

Genetics and Genomics Interventions for Promoting Millets as Functional Foods

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Abstract: Several crops, including millets with immense nutritional and therapeutic values, were once a part of our regular diet. However, due to domestication and selection pressures, many of them have become marginally cultivated crops confined to a particular region, race, or locality. Millets are a perfect example of neglected species that have the potential to address both food and nutritional insecurities prevalent among the ever-growing global population. Starvation and malnutrition contribute to a large number of health-related issues, being the main reason behind the occurrence of most of the severe diseases worldwide. These constraints are repeatedly disturbing both the social and economic health of global society. Naturally, millets are rich in minerals, nutrients, and bioactive compounds, and these crops are less dependent on synthetic fertilizers, systemic irrigation, and pest/weed control. Given this, the review emphasizes the nutritional values, health benefits, processing techniques, and genomic advancements of millets. In addition, it proposes a roadmap for enhancing the utility and commercialization of millets.

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1. INTRODUCTION

The current global population of 7.8 billion is projected to reach approximately 10 billion by the end of the year 2050. With this continuously expanding population size, nutritional deprivation is also prevailed in many parts of the world, especially in third-world countries. A properly balanced dietary supplement is mandatory for the health of a child to grow and develop properly. However, a disturbing number of 155 million children are reported to suffer from stunting, and 55 million are wasted globally due to malnutrition (UNICEF 2018). The maximum of such cases has occurred in various provinces of Asian (South-East Asia) and African continents (particularly, Kenya, Niger, Ethiopia, Nigeria, and Uganda) with low-mid income family belt [1]. Though the eradication of hunger from the global population is one of the mandates of the United Nations Sustainable Development Goals (SDGs), many countries are still far from reaching a satisfactory state to feed their population [2]. Further, a sedentary lifestyle, consumption of highly saturated fatty foods, obesity, environmental constraints, and fragile mental health have resulted in many chronic diseases. According to the global report on diabetes issued by World Health Organization (WHO), the total number of diabetic patients increased around four times to 422 million in 2014 since 1980.

Thus, a properly balanced diet is an essential element in maintaining society's overall health. Several neglected and underutilized crops such as millets can serve as the therapeutic diets to achieve the goal.

Millet is a general term used for small-seeded coarse grains which comprise crops from the grass family like pearl millet (*Pennisetum glaucum*), foxtail millet (*Setaria italica*), finger millet (*Eleusine coracana*), proso millet (*Panicum miliaceum*), barnyard millet (*Echinochloa crusgalli*), kodo millet (*Paspalum scrobiculatum*), tef (*Eragrostis tef*), and fonio (*Digitaria exilis*). Millets are cultivated worldwide, and with 11.56 million tonnes of gross yield (40.61% of the total global annual production), India was the largest producer of millet in the year 2017, followed by Niger (FAO 2018). Further, millets have a long history of domestication; foxtail millet and proso millet are known to be the most ancient crops with domestication history dating back to the Neolithic age. The archaeo-botanical macro remains at Neolithic sites in China provide evidence of the presence of proso millet from 8700-10000 years ago [3]. Foxtail millet was also estimated to be originated at Yellow River Valley in the northern province of China about 7,400-7,900 years before the present (BP) [4]. These findings indicate that millets have been an integral part of the diets from the ancient periods. Unfortunately, with time the production and consumption of millets have reduced drastically and limited to the selected regions of the globe. The green revolution has selectively emphasized the cultivation of crops like wheat and rice created an enormous drift in the farming practices of millets and other essential ancient food plants. However, with the most

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cultivated crops in tropical and subtropical parts of the world, millets are still a part of the staple diet of people living in arid and semi-arid regions. Thus, the robust behaviour, less water requirement, and the ability to grow in poorly fertile soils have made millets the ideal crops for cultivation in those areas. Apart from these agronomic attributes, millets are nutritionally rich and comparable or superior to other staple crops in most of the dietary aspects. Millet grains are rich in protein, carbohydrates, dietary fibers, vitamins, and minerals, hence commonly known as nutri-cereals [5, 6]. Also, several millets are rich in lignocellulosic biomass, and this can promote the production of lignocellulosic biofuels from secondary cell-wall biomass. Little millet, pearl millet, and foxtail millet are already being studied for their biofuel potential. Further, foxtail millet is genetically close to other biofuel grasses, including switchgrass and napiergrass, and thus, foxtail millet is now regarded as an experimental model for biofuel research.

2. NUTRITIONAL PROFILE OF MILLETS

In recent years, the health-benefiting nutritional values of millets have been noted, and it is considered a storehouse of nutrition [7]. Apart from carbohydrates and proteins, they are also rich in antioxidants, dietary fiber, phytochemicals, vitamins, and minerals [8]. Millets are a good source of protein, and the grains of proso-, foxtail-, and pearl millet have a significantly higher protein profile than rice, wheat, and maize. Further, millet proteins are reasonably abundant in essential amino acids and sulfur-containing amino acids, including cysteine and methionine [9]. Generally, cereal proteins are limited in tryptophan and lysine contents, but this could vary within varieties [10]. Thus, with the virtuous essential amino acid contents, the biological value of protein digested from millets is also more than other major cereals.

In cereals, the carbohydrate is existing in both structural and non-structural forms. The structural polysaccharide comprises cellulose and hemicellulose, whereas the non-structural form consists of free sugars and starch. Starch is the primary source of carbohydrates from plants. The starch content ranges from 56-75% in millets [11]. Starch is made up of two kinds of polyglucans: the linear polyglucan is linked through α -1,4 linkages and is known as amylose, whereas in the branched amylopectin, linear polyglucan chains are linked through α -1,6 bond at the branching points. Both the forms are arranged in a highly organized order to attain the spherical granular structures in the endosperm. Amylose comprises 20-30% of the starch fraction, while 70-80% of the starch is formed of branched amylopectin. Based on time taken for digestion, starch has been classified into three classes, rapidly digesting starch, slow-digesting starch, and thirdly, Resistant Starch (RS) that evades the normal digestion process in the small intestine and gets fermented in the large intestine to produce short-chain fatty acids [12]. The resistant starch is valuable for maintaining gut microbes and controls the glucose level after carbohydrate ingestion. The proportion of RS was estimated to be much higher in small

millets than the commonly consumed cereal grains such as rice, maize, and wheat [13].

Furthermore, millets are also rich in dietary fibers and low glycaemic index (GI) polysaccharides. Lipids are nonpolar biomolecules that include biomolecules like sterols, fatty acids, waxes, monoglycerides, diglycerides, triglycerides, phospholipids. Millets are a good source of essential fatty acids like linoleic acid, linolenic acid, and arachidonic acid. The fat content in millets is found to be between 1-5%. Fig. (1) presents the comprehensive illustration of nutritional profiles of popularly cultivating millet species, rice, and wheat.

3. HEALTH BENEFITS OF MILLETS CONSUMPTION

3.1. Millets for Diabetes Mellitus

Diabetes is a chronic health disorder characterized by hyperglycemia in the blood due to metabolic alteration. The rise in blood glucose levels can be linked to insulin deficiency or impaired insulin action. Diabetes can be further divided into diabetes insipidus (type 1) and diabetes mellitus (type 2). Type 1 diabetes is an autoimmune disorder where the beta cells of the pancreas are annihilated, and thus, the body experiences insulin. On the other hand, the primary cause of type 2 diabetes is insulin resistance and its secretory response. Several studies have been carried out to decipher the role of millets in controlling the effect of diabetes. A supplement of 33 and 66% (w/v) pearl millet to diabetes mellitus affected rats has significantly decreased the blood glucose level and serum lipid profile [14]. Further, the finger millet diet supplement was found to induce wound healing in diabetic rats [15]. Altered enzymatic activities of antioxidants, including superoxide dismutase (SOD) and catalase (CAT), were also recorded. Histological and microscopic evaluations distinguished the epithelialization, enhanced collagen synthesis, activation of fibroblasts, and mast cells in finger millet-fed diabetic animals.

The extracts from barnyard millet were found to inhibit the activity of α -glucosidase of *Saccharomyces cerevisiae* [16]. Out of eight phenolic extracts from barnyard millet, N-p-coumaroyl serotonin (CS), feruloyl serotonin (FS), and luteolin displayed the α -glucosidase inhibitory activity. The CS and FS had the potential to decrease intestinal sucrase activity and reduced the glucose content in Caco-2 (human intestinal epithelial) cells [16]. The combination of millet and wheat flours has significantly lowered the blood glucose level compared to wheat flour alone [17]. The type 2 diabetic KK-Ay mice fed with foxtail millet diets for three weeks resulted in a significantly decreased insulin level, whereas the concentration of adiponectin and high-density cholesterol enhanced in the serum [18]. Similarly, observations have also been obtained with proso millet where insulin and glucose levels subsided in the serum and increased adiponectin and high-density lipoprotein (HDL) cholesterol level [19]. Adiponectin and HDL cholesterol play a pivotal role in improving and ameliorating type 2 diabetes, obesity, and cardiovascular disease. Apart from the dehusked seeds, the

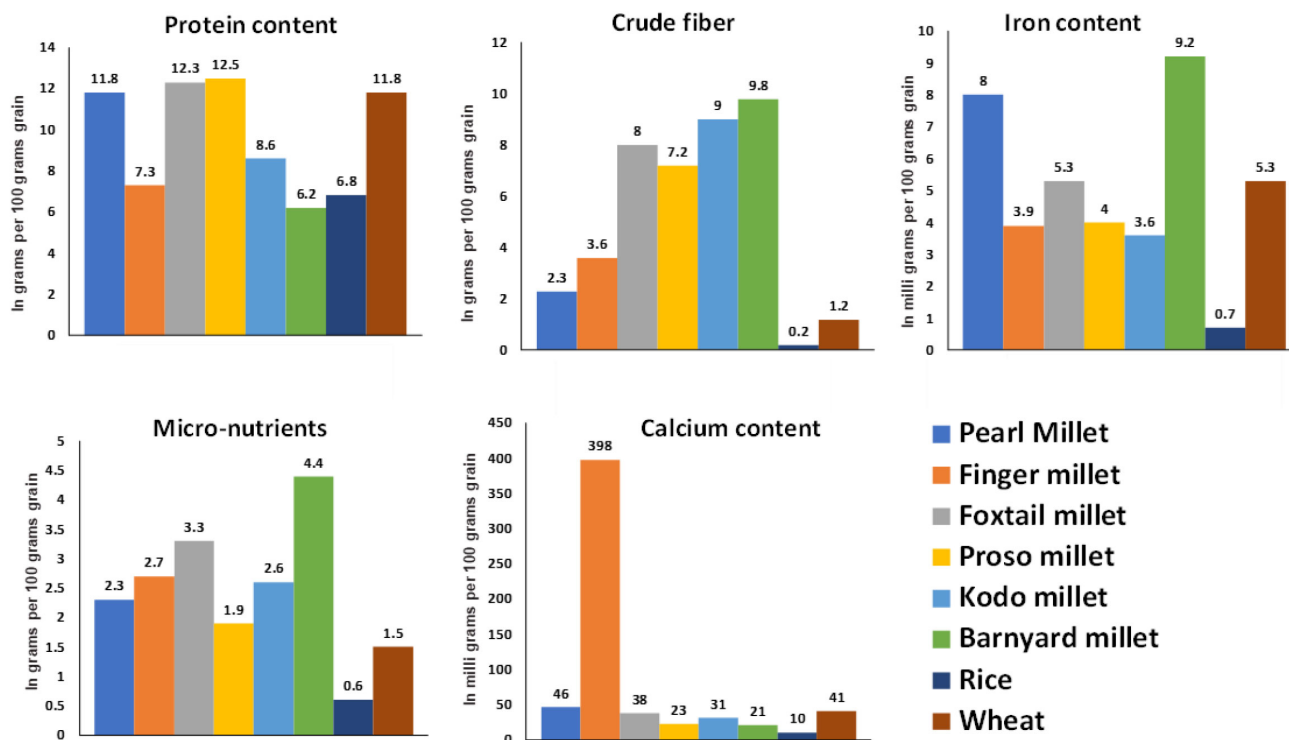


Fig. (1). Comparative illustration of the nutritional content of millet seeds (per 100 g grain weight) with rice and wheat [7]. The higher protein, crude fiber, iron, calcium, and micronutrient contents make the millet a nutri-rich cereal grain. The figure shows only the maximum values reported in each crop [7]; however, a great variation exists within the species with respect to genotype and environmental growth conditions. (A higher resolution / colour version of this figure is available in the electronic copy of the article).

seed coat also exhibits anti-diabetic properties. The application of seed coat matter of black finger millet had inhibited the activity of α -glucosidase and depicted reduced diabetic activity in streptozotocin-induced diabetic mice [20].

3.2. Cardiovascular Diseases and Dyslipidaemia

The impaired lipid metabolism results in the rise of low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and higher cholesterol (HC) levels while it lowers the HDL content in the blood serum. The irregular metabolic conditions eventually lead to cardiovascular diseases and hypertension. Several reports are suggesting the use of millet-based diets in refining these metabolic disorders. When type 2 diabetic patients fed with low GI biscuits made up of foxtail millet, a decrease in serum glucose, cholesterol, LDL, triglycerides, and VLDL was observed [21]. A similar pattern was also observed with the consumption of a functional non-alcoholic beverage formed from fermented sorghum and millet malts. The beverage also augmented the activities of superoxide dismutase, glutathione peroxidase, catalase, glutathione reductase, and glucose 6-phosphate dehydrogenase in the liver of rats [22]. Millet may exhibit a hypolipidemic effect by modulating the expression of lipid metabolism-related genes SREBP-1C, FAS, HMGCR, or gut microbiota composition [23]. Additionally, the lower cholesterol levels in serums could be due to

the higher amount of dietary fibers in the millet grains. The abundance of chlorogenic acid in proso millet has been proven to lower the cholesterol levels in the serum [24]. The study also suggests that reducing blood LDL can be due to the down-regulated tumor-necrosis-factor alpha (TNF-alpha) gene expression. The C-reactive protein (CRP) is an indicator of heart-related ailments, and people with a higher level of CRP have three times more chance of facing heart disorders. Foxtail millet consumption can also decrease the chances of cardiovascular diseases by controlling the levels of CRP in the serum of hyperlipidemic rats [25]. The high magnesium content of millet grains may be beneficial in maintaining optimal blood pressure in the body.

3.3. Cancer

Cancer has become a predominant life-threatening health disorder in which the body witnesses uncontrolled growth of cells impairing many metabolic functions. The cause of these conditions is either genetic and/or environmental factors. Along with therapeutic treatments, several dietary supplements can minimize the occurrence of cancer, and millets are one of those. The insoluble bound phenolics from commonly cultivated millets can significantly inhibit the proliferation of cancerous cells [26]. Phenolics compounds are often called natural scavengers of reactive oxygen species (ROS) and free radicals. Polyphenols from the

foxtail millet bran are reported to control the growth of cancerous human colorectal HCT-116 cells through the generation of oxidative stress that triggers the caspase regulated apoptosis in the malignant cell lines [27]. Additionally, the NF- κ B pathway was inhibited by the ROS that plays an essential role in tumour generation. The proliferation of MDA human breast cancer and HepG2 liver cancer cell lines was significantly inhibited by the dose-dependent exposure of foxtail millet polyphenolic extracts [28]. The primary constituents of foxtail millet polyphenolics are ferulic acid, caffeic acid, chlorogenic acid, syringic acid, p-coumaric acid, and carotenoid. A novel protein named foxtail millet bran protein (FMBP) exhibits anti-cancerous properties by introducing the G1 phase arrest in the cell cycle [29]. FMBP also induces caspase-dependent apoptosis through the loss of mitochondrial transmembrane potential in colon cancer cells. Millets containing linoleic acid possess anti-tumor activity. It is the potent inhibitor of a crucial histone modifier enzyme, histone deacetylases (HDACs). The cytotoxic effect of linoleic extract from proso and Japanese millet towards human leukaemia and prostate cancer cells has already been established [30]. Colon cancer is the second-highest occurring cancer in the human population. A high sugar diet and a sedentary lifestyle can surge the risk of colon cancer; on the other hand, a diet high in edible fibres, folate, cereals, vegetables, and fruits can reduce the appearance of colon cancer [31]. Millets extracts exhibit high antioxidant properties that suppressed HT-29 adenocarcinoma cells' proliferation in a time and dose-dependent manner [32]. The short-chain fatty acids resulting from the fermentation of RS act as a prebiotic to the gut microbiota, which contributes significantly to reducing the chance of colon cancer [33]. Thus, it can be concluded that millets can serve the purpose of an excellent nutraceutical agent to prevent the occurrence and restrict the increment of the cancerous mass.

3.4. Celiac Diseases

A large number of people have the celiac disease due to gluten intolerance and other allergic disorders. Gluten intolerance is an enteropathy prompted by the ingestion of seed storage protein, prolamin present in wheat, barley, and rye [34]. Gluten proteins are resistant to human gastrointestinal enzymes because of their characteristically high glutamine (26-53%) and proline (10-29%) contents [35]. The celiac disorder can be tackled by switching the high gluten to a strict gluten-free diet [36]. Since millet grains are gluten-free, they are progressively gaining popularity amongst people for their nutritional and health-benefiting properties [37]. The global marketing of gluten-free products has reached approximately 5 billion USD in 2017, which is expected to reach about 6.5 billion USD by 2023. Apart from millet grains, several other cereals like corn, sorghum, and pseudocereals, including amaranth, quinoa, and teff, constitute together a gluten-free diet group. The alcohol-soluble protein fraction from millets, teff, amaranth, and quinoa produces no immunological reaction in duodenal cultures from celiac disease patients [38].

3.5. Antioxidative Properties of Millet Grains

The higher amounts of polyphenol content in millet grains impart massive health benefits, including antioxidative properties, metabolic syndrome, and aging-related problems [39]. The bioactive compounds extracted from millet grains include gallic acid, caffeic acid, gentisic acid, p-coumaric acid, p-hydroxybenzoic acid, vanillic acid, syringic acid, sinapic acid, salicylic acid, ascorbic acid, chlorogenic acid, catechol, and kaempferol [40-42]. These phenolic compounds subsidize health benefits by ceasing the auto-oxidation in unsaturated fats by providing the means of reducing agents [43]. The flour from germinated foxtail, barnyard, and kodo millets showed higher antioxidant activities than raw flours [44]. The seed coat matter from finger millet has been shown to reduce oxidative stress damage in streptozotocin-induced diabetic rats [20]. The activities of catalase (CAT) and superoxide dismutase (SOD) were found to increase in the millet-fed streptozotocin (STZ) induced diabetic rats. High-performance liquid chromatography (HPLC) analysis of millet phenolic extracts revealed that the bound fractions contained a higher proportion of ferulic and p-coumaric acids than their soluble counterparts [26]. Interestingly, the antioxidant activities of the phenolic compounds vary with the malting process of the grains. The phenolic acids and their activities differ with the time-points and mode of the process [11]. Free radical scavenging activities of phenolic compounds from different millets have shown LDL cholesterol oxidation inhibition by up to 41% [45]. Kodo millet exhibited the highest inhibitory effects on lipid oxidation than other millet species. Thus, millets may potentially serve as a natural source of various antioxidants and nutraceutical food ingredients.

3.6. Antimicrobial Activity

Millet grain extracts are shown to have natural antimicrobial activities. The phenolic extract from the seed coats of finger millet showed potent antimicrobial activity against *Bacillus cereus* and *Aspergillus flavus* [46]. A novel antifungal peptide with a molecular mass of 26.9 kDa was identified from foxtail millet seeds exhibited inhibitory activity against *Alternaria alternata*, *Botrytis cinerea*, *Trichoderma viride*, and *Fusarium oxysporum* [47]. Similarly, peptides fractionated through the RP-HPLC method of fermented foxtail millet extract have demonstrated antioxidative and antimicrobial activity [48]. Lactic acid bacteria (LAB) identified from the fermenting millet gruel exhibit a broad range of antimicrobial activity. The isolated LAB unveiled inhibitory effects on the growth of *Escherichia coli*, *Bacillus licheniformis*, *Bacillus cereus*, *Staphylococcus aureus*, *Salmonella* spp.; *Pseudomonas fluorescens*, *Pseudomonas syringae*, *Pseudomonas aeruginosa*, *Proteus* spp. and *Serratia* spp [49]. The metabolites from these fermenting bacteria are an excellent alternative to preservatives because of their natural source and no harmful side effects. Hence, phytochemicals from millets can prove to be an excellent source of natural antimicrobial agents, and further investigations could be carried out to exploit these as natural preservatives in the food industry.

4. PROCESSING AND FOOD PREPARATION OF MILLETS

Although millets are the storehouse of nutrients, before consuming as food products, it requires a set of food processing to increase the bioavailability of nutrients inside the human body. Millet processing techniques involve decortication, milling, malting, fermentation, roasting, and grinding. Food processing enhances the alimentary properties and reduces the antinutrient contents such as phytate [50]. The decortication of millets is always tricky due to their small-sized grains. However, hydrothermal treatment hardens the endosperm texture and capacitates its decortication. Noteworthy, a substantial alteration of carbohydrate, proteins, and lipid contents was observed upon decortication of hydrothermally processed finger millet seeds [51]. Dehulling of millets results in reducing phytic acid, tannin, polyphenols, and mineral concentrations while improving protein digestibility [52, 53]. Therefore, food processing through decortication has limited use in millet; instead, flour-based products are premounted. Millet-based recipes involving whole grain and flour are now available for preparing healthy and nutritious foods. Also, millet flour can be added with other flours (wheat or multigrain) to produce healthy bakery products.

There is now scope for innovation in methodologies for millet grain decortication without the expense of nutrient values. The milling process can eliminate the bran and germ of the grains, which contain some essential nutrients. The use of semi-refined flours of pearl millet was recommended, which maintained the low antinutrients and improved mineral bioaccessibility [54]. Sieved and whole flours also differ in their nutritional properties as sieving reduced the content of both nutrients and antinutrients but enhanced digestibility [55]. Germination or malting of grains usually results in altered biochemical properties and produces malt with improved nutritional quality. Effect of malting with three days of germination depicted an improvement of *in vitro* protein and starch digestibility by 14-26 and 86-112%, respectively, in pearl millet [56]. The use of malted or germinated millets in traditional recipes is in practice worldwide for since long. Different kinds of fermented food products are produced from the millet grains in various countries of Asia and Africa. The bran and germ as the by-products of grain milling can be served as a substrate for fermentation processes. The sixteen-hour fermentation of pearl millet resulted in enhanced crude proteins and flavonoids whereas reduction in coarse fibers and fats was detected [57]. The benefits associated with grain fortification and supplementation have also been explored in millets. The use of natural products for millet fortification has been proven to be more promising than artificial substitutes. Food-to-food fortification of pearl millet with moringa leaves, roselle calyces, and baobab fruit pulp has substantially improved the bioaccessibility of zinc and iron [58]. Thus, supplementation of millet grains with natural products may magnify their nutritional values at a cost-effective demeanour.

5. ADVANCES IN THE GENETICS AND GENOMICS OF MILLET RESEARCH

Exploring genetic and genomic resources is an integral part of millet improvement programmes. These include genome sequencing, molecular marker developments, functional genomic analysis, genome-wide association mapping, genomic-assisted breeding, and biotechnological advances. The motive behind the development of genetic resources is to explore the overall diversity within the population and maximize the credentials of potential donor genotypes for crop improvement. High-throughput genomic resources are a prerequisite for harnessing the trait-associated genomic regions for introgression into elite cultivars through molecular breeding or genetic engineering approaches. International Crop Research Institute for Semi-Arid Tropics (ICRISAT) is a non-profit institutional body with an excellent repertoire of millet germplasm from various parts of the globe. With a total number of 23,092 accessions, including 750 wild varieties, pearl millet shares the maximum proportion of germplasm collection at ICRISAT, followed by finger-, foxtail-, kodo-, little-, proso-, barnyard millet [59-61]. The genetic diversity in accessions or within a population can be analysed through the molecular markers such as single nucleotide polymorphism (SNPs), simple sequence repeats (SSRs), cleaved amplified polymorphic sequences (dCAPS), restriction fragment length polymorphisms (RFLPs), and amplified fragment length polymorphisms (AFLPs). The available genomic resource and their application in millet improvement are comprehensively reviewed by Muthamilarasan and Prasad [62], Singh *et al.* [63, 64], and Singh and Prasad [65]. The available draft genome sequences of foxtail millet [66, 67], pearl millet [68], finger millet [69], and broomcorn millet [70] providing an excellent opportunity for their genetic evaluation. The small-sized genome (~515 Mb) of foxtail millet together with the short life cycle, inbreeding nature, profound seed profile, and extensively available genomic resources, foxtail millet is considered as a C₄ model plant for abiotic stress, biofuel trait, and photosynthesis research [71, 72].

The establishment of an efficient genetic transformation system is essential for crop genetic improvement. The development of a competent *Agrobacterium*-mediated transformation system has already been established for pearl-, foxtail- and finger millet [73, 74]. A recently developed *Agrobacterium*-mediated genetic transformation system in foxtail millet with approximately 27% gene integration frequency is expected to expedite the millet transgenic research to an extreme altitude [75]. A foxtail mosaic virus-based gene delivery system has been established for functional characterization of genes using a virus-induced gene silencing approach [76-82]. This system has been proven successful in foxtail millet as well as other cereal crops to silence the expression of candidate genes. On the other hand, there are limited reports available on the use of other molecular techniques like RNA interference and genome editing tools such as clustered regularly interspaced short palindromic repeats (CRISPR), zinc finger nucleases (ZFNs), and transcription activator-like effector nucleases (TALENs). Effective deployment

of these approaches is required to accelerate the biofortification and quality improvement of millet grains [76].

6. CHALLENGES AND PROPOSED FRAMEWORK FOR MILLET DEVELOPMENT

Despite early domestication and the climate-resilient nature of millets, the green revolution and other crop improvement programmes principally focused on crops like rice and wheat. This resulted in the disappearance of the traditional millet crops from the food basket of the typical families. Ignorance and reckless attitude towards millets have led to them in a category of neglected and underutilized crops, which was further retrograded because of the meagrely developed agribusiness and food processing models. For exam-

ple, in the highest millet producer country like India, the market cost millets are more than double of other major cereals like rice, wheat, or maize (<https://agmarknet.gov.in/>). The lack of proper supply channels between producer, distributor, and trader, together with consumer awareness, hinders the flourishing of millets. A collaborative effort from every dimension, including production, planning, marketing, and innovations are must require establishing the central position of millets in the global agri-economic sector (Fig. 2). The diversification of healthful and nutrient-rich food crops must be encouraged both at the international and local levels. Considering its socio-economic and nutritional prospects, the Food and Agriculture Organisation (FAO) of the United Nations has declared the year 2023 as the 'International Year of Millets'.



Fig. (2). A detailed roadmap for the development and commercialization of millet-based food products. (A higher resolution / colour version of this figure is available in the electronic copy of the article).

CONCLUSION

The rekindling of millet grains is necessary since malnutrition and nutrient deficiency is striking at an alarming rate, especially in developing countries. The jeopardizing environmental conditions and lack of public awareness, inappropriate policies, and slow economic development add more to the instability. Climate and global warming are posing additional adverse constraints on agriculture and food security. In this scenario, the small-scale farmers of developing nations are the most suffered ones. Mainstreaming millet cultivation and consumption is also equally crucial at this point-of-time, where we are set to reach an additional ~2-2.5 billion people by 2050. The time has also arrived to invest more in millet and value-added food crop research. They have the potential to ensure food, nutrition, and health security through maintaining uninterrupted supply even under the adverse conditions of global climate change. Concerted efforts from the government side are also required, such as subsidies for farmers in millet cultivation, the establishment of public-private partnerships for commercialization, and general consumer awareness.

CONSENT FOR PUBLICATION

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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