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Review Article

Nutrients Anti-Nutrients Interaction in Millets and its Effect on Malnutrition

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Abstract

Malnutrition problem, which is derived from having insufficient amount of nutrients like minerals, essential vitamins and other macronutrients (proteins and carbohydrates) in our daily diet. After the pandemic, the prevalence of under nourishment jumped from 8.0 in 2019 to around 9.3 percent in 2020 and continued to rise in 2021. Malnutrition problem can be reduced by adding the nutrients in our daily diet. Millets are the excellent source of minerals, vitamins, proteins and carbohydrates. But some anti-nutrients (oxalate, phytate) present on them interact with nutrients (like minerals, vitamins) and reduce its bioavailability in millets. To overcome this malnutrition problem, anti-nutrients should be removed in crops like millets. There are many biofortification methods used by scientists to improve the nutritional content time to time. However, it is necessary to know the current status of these anti-nutrients and identify those genes which are responsible for the accumulation of these anti-nutrients in millets. Thus, for better human health and physical wellbeing, it is most important to take bio-fortified foods containing fewer anti-nutrients.

Keywords: Nutrients; Anti-Nutrients; Malnutrition; Millets

Introduction

Malnutrition problem in a community is the major obstruction in the development of a nation and large population of the world suffers from this. Malnutrition is a common issue that results from having low nutrients in our daily life. According to UN report, after a prolonged decline there is an increase in the world's population that suffers from hunger or undernourishment. From 2015 to 2016, there was an increase in the number of nutrient deficient people in the world to 815 million up from 777 million [1] and reached higher to821 million in 2017 [2]. According to a report publish in 2017, it was estimated that around 5.9 million people are still considered acutely food insecure and around 3.9 million children are suffering from acute malnutrition and among them 1.9 million are extremely malnourished [3]. Malnutrition is estimated for the cause of more than one third of all child deaths [4]. In 2021, an estimated29.3 % of the global population, 2.3 billion people were moderately or severely food insecure and 11.7% (923.7 million people) faced severe food insecurity [5]. In the last few years many countries shows his concern towards it and takes up a serious challenge for international commitments to end hunger and malnutrition problem by 2030. Food insecurity and malnutrition in all its forms has multiple and diverse negative effects on health and wellbeing [6].

Dietary intakes of peoples below the poverty line are deficient in several divalent cations such as calcium (Ca), iron (Fe), Magnesium (Mg), zinc (Zn), and also in other nutrients (proteins and vitamins). Children, pregnant and lactating women need these nutrients more than any others. Sometimes these nutrient deficiencies are reflected in diseases like Kwashiorkor, anemia, scurvy, rickets and other minerals deficiency diseases. The overall malnutrition and nutrient deficiency rates may vary province to province, but no such differences in malnutrition and nutrient deficiency rates are found in relation to genders, says FAO. For solving this malnutrition problem, dietary intake of macro and micro-nutrients in our food should be improved. Dietary nutrient quality of food should be taken into consideration for maintaining human health and physical wellbeing [7]. For human growth and wellbeing, currently 49 nutritional components are considered to be essential [8]. Mineral nutrition is important for health and development for all human beings as well as animals.

Plant based foods in various forms are an essential component of our daily dietary intake in many parts of the world. These foods contain an important source of vitamins, proteins, minerals, carbohydrates, dietary fiber and non-nutrients [9]. Millets can be a good alternative of wheat, rice and cereals because it is rich in minerals and proteins. Millets are the good source of minerals, proteins, energy, fat, carbohydrates and vitamins which are comparable to cereals [10-12]. It is also a cheap source of food for poor people and it is easy to cultivate. Due to its nutritional and other importance, millets can be an alternative food source in comparison of cereals as the consumption of cereals by Indians are more that constitute 70-80% of the total energy intake [13]. But these nutrients interact with antinutrient like oxalates, phytates, polyphenols, tannins and digestive enzyme inhibitors and these interactions reduces the minerals absorption [7]. According to earlier studies the presence of nutrient like calcium in plants exists primarily as a complex form in which it is bound with anti-nutrients such as phytate, oxalate along with proteins and other nutrient factors [14]. Thus, it is also one of the important and key factor for the reduction of nutrients in our daily diet and it has indirect effect on malnutrition.

Production and availability

Millets are considered as one of the oldest, cheapest and ancient foods known to humans but they were ignored in comparison of rice and wheat. In the last decade, the govt. policies are currently to be in favor of the millets and government also trying to increase the popularity of millets among peoples. Overall, the production of millets is expected to increase in the coming years. For example, the overall production of barley, rice and corn were better and almost same in the year of 2016-17 but the production of madua/ragi (finger millet), Jowar (Sorghum) and bajra (pearl millet) were lower [15] (Figure 1). On the other hand, the population of 1.343 billion, household cereal demand works out to 221 million tons and for food grains 241 million tons in India (overall in 2020) [16]. However, an estimated in the production of sorghum will be 35.0 million tons, which will contribute alone 68% of total production of rabi. Similarly the estimated production of pearl millet will be 37.50 million tons, 10.0 tons for finger millet, 3.0 million tons for other small millets will be expected with overall gross production of 85.50 million tons for all (Sorghum, pearl millet and other millets) by the end of 2050 AD [18] (Figure 1).

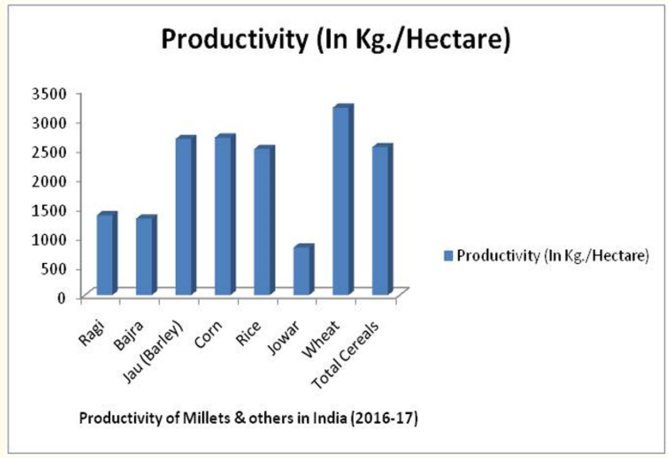

Figure 1: Production of millets and other cereals in the year 2016-17 [15].

Nutritional quality in millets

Plant nutrients are commonly used in the food industry. Macronutrients (such as carbohydrates, fats and proteins) as well as micronutrients (minerals and vitamins) deficiencies are seen every wherein most of the countries. Cereals and millets constitute a major source of daily dietary nutrients worldwide [18]. For improving the nutritional quality, millets are receiving attention in many countries for its high economic and medicinal values. Millets has the potential for accelerating the agricultural productivity to achieve green revolution that India needs again. Millets are the drought resistant crop and can be grown in low rain fed areas under extreme environmental conditions in which major cereals fail to give substantial yields [19]. Millets are the rich source of carbohydrates, proteins, energy, fat, minerals and vitamins which is comparable to cereals [10,11]. The average protein content of small millet is reported to be from 7.7-11.8% [20]. Generally, cereal proteins including millets are limited in lysine and tryptophan content except finger millet, which has higher amount of methionine, lysine and tryptophan [21]. Foxtail millet and its bran is rich in poly-unsaturated fatty acid (PUFA) such as linoleic acid and a good source of dietary fiber and several minerals. Beside this, the number of antioxidants present in foxtail millet exhibit effective inhibition of free radicals action [22]. Foxtail millet also has a high amount of protein (11%) and fat (4%). Protein in millets has three main fractions: prolamins (39.4%), albumins and globulins (13%), and glutelin's (9.9%). It is thus recommended as an ideal food for diabetics [12]. Pearl millet have a successfully developed biofortified variety Dhana shakti and also have some hybrids (HHB 299, HHB 311, RBH 238 and AHB 1200). These varieties/hybrids have significant amount of iron (Fe) and zinc (Zn), this higher amount will fulfill 70% of daily requirement of an adult (if 200gm consumed per day) [23]. Pearl millet and sorghum are also good source of dietary fiber [24]. Due to its high protein and high fiber content, millets are considered one of the favorite foods among peoples having diabetes and cardiovascular diseases [25]. A successful attempt were also made to create gluten free biscuits which is less in fat and table sugar for obese and diabetic individuals [26]. The nutritional composition of protein content, fat, total dietary fiber, minerals and trace elements has been compared with other cereals and millets in figure 2.

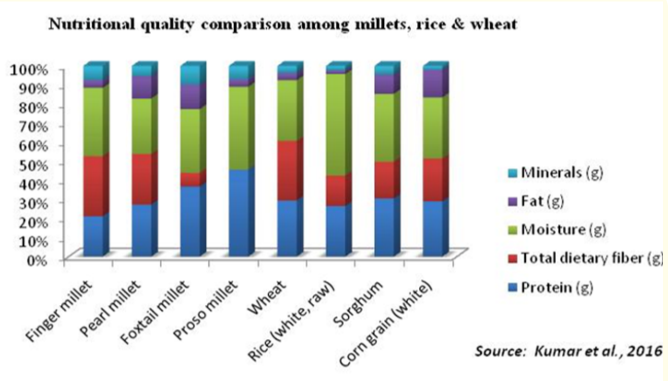

Figure 2: Nutrient comparison among millets, rice and wheat.

Among other millets, from nutritional point of view, finger millet is also considered as model crop for its higher amount of macro and micronutrients [27,28]. Finger millet is also a very good source of variety of phenolic compounds which may have health benefits [29]. Besides high amount of calcium, the grains of finger millet also has high seed storage proteins (albumins, globulins and prolamins) and other quality proteins having significant amount of cysteine, trptophan and methionine etc. and phytochemicals, fibers and other minerals [30,31]. In addition, black finger millet contains 8.71 mg/g dry weight fatty acid and 8.47 mg/g dry weight protein [32]. From nutritional point of view, small millets like kodo and little millets are also superior to rice and wheat as it is a good source of dietary fiber and some minerals. According to a study, antioxidant activities of phenolic extracts of kodo millet were higher in comparison of pearl millet [33]. Kodo millet and little millet also have higher amount of dietary fiber in comparison of cereals; and the fat has higher polyunsaturated fatty acids [34]. Beside this nutritional significance, millets also have anti-nutrients like oxalate, phytate, polyphenols and tannins which render the bioavailability of minerals.

Antinutritional factors in millets

Antinutritional factors affect the bioavailability of minerals and proteins in plants. Millets, which are an excellent source of nutrients and other minerals but its nutritional quality is considerably lowered by the presence of anti-nutrients and reduction of these minerals and proteins will effect of our daily diet. Anti-nutrients such as dietary fibers, oxalate, phytate and calcium binding proteins that reduce the bioavailability of essential nutrients like calcium [35]. Millets are also rich in photochemical (polyphenols, tannins, phytosterols) and antioxidants; however, they do contain some anti-nutritional factors that can be reduced by certain processing treatments [36]. Mostly secondary metabolites which functions as anti-nutrients may cause harmful biological activities, these anti-nutrients can be eliminated by pre-processing techniques (DE branning, soaking, sprouting, fermentation etc.) in millets [26,37]. These pre-processing techniques reduces significant amount of anti-nutrients in crops like millets. In finger millet, besides nutrients it also contains oxalate, phytate, polyphenols, tannins, dietary fiber and trypsin inhibitory factors, these were called as 'Anti-nutrients' for their metal chelating and enzyme inhibition activities [7]. According to earlier studies the presence of nutrient like calcium in plants exists primarily as a complex form in which it is bound with anti-nutrients such as phytate, oxalate [38,39] along with proteins and other nutrient factors. Legumes and cereals also contains anti-nutritional factors like phytic acid, saponins, tannins, gossypol, lectins, protease inhibitors, amylase inhibitor, and goitrogens [40]. The removal of anti-nutrients from plants can increase bioavailability of minerals and improves our daily diet. Some plant breeding and genetic engineering methods have made several attempts in decreasing the levels of these anti-nutrients; however, these anti-nutrients have roles in plant development and defense thus its complete removal is problematic [41,42]. There are some important anti-nutritional factors in millets that render the bioavailability of minerals

- **Oxalate:** Oxalate or oxalic acid is an anti-nutrient which renders the calcium as well as other mineral ions and makes it unavailable for nutritional absorption [43,44]. Oxalate is a major component in plants; important aspects of its synthesis and accumulation in most crop plants are unresolved. Oxalic acid binds with minerals like calcium, sodium, potassium, magnesium and forms oxalate salts. Among these oxalate salts, some of them are soluble like potassium and sodium whereas calcium oxalate salts are insoluble [45]. In case of calcium (Ca), the substance to which Ca is bound can deposits in many forms such as Ca phosphate, Ca carbonate, Ca-sulphate, Ca chloride, Ca-gluconate and others. In these compounds some of them are soluble but calcium-oxalates are insoluble [46]. Highest conc. of this bound calcium is commonly found in crystalline forms, such as calcium oxalate (Ca-Ox) [47] and it is the main anti-nutrient which reduces the calcium bioavailability in plants. Ca-Ox affects the absorption and utilization of calcium also in the animal body. But on other side both soluble oxalic acid and insoluble Ca oxalate also provide self-defense to plants against insect pests and grazing animals [48]. The absorption of calcium depends on the oxalic acid content in food and it seems inversely proportional. For example, spinach contains low Ca and high oxalate content which has lower the bioavailability of Ca; however, kale which contains high Ca and low oxalate levels has higher bioavailability of Ca [44]. There are several hypotheses attempting to explain the role of anti-nutrients like oxalate in plants [14,42,49-51] (Figure 3). There are three different oxalic acid biosynthesis pathways reported in various organisms [42]. Among them, ascorbate-oxalate and glyoxalate-oxalate conversion pathways are generally found in many plant species [42,52] (Figure 3). These oxalate ions will further binds with minerals, proteins and other nutrient ions and makes it unavailable for absorption.

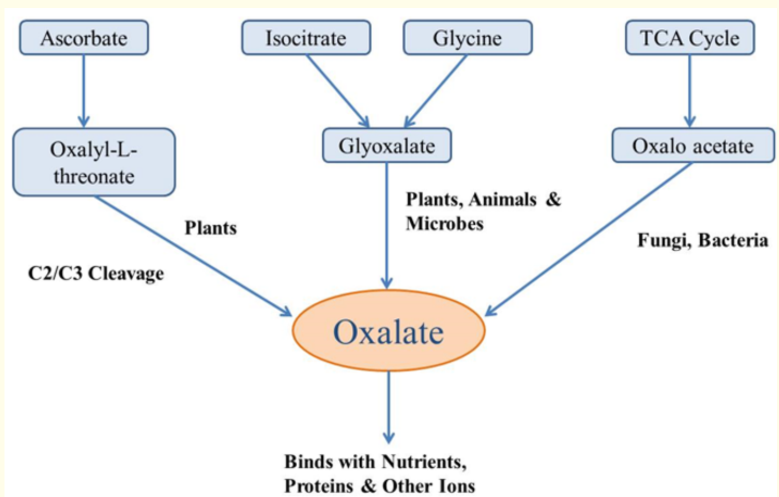

Figure 3: Representation of oxalic acid biosynthesis pathway in different organisms (Source: 14; 42).

- **Phytate:** Phytate (Inositol hexa-kisphosphate, InsP6) is the salt form of phytic acid, are found in animals, humans, plants and soil. Phytate or phytic acid is formed either from myo-inositol-1-phosphate or it is formed from phosphatidyl inositol in most plant species [53,54] (Figure 4). It is primarily present as a salt and reduces the bioavailability of ions like Ca^{2+}, Mg^{2+} and K^{+} and accumulates mostly at the time of the ripening period in the seeds. Anti-nutrient phytic acid is one of the sources of phosphorus in seeds which interacts with the other nutrient cations in protein storage vacuoles [55,56]. Phytate attaches with magnesium, calcium and potassium salt for degrading the nutrients. Phytate generally binds with some divalent cation molecules viz; calcium and iron to form insoluble complexes, reducing their bioavailability but increases the zinc content [57]. In a recent studies, a nod based sulfate transporter (SULTR)-like phosphorus distribution transporter (SPDT) were identified in rice to control phosphorus allocation to the grains and reducing the phosphorus (P) accumulation as well as phytate excretion-associated pollution [58,59]. Higher intake of phytate reduced the minerals bioavailability and in some areas where cereal proteins are the main source of daily diet, the associated phytate intake

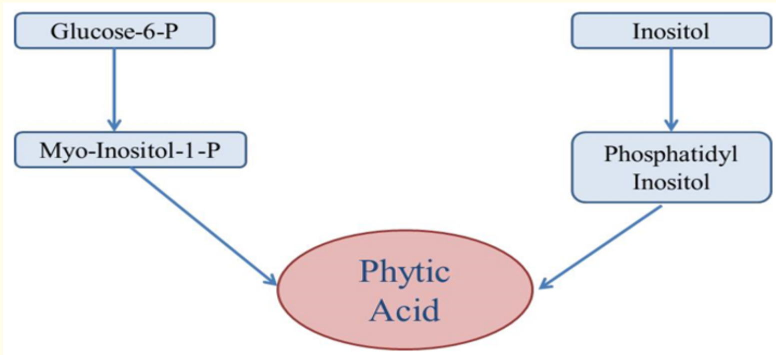

Figure 4: Representation of phytic acid metabolic pathway in different plant species (Source: 53; 54).

is a cause for concern [60]. In a study on finger millet's phytic acid analysis reveals that the accumulation of phytic acid increases with the increasing concentration of exogenous calcium but the amount of phytic acid may vary from genotype to genotype [61]. The phytic acid complexes are non-absorbable by the human digestive system so the formation of insoluble phytic acid complexes with minerals at different physiological pH is regarded as the main reason for the poor mineral bioavailability.

- **Calcium binding proteins:** Calcium also stored mostly in bound form with calcium binding proteins (CaBPs). Cells activates several types of calcium binding proteins which include Calmodulin (CaM), CaM-like proteins, Calcineurin-B, Calreticulin and calcium dependent protein kineses (CDPKs) [62,63] among these calreticulin is main which responsible for binding with the free calcium [64]. Calcium binding proteins reduce the bioavailability of calcium in some plants by binding free cytosolic calcium [65,66]. But on the other side the over expression of calreticulin in Arabidopsis increased the calcium content in tissues [67]. As a candidate gene to improve calcium accumulation the use of calcium binding proteins hasn't sufficiently work as compare to CAX transporter [68]. In finger millet seeds two calcium binding proteins (Calcineurin-B and Careticulin) were identified through proteomics approaches [63]. In earlier work, the characterization of Calmodulin (CaM) had done and attempts were made to increase the seed calcium content in finger millet [69]. Calcium-ion binding agents are good inactivators of α-amylase enzyme in little millet which plays important role in starch biosynthesis [70]. However, the work of these calcium binding proteins or agents is not completely identified in most of the millets which reduce or increase the bioavailability of calcium and others minerals. There is a need to work in this area to identify the role of these calcium binding proteins in millets.
- **Other antinutritional factors:** There are some other nutrient inhibitors and phenolic substances are found in many plant species as well as in millets. These nutritional inhibitors render the bioavailability of minerals and ions in millets. Other than oxalate and phytate (which were considered as main antinutrient), millets also contain tannins, saponins, trypsin inhibitors and dietary fiber [7,71]. In a comparative study on foxtail millet shows reduction in the amount of anti-nutrients after pre-processing treatment, which is a smart approach to increase the bioavailability of crop [72]. However, fermentation is the best way among all pre-processing treatments which reduced 80% of phytic acid and 90% of tannin in pearl millet, finger millet and sorghum [73]. Among millets, brown varieties of finger millet were reported high amount of tannins (tannic acid) as compared with white varieties of finger millet [74]. These tannic acids are responsible for the reduction of iron in millets. However, boiling and high-pressure cooking can reduce the tannin content in millets [75]. Some digestive inhibitors like amylase, protease and trypsin have been identified in sorghum and millets [76]. According to this study, pearl millet inhibits the proteolytic enzymes of both human and bovine pancreatic preparations. Some anti-nutrients of millets and other similar crops were listed below in the table 1. There is a lack of complete information on antinu-

S. No.	Millets and other cereals	Oxalic acid (Total) (mg/100g)	Phytic acid (mg/100g)	Saponins	Dietary fiber (Total) (gm/100g)
1	Finger Millet *(Eleusinecoracana)*	39.58 ± 6.47	306 ± 6.9	-	11.18 ± 1.14
2	Pearl Millet *(Pennisetumtyphoideum)*	53.13 ± 5.34	485 ± 12.1	-	11.49 ± 0.62
3	Sorghum *(Sorghum vulgare)*	28.38 ± 2.65	549 ± 27.2	-	10.22 ± 0.49
4	Foxtail Millet (Setariaitalica)	3.48 ± 0.17	452 ± 6.5	-	6.39 ± 0.60
5	Little Millet (Panicummiliare)	6.74 ± 0.98	265 ± 20.1	0.44 ± 0.04	7.72 ± 0.92
6	Maize, Dry (Zea mays)	15.26 ± 1.78	646 ± 19.4	-	12.24 ± 0.93
7	Rice flakes (Oryza sativa)	10.97 ± 0.60	474 ± 21.1	-	3.46 ± 0.32
8	Rice, raw, brown (Oryza sativa)	12.06 ± 1.05	742 ± 14.5	-	4.43 ± 0.54
9	Wheat, whole (Triticumaestivum)	52.46 ± 3.32	638 ± 29.2	-	11.23 ± 0.77
10	Barley (Hordeum vulgare)	10.98 ± 1.31	386 ± 18.2	-	15.64 ± 0.64

Table 1: Major anti-nutrient's content in millets, rice, maize and wheat.

Source: National Institute of Nutrition, 2017 (84).

trient's content in all millets so there is a need to investigate all the antinutritional factors in millets. These anti-nutrients interact with nutrients and make it unavailable for humans which lead to malnutrition.

- **Nutrient-Antinutrient interactions:** Mostly, plants contain some anti-nutrients in their seeds as well as other parts of plants to support their defence mechanism. A plant with poor defenses faces the possibility of severe foliage damage, rendering it incapable of performing an adequate amount of physiological or reproductive measures to survive. Plants defend themselves using a variety of preformed and induced chemical and/or physical barriers. Anti-nutrients play an important role to improve the defence mechainism of plant. The nutrients interact with antinutrient like oxalates, phytates, polyphenols, tannins and digestive enzyme inhibitors and these interactions reduces the minerals absorption. These anti-nutrients like polyphenols have been useful to those who suffering from metabolic disorders like diabetes and obesity [77]. The concentration, ratios of ions and interaction can influence the uptake and transport of a particular nutrient in the root [78]. Minerals with chemical similarities can compete for transport proteins, facilitating or hindering absorptions, and other uptake mechanisms. The interaction of mineral like Ca also affects the absorption of other essential ions. Calcium is not only maintained integrity of the selective ion transport mechanisms but is also important for selective ions uptakes [79]. For example, high Na concentration in the soil solution inhibits the absorption K, Rb and other ions by plant root. Being an important nutrient Care placed the other toxic cations around ion channels reduces the inhibitory effects of Na and thus facilitates the regulation and uptake of other minerals and ions [80,81]. In addition, a study on millets has demonstrated that phenolics may be effective in the prevention of cancer initiation and progression [33]. But on the other side, anti-nutrients are the phyto-chemicals which reduce the maximum utilization of nutrients especially minerals such as calcium, magnesium and trace elements such as zinc, iron, copper and other nutrients like proteins and carbohydrates [7,12,45,82]. In millets, which are the excellent source of nutrients, nutritional quality is considerably lowered by the presence of anti-nutrients. Antinutrient phytic acid is one of the sources of phosphorus in seeds which interacts with the other nutrient cations in protein storage vacuoles. Measurements have revealed 208 to 246 mg of phytic acid/100 g in finger millet, which is higher than rice [83]. According to earlier studies the presence of nutrient like calcium in plants exists primarily as a complex form in which it is bound with anti-nutrients such as phytate, oxalate along with proteins and other nutrient factors. Millets has wide range of anti-nutrients and nutrients, these nutrient-antinutrient interactions provide nutritional balance for different foods sometimes it is beneficial, but most of the times it is harmful. If the nutritional status of millets improves then it will surely affect the malnutrition problem and it also improves our daily diet.

Conclusion

The COVID-19 pandemic and war in Ukraine threaten the progress in the achieving the 2030 global nutrition targets. Risk of malnutrition is rising and everyone realize the human right to access the quantity and quality of food. However, available food has insufficient number of macronutrients and micronutrients in our daily diet. To improve nutrient's deficiencies and treat undernutrition, many nutritionally rich health products are used in public health sector. On the other hand, scientists are also improving the nutrients status in crops like millets by traditional plant breeding methods, pre-processing techniques, marker assisted selection method, molecular gene cloning etc. It is very important to break the cycle of malnutrition and boost the nutritional status in adults as well as in young ones by reducing the anti-nutrients in crops like millets. Thus, there is a need to research and scaling-up nutrition programs which are also focused on 'Anti-nutrients' as well as 'Millets'. Millets can be an alternative source of rice, wheat and other cereals because it is nutrient rich, cheap and easy to cultivate. By doing this we can ensure a good future of our children and the young ones.

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