor (TNF)-alpha, and C-reactive proteins (Singh et al. 2020). Zhang et al. (2022) identified 22 potential bio-peptides from foxtail millet protein hydrolysates (FMPH) using UPLC MS/MS. The bio-peptides play a critical role in reducing disease activity index (DAI) by inhibiting Th17 cell differentiation and activating inflammasome, thereby improving colitis in mice (Zhang et al. 2022).

In addition to imparting neuroprotective effects, foxtail millet consumption has also been linked with enhanced cognitive abilities and synaptic plasticity. BDNF (Brain-derived neurotrophic factor) is a neurotrophin that ensures normal brain development, function, and maintenance. BDNF is secreted and expressed by physical exercise (Colucci-D'Amato et al. 2020). Foxtail millet methanol extracts led to increased secretion of BDNF in ACHN human kidney adenocarcinoma cells (Nakajima et al. 2020). Interestingly, a recent study highlighted that methanol extracts of red foxtail millet increased BDNF levels significantly as compared to white foxtail millet (Nakajima et al. 2023).

Antioxidant activity

The capability of donating electrons is also referred to as the reduction power. These electrons convert free radicals into stable products and attenuate the radical chain reaction. Antioxidants, termed by Gutteridge and Halliwell (1989), are substances that prevent the oxidation of oxidizable substrates. The generation of free radicals, reactive nitrogen and oxygen nitrogen species (RNS and ROS) in vivo causes significant damage to the cells and biomolecules. Various endogenous antioxidant-based defense systems are induced such as H_2O_2-removing enzymes, superoxide dismutases, and metal-binding proteins. The mode of action of antioxidants includes the scavenging of ROS and RNS, removal of O_2, and inhibiting ROS-RNS formation by binding to the metal ions, which are needed for the catalysis of ROS (Halliwell 1996). These ROS play a role in the progression of inflammatory diseases and cancer through damaging DNA (Wiseman and Halliwell 1996). These endogenous antioxidant defenses seem to be inadequate to prevent damage completely, which underlines the importance of diet-derived antioxidants. Many dietary components have been found to act as potential antioxidants, including millet bran.

A considerable amount of reduction power was observed in the ethanolic extract of defatted foxtail millet bran (DFMB). The scavenging property of DFMB was considered to play an important role in preventing oxidative stress and inducing hydroxyl radical scavenging activity (Halliwell and Gutteridge 1999; Fardet et al. 2008). The IC50 value of DFMB aqueous extract indicated the highest proton donating ability. Antioxidants were reported to be highest in the methanolic extracts of whole flour and bran-rich fraction of foxtail millet exhibiting significantly higher radical scavenging activity and reducing power (Suma and Urooj 2012). Several pieces of evidence suggest that millets are rich in endogenous antioxidants like total carotenoids, vitamin E, and γ- and α-tocopherols, which might help in lowering oxidative stress. These beneficial effects of millets are associated with the enzyme-inhibitory properties of seed coat phenolics which may cause the inhibition of α-Glucosidase and pancreatic amylase indicating a hepato-protective role. Peptides derived from *Lactobacillus paracasei* Fn032 fermented foxtail millet meal were purified using RP-HPLC followed by LC–MS. These peptides were reported to be trypsin-resistant and exhibited antimicrobial and antioxidant activities (Amadou et al. 2013). In a clinical trial, millet-based functional food imparted a significant decline in oxidative stress along with an increase in antioxidant vitamins A, E, and C as well as β-carotene (Singh et al. 2020).

These reports warrant a comprehensive study on the role of foxtail millet in combating chronic diseases, emphasizing nutrient profile and bioactive components, such as phenolics, fibers, and antioxidants. Studies focusing on gaining molecular insights by exploring the mode of action of these compounds to prevent or manage conditions like diabetes, cardiovascular diseases, and obesity are important. Following this, clinical trials will investigate the impact of foxtail millet-derived molecules on human health, providing evidence for its use in dietary interventions.

Resistant starch as a functional food component

Resistant starch (RS) is a complex molecule, which is known to resist enzymatic digestion in the small intestine and escapes to the colon where it undergoes fermentation by the gut microbiota to yield short-chain fatty acids (SCFAs). These SCFAs, particularly, butyrate, propionate, and acetate are well reported for their role in imparting therapeutic effects. The slow digestion rate and fermentation of RS due to its high fiber content explain the anti-hyperglycaemic effect of RS, which in turn has been linked to the prevention of type 2 diabetes (Li et al. 2020). Hu et al. (2020) suggested

that these SCFAs also improve pancreatic β-cell metabolism under oxidative stress. RS is well-studied for its role in preventing inflammation and aging and poses anti-cancer effects (Grubben et al. 2001; Le Leu et al. 2010; Vahdat et al. 2020; Warman et al. 2022; Wei et al. 2022; Mathers et al. 2022). Haghikia et al. (2022) associated the therapeutic effects of RS on lipid profile and liver health with the generation of SCFAs. Owing to these properties, RS acts as dietary fiber and helps in imparting various therapeutic effects. RS incorporation into diet leads to reduced glycaemic levels, heart rate, and inflammatory biomarkers (Maiya et al. 2023). The SCFAs generated post-fermentation also aid in maintaining healthy gut microbiota (Liu et al. 2022a, b; Li et al. 2024). RS has been well explored in cereals like rice and maize and vegetables like potato, etc. concerning its genetic and genomic aspects. However, the research progress focusing millet-resistant starch remains in its infancy. Further studies dedicated to millet RS shall be conducted to explore and accelerate the understanding of the mechanisms underlying the therapeutic effects of foxtail millet-derived RS.

Conclusions and future prospects

Owing to its small genome size, rich nutritional profile, and considerable tolerance to biotic and abiotic stressors, foxtail millet has gained worldwide attention. It is being considered as "Nutri-cereal' due to its excellent nutritional and nutraceutical properties. To date, the majority of the studies evidencing the nutraceutical properties of foxtail millet are focused on a few components of the grain, such as bran extracts, bran-derived bio-peptides, protein hydrolysates, phenolics, and inner shell-bound polyphenols. While these components are shown to be considerably associated with the nutraceutical potential of foxtail millet, other important components, similar to those studied in cereals like rice, need to be explored such as bran lipids, bran oil, bran wax, bran-related flavones, ferulate compounds, terpenoids, anthocyanidins, cyanidins, peonidins, tricins and its derivatives, transferulic acid, and tocopherols (Jia et al. 2013; Burlando and Cornara 2014). Further, advanced omics technologies shall be employed to characterize the therapeutic biomolecules and identify their genetic determinants. With the expansion of whole genome sequencing technologies, in addition to the release of pangenome, the reference genome of foxtail millet is expected to be refined to the 'gold standard' for a better understanding of the specific genes regulating the pathways that are of importance in regard to the crop's nutraceutical properties. The combination of these approaches would be imperative to determine the key compounds that may serve as nutraceutical biomarkers that would help to harness the nutraceutical potential of foxtail millet efficiently. Additionally, breeding programs should aim to develop foxtail millet varieties with enhanced bioactive profiles, catering to the increasing demand for health-promoting foods. Processing technologies must be refined to ensure the retention and stability of these bioactive components in various food products, making foxtail millet more accessible and appealing to consumers. Altogether, foxtail millet holds great promise in the realm of nutraceuticals, and continued research and innovation will be key to realizing its potential to enhance human health and well-being.

Author contributions MM designed and conceptualized the manuscript. PS wrote the first draft and prepared table and figure. PRA critically improved the manuscript. PC edited the manuscript. All the authors have read and approved the final manuscript.

Funding Authors' work on millet genomics is funded by the Innovative Young Biotechnologist Fellowship grant from the Department of Biotechnology, Govt. of India (file no.: HRD-17011/4/2023-HRD-DBT), and Science and Engineering Research Board, Department of Science and Technology, Govt. of India (file no.: EEQ/2023/000467). Authors' work is also supported by the Institute of Eminence grant (project no.: UoH-IoE-RC2-21-014) awarded to the University of Hyderabad by the Ministry of Education, Govt. of India [Ref. no.: F11/9/2019-U3(A)].

Declarations

Conflict of interest The authors declare that the research was conducted in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

Ethical approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

References

Amadou, I., Amza, T., Shi, Y.H., Le, G.W.: Chemical analysis and antioxidant properties of foxtail millet bran extracts. Warasan Songkhla Nakharin **33** (2011)

Amadou, I., Le, G.W., Amza, T., Sun, J., Shi, Y.H.: Purification and characterization of foxtail millet-derived peptides with antioxidant and antimicrobial activities. Food Res. Int. **51**, 422–428 (2013)

Anitha, S., Botha, R., Kane-Potaka, J., Givens, D.I., Rajendran, A., Tsusaka, T.W., Bhandari, R.K.: Can millet consumption help manage hyperlipidemia and obesity?: a systematic review and meta-analysis. Front. Nutr. **478** (2021)

Anitha, S., Kane-Potaka, J., Botha, R., Givens, D.I., Sulaiman, N.L., Upadhyay, S., Vetriventhan, M., Tsusaka, T.W., Parasannanavar, D.J., Longvah, T., Rajendran, A.: Millets can have a major impact on improving iron status, hemoglobin level, and in reducing iron deficiency anemia—a systematic review and meta-analysis. Front. Nutr. **712** (2021)

Bayazid, A.B., Lim, B.O.: Therapeutic effects of plant anthocyanin against Alzheimer's disease and modulate gut health, short-chain fatty acids. Nutrients **16**, 1554 (2024)

Bijalwan, V., Ali, U., Kesarwani, A.K., Yadav, K., Mazumder, K.: Hydroxycinnamic acid bound arabinoxylans from millet

brans-structural features and antioxidant activity. Int. J. Biol. Macromol. **88**, 296–305 (2016)
Birt, D.F., Boylston, T., Hendrich, S., Jane, J.L., Hollis, J., Li, L., McClelland, J., Moore, S., Phillips, G.J., Rowling, M., Schalinske, K.: Resistant starch: promise for improving human health. Adv. Nutr. **4**, 587–601 (2013)
Bohn, T., Balbuena, E., Ulus, H., Iddir, M., Wang, G., Crook, N., Eroglu, A.: Carotenoids in health as studied by omics-related endpoints. Adv. Nutr. (2023)
Brunda, S.M., Kamatar, M.Y., Naveenkumar, K.L., Hundekar, R.: Genetic variability in the foxtail millet (Setaria italica) germplasm as determined by nutritional traits. In: III International Symposium on Underutilized Plant Species, vol. 1241, pp. 113–120 (2015)
Burlando, B., Cornara, L.: Therapeutic properties of rice constituents and derivatives (Oryza sativa L.): a review update. Trends Food Sci. Technol. **40**, 82–98 (2014)
Byers, T.: The role of nutrition and nutrients in the prevention of chronic diseases. Prim. Care **29**, 615–627 (2002)
Chandrasekara, A., Shahidi, F.: Antiproliferative potential and DNA scission inhibitory activity of phenolics from whole millet grains. J. Funct. Foods **3**, 159–170 (2011)
Chandrasekara, A., Shahidi, F.: Antioxidant phenolics of millet control lipid peroxidation in human LDL cholesterol and food systems. J. Am. Oil Chem. Soc. **89**, 275–285 (2012a)
Chandrasekara, A., Shahidi, F.: Bioaccessibility and antioxidant potential of millet grain phenolics as affected by simulated in vitro digestion and microbial fermentation. J. Funct. Foods. **4**, 226–237 (2012b)
Chen, J., Duan, W., Ren, X., Wang, C., Pan, Z., Diao, X., Shen, Q.: Effect of foxtail millet protein hydrolysates on lowering blood pressure in spontaneously hypertensive rats. Eur. J. Nutr. **56**, 2129–2138 (2017)
Choi, Y.Y., Osada, K., Ito, Y., Nagasawa, T., Choi, M.R., Nishizawa, N.: Effects of dietary protein of Korean foxtail millet on plasma adiponectin, HDL-cholesterol, and insulin levels in genetically type 2 diabetic mice. Biosci. Biotechnol. Biochem. **69**, 31–37 (2005)
Colucci-D'Amato, L., Speranza, L., Volpicelli, F.: Neurotrophic factor BDNF, physiological functions and therapeutic potential in depression, neurodegeneration and brain cancer. Int. J. Mol. Sci. **21**, 7777 (2020)
Cui, K., Wu, H., Fan, J., Zhang, L., Li, H., Guo, H., Yang, R., Li, Z.: The mixture of ferulic acid and P-coumaric acid suppresses colorectal cancer through lncRNA 495810/PKM2 mediated aerobic glycolysis. Int. J. Mol. Sci. **23**, 12106 (2022)
Devisetti, R., Yadahally, S.N., Bhattacharya, S.: Nutrients and antinutrients in foxtail and proso millet milled fractions: evaluation of their flour functionality. LWT **59**, 889–895 (2014)
Dong, J.L., Wang, L., Lü, J., Zhu, Y.Y., Shen, R.L.: Structural, antioxidant and adsorption properties of dietary fiber from foxtail millet (Setaria italica) bran. J. Sci. Food Agric. **99**, 3886–3894 (2019)
Doust, A.N., Kellogg, E.A., Devos, K.M., Bennetzen, J.L.: Foxtail millet: a sequence-driven grass model system. Plant Physiol. **149**, 137–141 (2009)
Fardet, A., Rock, E., Rémésy, C.: Is the in vitro antioxidant potential of whole-grain cereals and cereal products well reflected in vivo? J. Cereal Sci. **48**, 258–276 (2008)
Fu, Y., Yin, R., Liu, Z., Niu, Y., Guo, E., Cheng, R., Diao, X., Xue, Y., Shen, Q.: Hypoglycemic effect of prolamin from cooked foxtail millet (Setaria italica) on streptozotocin-induced diabetic mice. Nutrients **12**, 3452 (2020)
Godos, J., Sinatra, D., Blanco, I., Mulè, S., La Verde, M., Marranzano, M.: Association between dietary phenolic acids and hypertension in a mediterranean cohort. Nutrients **9**, 1069 (2017)
Gonçalves, A.C., Nunes, A.R., Falcão, A., Alves, G., Silva, L.R.: Dietary effects of anthocyanins in human health: a comprehensive review. Pharmaceuticals. **14**, 690 (2021)
Gowda, N.N., Siliveru, K., Prasad, P.V., Bhatt, Y., Netravati, B.P., Gurikar, C.: Modern processing of Indian millets: a perspective on changes in nutritional properties. Foods **11**, 499 (2022)
Grubben, M.J., Braak, C.V., Essenberg, M.V., Olthof, M., Tangerman, A., Katan, M.B., Nagengast, F.M.: Effect of resistant starch on potential biomarkers for colonic cancer risk in patients with colonic adenomas. Dig. Dis. Sci. **46**, 750–756 (2001)
Guo, X., Sha, X., Rahman, E., Wang, Y., Ji, B., Wu, W., Zhou, F.: Antioxidant capacity and amino acid profile of millet bran wine and the synergistic interaction between major polyphenols. J. Food Sci. Technol. **55**, 1010–1020 (2018)
Guo, J., Gutierrez, A., Tan, L., Kong, L.: Considerations and strategies for optimizing health benefits of resistant starch. Curr. Opin. Food Sci. **51**, 101008 (2023)
Gutteridge, J.M., Halliwell, B.: 1 Iron toxicity and oxygen radicals. Bailliere's Clin. Haematol. **2**, 195–256 (1989)
Haghikia, A., Zimmermann, F., Schumann, P., Jasina, A., Roessler, J., et al.: Propionate attenuates atherosclerosis by immune-dependent regulation of intestinal cholesterol metabolism. Eur. Heart J. **43**, 518–533 (2022)
Halliwell, B.: Antioxidants in human health and disease. Annu. Rev. Nutr. **16**, 33–50 (1996)
Halliwell, B., Gutteridge, J.M.C.: Free radicals in biology and medicine. In: Halliwell, B., Gutteridge, J.M.C. (eds.) Free Radicals in Biology and Medicine, 3rd edn., pp. 1–25. Oxford University Press, Oxford (1999)
He, R., Liu, M., Zou, Z., Wang, M., Wang, Z., Ju, X., Hao, G.: Anti-inflammatory activity of peptides derived from millet bran in vitro and in vivo. Food Funct. **13**, 1881–1889 (2022)
Hou, D., Chen, J., Ren, X., Wang, C., Diao, X., Hu, X., Zhang, Y., Shen, Q.: A whole foxtail millet diet reduces blood pressure in subjects with mild hypertension. J. Cereal Sci. **84**, 13–19 (2018)
Hu, S., Kuwabara, R., de Haan, B.J., Smink, A.M., de Vos, P.: Acetate and butyrate improve β-cell metabolism and mitochondrial respiration under oxidative stress. Int. J. Mol. Sci. **21**, 1542 (2020)
Ingle, K.P., Suprasanna, P., Narkhede, G.W., Ceasar, A., Abdi, G., Raina, A., Moharil, M.P., Singh, A.: Biofortified foxtail millet: towards a more nourishing future. Plant Growth Regul. **99**, 25–34 (2023)
Jali, M.V., Kamatar, M.Y., Jali, S.M., Hiremath, M.B., Naik, R.K.: Efficacy of value added foxtail millet therapeutic food in the management of diabetes and dyslipidamea in type 2 diabetic patients. Recent Res. Sci. Technol. **4**, 3–4 (2012)
Ji, J., Liu, Y., Ge, Z., Zhang, Y., Wang, X.: Oleochemical properties for different fractions of foxtail millet bran. J. Oleo Sci. **68**, 709–718 (2019)
Jia, H., Chen, W., Yu, X., Wu, X., Li, S., Liu, H., Liao, J., Liu, W., Mi, M., Liu, L., Cheng, D.: Black rice anthocyanidins prevent retinal photochemical damage via involvement of the AP-1/NF-κB/Caspase-1 pathway in Sprague-Dawley rats. J. Vet. Sci. **14**, 345–353 (2013)
Johnston, K.L., Thomas, E.L., Bell, J.D., Frost, G.S., Robertson, M.D.: Resistant starch improves insulin sensitivity in metabolic syndrome. Diabet. Med. **27**, 391–397 (2010)
Kalsi, R., Bhasin, J.K.: Nutritional exploration of foxtail millet (Setaria italica) in addressing food security and its utilization trends in food system. eFood **4**, e111 (2023)
Kamatar, M.Y., Brunda, S.M., Rajaput, S., Hundekar, R.: Nutritional composition of seventy five, elite germplasm of foxtail millet (Setaria italica). Int. J. Adv. Res. Technol. **4**, 1–6 (2015)
Karpagapandi, L., Kalaiselvan, A., Baskaran, V.: Nutraceutical and functional attributes of foxtail millet (Setaria italica). Nutri-Cereals 141–177 (2023)

Kirwan, J.P., Malin, S.K., Scelsi, A.R., Kullman, E.L., Navaneethan, S.D., Pagadala, M.R., Haus, J.M., Filion, J., Godin, J.P., Kochhar, S., Ross, A.B.: A whole-grain diet reduces cardiovascular risk factors in overweight and obese adults: a randomized controlled trial. J. Nutr. **146**, 2244–2251 (2016)

Kouhestani, B., Azizkhani, M.: Evaluation of the prebiotic effect of oat, rice, and barley bran on growth and activity of probiotic bacteria. Food Res. J. **34**, 35–53 (2024)

Kuruburu, M.G., Bovilla, V.R., Leihang, Z., Madhunapantula, S.V.: Phytochemical-rich fractions from foxtail millet (Setaria italica (L.) P. Beauv) seeds exhibited antioxidant activity and reduced the viability of breast cancer cells in vitro by inducing DNA fragmentation and promoting cell cycle arrest. Anti-Cancer Agent. Med. Chem. **22**, 2477–93 (2022)

Lata, C., Gupta, S., Prasad, M.: Foxtail millet: a model crop for genetic and genomic studies in bioenergy grasses. Crit. Rev. Biotechnol. **33**, 328–343 (2013)

Le Leu, R.K., Hu, Y., Brown, I.L., Woodman, R.J., Young, G.P.: Synbiotic intervention of Bifidobacterium lactis and resistant starch protects against colorectal cancer development in rats. Carcinogenesis **31**, 246–251 (2010)

Lehmann, U., Robin, F.: Slowly digestible starch—its structure and health implications: a review. Trends Food Sci. Technol. **18**, 346–355 (2007)

Li, S., Xian, F., Guan, X., Huang, K., Yu, W., Liu, D.: Neural protective effects of millet and millet polyphenols on high-fat diet-induced oxidative stress in the brain. Plant Foods Hum. Nutr. **75**, 208–214 (2020)

Li, N., Niu, L., Liu, Y., Wang, Y., Su, X., Xu, C., Sun, Z., Guo, H., Gong, J., Shen, S.: Taking SCFAs produced by Lactobacillus reuteri orally reshapes gut microbiota and elicits antitumor responses. J. Nanobiotechnology **22**, 241 (2024)

Liang, S., Yang, G., Ma, Y.: Chemical characteristics and fatty acid profile of foxtail millet bran oil. J. Am. Oil Chem. Soc. **87**, 63–67 (2010)

Lin, H.C., Sheu, S.Y., Sheen, L.Y., Sheu, P.W., Chiang, W., Kuo, T.F.: The gastroprotective effect of the foxtail millet and adlay processing product against stress-induced gastric mucosal lesions in rats. J. Tradit. Complement. Med. **10**, 336–344 (2020)

Liu, F., Shan, S., Li, H., Li, Z.: Treatment of peroxidase derived from foxtail millet bran attenuates atherosclerosis by inhibition of CD36 and STAT3 in vitro and in vivo. J. Agric. Food Chem. **68**, 1276–1285 (2020a)

Liu, H., Zhang, M., Ma, Q., Tian, B., Nie, C., Chen, Z., Li, J.: Health beneficial effects of resistant starch on diabetes and obesity via regulation of gut microbiota: a review. Food Funct. **11**, 5749–5767 (2020b)

Liu, J., Tan, Y., Cheng, H., Zhang, D., Feng, W., Peng, C.: Functions of gut microbiota metabolites, current status and future perspectives. Aging Dis. **13**, 1106 (2022a)

Liu, X., Qiu, B., Liu, W., Zhang, Y., Wang, X., Li, X., Li, L., Zhang, D.: The preventive effects of fermented and germinated foxtail millet whole grain on kidney damage in a diabetic mouse model. Front. Nutr. **9**, 940404 (2022b)

Lu, Y., Shan, S., Li, H., Shi, J., Zhang, X., Li, Z.: Reversal effects of bound polyphenol from foxtail millet bran on multidrug resistance in human HCT-8/Fu colorectal cancer cell. J. Agric. Food Chem. **66**, 5190–5199 (2018)

Luithui, Y., Baghya Nisha, R., Meera, M.S.: Cereal by-products as an important functional ingredient: effect of processing. J. Food Sci. Technol. **56**, 1–11 (2019)

Maiya, M., Adorno, A., Toulabi, S.B., Tucker, W.J., Patterson, M.A.: Resistant starch improves cardiometabolic disease outcomes: a narrative review of randomized trials. Nutr. Res. **114**, 20–40 (2023)

Manders, R.J., Koopman, R., Sluijsmans, W.E., van den Berg, R., Verbeek, K., Saris, W.H., Wagenmakers, A.J., van Loon, L.J.: Co-ingestion of a protein hydrolysate with or without additional leucine effectively reduces postprandial blood glucose excursions in Type 2 diabetic men. J. Nutr. **136**, 1294–1299 (2006)

Mathers, J.C., Elliott, F., Macrae, F., Mecklin, J.P., Möslein, G., McRonald, F.E., Bertario, L., Evans, D.G., Gerdes, A.M., Ho, J.W., Lindblom, A.: Cancer prevention with resistant starch in Lynch syndrome patients in the CAPP2-randomized placebo controlled trial: planned 10-year follow-up. Cancer Prev. Res. **15**, 623–634 (2022)

Matsumura, Y., Kitabatake, M., Kayano, S.I., Ito, T.: Dietary phenolic compounds: their health benefits and association with the gut microbiota. Antioxidants **12**, 880 (2023)

Mozos, I., Flangea, C., Vlad, D.C., Gug, C., Mozos, C., Stoian, D., Luca, C.T., Horbańczuk, J.O., Horbańczuk, O.K., Atanasov, A.G.: Effects of anthocyanins on vascular health. Biomolecules **11**, 811 (2021)

Muthamilarasan, M., Prasad, M.: Advances in Setaria genomics for genetic improvement of cereals and bioenergy grasses. Theor. Appl. Genet. **128**, 1–4 (2015)

Nakajima, K., Oiso, S., Kariyazono, H.: Brain-derived neurotrophic factor up-regulation by the methanol extract of foxtail millet in human peripheral cells. J. Nutr. Sci. Vitaminol. **66**, 284–288 (2020)

Nakajima, K., Tomohiro, H., Oiso, S.: Red foxtail millet upregulates brain-derived neurotrophic factor levels in vitro and in vivo. Biomed. Res. **44**, 97–104 (2023)

Norton, L., Norton, K., Lewis, N.: Exercise training improves fasting glucose control. Open Access J. Sports Med. 209–214 (2012)

Ojo, O.: Nutrition and chronic conditions. Nutrients **11**, 459 (2019)

Onteddu, P.R., Sajja, S., Gajala, B., Edavaluru, S., Kandula, C.: Effect of foxtail millet supplementation in comparison to atorvastatin on high-fat diet-induced hyperlipidemia in rats. Asian J. Med. Sci. **14**, 50–55 (2023)

Oteiza, P.I., Cremonini, E., Fraga, C.G.: Anthocyanin actions at the gastrointestinal tract: relevance to their health benefits. Mol. Aspects Med. **89**, 101156 (2023)

Pang, M., He, S., Wang, L., Cao, X., Cao, L., Jiang, S.: Physicochemical properties, antioxidant activities and protective effect against acute ethanol-induced hepatic injury in mice of foxtail millet (Setaria italica) bran oil. Food Funct. **5**, 1763–1770 (2014)

Parulekar, Y.R., Haldankar, P.M., Dalvi, N.V., Salvi, B.R., Bhattacharyya, T.: Nutraceuticals and their biofortification in vegetable crops: a review. Adv. Agric. Res. Technol. J. **3**, 219–229 (2019)

Patel, S.: Cereal bran: the next super food with significant antioxidant and anticancer potential. Med. J. Nutr. Metab. **5**, 91–104 (2012)

Ren, X., Chen, J., Molla, M.M., Wang, C., Diao, X., Shen, Q.: In vitro starch digestibility and in vivo glycemic response of foxtail millet and its products. Food Funct. **7**, 372–379 (2016)

Ren, X., Yin, R., Hou, D., Xue, Y., Zhang, M., Diao, X., Zhang, Y., Wu, J., Hu, J., Hu, X., Shen, Q.: The glucose-lowering effect of foxtail millet in subjects with impaired glucose tolerance: A self-controlled clinical trial. Nutrients 10, 1509(2018)

Ren, X., Wang, L., Chen, Z., Zhang, M., Hou, D., Xue, Y., Diao, X., Liu, R., Shen, Q.: Foxtail millet supplementation improves glucose metabolism and gut microbiota in rats with high-fat diet/streptozotocin-induced diabetes. Food Sci. Hum. Wellness. **11**, 119–128 (2022)

Saini, S., Saxena, S., Samtiya, M., Puniya, M., Dhewa, T.: Potential of underutilized millets as Nutri-cereal: an overview. J. Food Sci. Technol. **58**, 4465–4477 (2021)

Saleh, A.S., Zhang, Q., Chen, J., Shen, Q.: Millet grains: nutritional quality, processing, and potential health benefits. Comp. Rev. Food. Sci. Food. Saf. **12**, 281–295 (2013)

Shahidi, F., Chandrasekara, A.: Millet grain phenolics and their role in disease risk reduction and health promotion: a review. J. Funct. Foods **5**, 570–581 (2013)

Shahidi, F., Chandrasekara, A. (2017) Interaction of phenolics and their association with dietary fiber. In: Dietary Fiber Functionality in Food and Nutraceuticals: From Plant to Gut, vol. 27, pp. 21–44

Shan, S., Li, Z., Newton, I.P., Zhao, C., Li, Z., Guo, M.: A novel protein extracted from foxtail millet bran displays anti-carcinogenic effects in human colon cancer cells. Toxicol. Lett. **227**, 129–138 (2014a)

Shan, S., Yin, R., Shi, J., Zhang, L., Liu, F., Qiao, Q., Li, Z.: Bowman-Birk major type trypsin inhibitor derived from foxtail millet bran attenuate atherosclerosis via remodeling gut microbiota in ApoE–/– mice. J. Agric. Food Chem. **70**, 507–519 (2022)

Shan, S., Zhou, J., Yin, R., Zhang, L., Shi, J., Qiao, Q., Li, Z.: Millet bran protein hydrolysate displays the anti-non-alcoholic fatty liver disease effect via activating peroxisome proliferator-activated receptor γ to restrain fatty acid uptake. J. Agric. Food Chem. **71**, 1628–1642 (2023)

Sharma, I., Khare, N., Rai, A.: Arotenoids: sources, bioavailability and their role in human nutrition. In: Dietary Carotenoids-Sources, Properties, and Role in Human Health. IntechOpen (2024)

Shi, J., Shan, S., Li, Z., Li, H., Li, X., Li, Z.: Bound polyphenol from foxtail millet bran induces apoptosis in HCT-116 cell through ROS generation. J. Funct. Foods **17**, 958–968 (2015)

Shi, J., Shan, S., Zhou, G., Li, H., Song, G., Li, Z., Yang, D.: Bound polyphenol from foxtail millet bran exhibits an antiproliferative activity in HT-29 cells by reprogramming miR-149-mediated aerobic glycolysis. J. Funct. Foods **56**, 246–254 (2019)

Singh, R.M., Fedacko, J., Mojto, V., Isaza, A., Dewim, M., Watanabe, S.: Effects of millet based functional foods rich diet on coronary risk factors among subjects with diabetes mellitus: a single arm real world observation from hospital registry. MOJ Public Health **9**, 18–25 (2020)

Singh, D., Lawrence, K., Singh, S., Ercisli, S., Choudhary, R.: In-vivo hyperglycemic, antioxidant, histopathological changes, and simultaneous measurement of kaempferol verified by high-performance thin layer chromatography of *Setaria italica* in streptozotocin-induced diabetic rats. Saudi J. Biol. Sci. **29**, 3772–3790 (2022)

Sireesha, Y., Kasetti, R.B., Nabi, S.A., Swapna, S., Apparao, C.: Anti-hyperglycemic and hypolipidemic activities of Setaria italica seeds in STZ diabetic rats. Pathophysiology **18**, 159–164 (2011)

Srinivasan, A., Ekambaram, S.P., Perumal, S.S., Aruldhas, J., Erusappan, T.: Chemical characterization and immunostimulatory activity of phenolic acid bound arabinoxylans derived from foxtail and barnyard millets. J. Food Biochem. **44**, e13116 (2020)

Suma, P., Urooj, A.: Antioxidant activity of extracts from foxtail millet (Setaria italica). J. Food Sci. Technol. **49**, 500–504 (2012)

Thathola, A., Srivastava, S., Singh, G.: Effect of foxtail millet (Setaria italica) supplementation on serum glucose, serum lipids and glycosylated hemoglobin in type 2 diabetics. Diabetol. Croat. **40**, 23–29 (2011)

Vahdat, M., Hosseini, S.A., Khalatbari Mohseni, G., Heshmati, J., Rahimlou, M.: Effects of resistant starch interventions on circulating inflammatory biomarkers: a systematic review and meta-analysis of randomized controlled trials. Nutr. J. **19**, 1 (2020)

Wang, C., Li, Z., Xiang, J., Johnson, J.B., Zheng, B., Luo, L., Beta, T.: From foxtail millet husk (waste) to bioactive phenolic extracts using deep eutectic solvent extraction and evaluation of antioxidant, acetylcholinesterase, and α-glucosidase inhibitory activities. Foods **12**, 1144 (2023)

Warman, D.J., Jia, H., Kato, H.: The potential roles of probiotics, resistant starch, and resistant proteins in ameliorating inflammation during aging (inflammaging). Nutrients **14**, 747 (2022)

Wei, Y., Zhang, X., Meng, Y., Wang, Q., Xu, H., Chen, L.: The effects of resistant starch on biomarkers of inflammation and oxidative stress: a systematic review and meta-analysis. Nutr. Cancer **74**, 2337–2350 (2022)

Wiseman, H., Halliwell, B.: Damage to DNA by reactive oxygen and nitrogen species: role in inflammatory disease and progression to cancer. Biochem. J. **313**, 17 (1996)

Xu, W., Wei, L., Qu, W., Liang, Z., Wang, J., Peng, X., Zhang, Y., Huang, K.: A novel antifungal peptide from foxtail millet seeds. J. Sci. Food Agric. **91**, 1630–1637 (2011)

Yang, R., Shan, S., Zhang, C., Shi, J., Li, H., Li, Z.: Inhibitory effects of bound polyphenol from foxtail millet bran on colitis-associated carcinogenesis by the restoration of gut microbiota in a mice model. J. Agric. Food Chem. **68**, 3506–3517 (2020)

Zhang, L.Z., Liu, R.H.: Phenolic and carotenoid profiles and antiproliferative activity of foxtail millet. Food Chem. **174**, 495–501 (2015)

Zhang, B., Xu, Y., Liu, S., Lv, H., Hu, Y., Wang, Y., Li, Z., Wang, J., Ji, X., Ma, H., Wang, X.: Dietary supplementation of foxtail millet ameliorates colitis-associated colorectal cancer in mice via activation of gut receptors and suppression of the STAT3 pathway. Nutrients **12**, 2367 (2020)

Zhang, B., Xu, Y., Zhao, C., Zhang, Y., Lv, H., Ji, X., Wang, J., Pang, W., Wang, X., Wang, S.: Protective effects of bioactive peptides in foxtail millet protein hydrolysates against experimental colitis in mice. Food Funct. **13**, 2594–2605 (2022)

Zhang, L.C., Liu, Y.N., La, X.Q., Li, S.T., Wen, L.N., Liu, T., Li, H.Q., Li, A.P., Wu, H., Wu, C.X., Li, Z.Y.: The bound polyphenols of foxtail millet (Setaria italica) inner shell inhibit breast cancer by promoting lipid accumulation-induced autophagic death. Food Chem. Toxicol. **177**, 113855 (2023)

Zhu, Y., Chu, J., Lu, Z., Lv, F., Bie, X., Zhang, C., Zhao, H.: Physicochemical and functional properties of dietary fiber from foxtail millet (Setaria italica) bran. J. Cereal Sci. **79**, 456–461 (2018)

Zhu, Y., He, C., Fan, H., Lu, Z., Lu, F., Zhao, H.: Modification of foxtail millet (Setaria italica) bran dietary fiber by xylanase-catalyzed hydrolysis improves its cholesterol-binding capacity. LWT **101**, 463–468 (2019)