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INVITED REVIEW

Biofortification of food crops: a novel strategy for reducing micronutrient malnutrition

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ABSTRACT

More than two billion people across the world are iron (Fe) and zinc (Zn) deficient, the majority of them are rural poor living in developing countries. Poor people cannot afford diversified diets, nutrient supplements and fortified foods. Thus, biofortification appears to be a good means of enriching micronutrients to food crops and it can be done through conventional breeding, transgenic or agronomic approach. Landraces and wild relatives having high mineral contents are used in the breeding programme to develop new varieties with high yield and elevated mineral characteristics. In conventional breeding, parent lines with high mineral levels are crossed and back-crossed over several generations to produce plants that have enhanced level of minerals. Transgenic approach has made it possible to transfer candidate gene from the same or a different species or organism to the intended crops that low in minerals. Internationally the 'HarvestPlus' programme has taken initiative to address micronutrient malnutrition of rural poor in developing countries through development of staple food crop varieties (rice, wheat, maize, cassava, pearl millet, beans and sweet potato) that rich in Fe, Zn and Vitamin A (β-carotene). The whole amount of minerals present in plant foods is not bioavailable to humans due to presence of antinutritional compounds (e.g. phytate) that interferes with the absorption of nutrients. Agronomic biofortification provides temporary micronutrient increase through fertilizer application. This approach could be complementary to breeding strategy for achieving greater success of breeding efforts for micronutrient enrichment of food crops. This paper presents a comprehensive review of the progress of biofortification research, indicating a sustainable strategy to enhance the micronutrient concentration in staple foods and thereby reducing micronutrient malnutrition.

Keywords: Biofortification, HarvestPlus, Iron, Malnutrition, Micronutrients, South Asia, Zinc

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1 Introduction

Micronutrient malnutrition is a great concern in the present day world. Access to food is not enough, access to nutritious food is important for a healthy nation. Humans require 10–15 mg Fe and 12 -15 mg Zn daily (Welch and Graham, 2004). The FAO has five objectives, of which objective 1 is to 'help eliminate hunger, food insecurity and malnutrition' (FAO, 2019). Biofortification means biological fortification. Thus, it is a biological process of adding micronutrients to food crops through breeding or agronomic approach. It is recognized as a good means of dietary improvement of malnourished rural population (Bouis, 2013; Garg et al., 2018). The agricultural system that produces foods in the developing world usually does not provide enough micronutrients (trace elements and vitamins) to meet the human needs, although the production of carbohydrates via cereal crops is adequate to feed the world (Welch et al., 1997). In developing countries, the staple cereals (rice, wheat, maize) are largely grown in micronutrient, particularly Zn deficient soils and the farmers do not regularly use micronutrient fertilizers, thus the grains contain low amount of micronutrients. Furthermore, minimum attention is given to the production of micronutrient-rich non-staples, such as pulses, vegetables and fruits. Again, the increased prices of vegetables and pulses have made it difficult for the poor to afford quality diet (Bouis et al., 2011a). Inadequate intake of micronutrients in diets can affect the normal functions of brain, immunity and reproductive systems (World Bank, 1994).

A number of studies have been done and are in progress regarding biofortification of cereals as in rice (Behura et al., 2011; Mubarak et al., 2015), wheat (Cakmak et al., 2010; Guzmán et al., 2014) and maize (Qin et al., 2012; Šimić et al., 2011). It is now well agreed that adoption of two strategies (agronomic and breeding) can increase the micronutrient concentrations of food crops and thus consumption of these foods can reduce the malnutrition of humans. Agronomic technique through fertilizer management can rapidly increase the micronutrient concentration of crop foods (Zuo and Zhang, 2011; Cakmak and Kutman, 2018) and breeding technique (conventional and transgenic) through developing new varieties can enhance the capacity of plant roots to take up nutrients from soil and accumulate them in edible parts (White and Broadley, 2009).

This article aims at reviewing the progress of biofortification research and identifying sustainable strategy to enhance micronutrient concentration in staple foods and thereby reducing the malnutrition of world poor. It is hypothesized that the breeding approach alone cannot adequately address micronutrients enrichment of food grains, agronomic approach via fertilizer application can effectively complement the breeding strategy.

2 Micronutrient malnutrition

2.1 Concept

Malnutrition can arise in three forms (Ritchie and Roser, 2020): (a) hunger and undernourishment, (b) obesity or overnourishment, and (c) micronutrient deficiencies. In this article, human malnutrition in the form of micronutrient deficiency has been addressed. Micronutrient refers to a substance that is essential in trace amounts for the growth and metabolism of a living organism. To a human nutritionist micronutrient could be a vitamin or a mineral, while plant scientists mean it only minerals. So, nutritionally micronutrient malnutrition is a dietary deficiency of minerals and vitamins.

2.2 Essential micronutrients

Humans need 11 trace elements (minerals) and 14 vitamins for their normal growth and health. Both animals and plants require eight essential trace elements, but not all the same. A list of minerals required for humans, livestock and crops is shown in Table 1 and the amount of requirement for humans is presented in Table 2. Each mineral nutrient has a definite role in human, animal and plant metabolisms. Of the essential micronutrients, the most frequently reported deficiencies for human health are Fe, Zn, I and vitamin A (Welch and Graham, 2004), the reason can be attributed to the smaller amount of micronutrients in cereal grains (Garg et al., 2018) and the higher amount of antinutrient substances e.g. phytic acid (White and Broadley, 2009), a substance that inhibits the absorption of mineral elements by the gut. The levels of trace elements like Cu, Zn, Mn, Fe and Mo in crops can be sufficient for optimum yields, but they may be sub-optimal to meet the needs of livestock (Shukla et al., 2018). Cobalt is essential for livestock and legume (pulse) crops. Humans need 14 vitamins which include water-soluble vitamins *viz.* ascorbic acid, biotin, cobalamin, folic acid, niacin, pantothenic acid, pyri-doxine, riboflavin and thiamin and fat-soluble vitamins *viz.* retinoic acid, calciferol, tocopherol, phylloquinone, and menoquinone (Graham et al., 2001).

2.3 Hidden hunger

Unlike energy-protein undernourishment, the health impact of micronutrient deficiency is not always visible; it is therefore also called 'hidden hunger'. Swaminathan (2014) states, 'Hidden hunger is one vibrant of hunger which arises from lack of micronutrients'. Pregnant women and children are at greater risk of micronutrient deficiencies. This is due to higher physiological requirements; pregnancy and childhood development often create demand for specific vitamins and minerals. Based on the global burden of disease estimates there are 26 major risk factors of human health, of them Fe deficiency ranks 9th, Zn deficiency 11th, and vitamin A deficiency 13th (Ezzati et al., 2002).

Poor diet is a major cause of hidden hunger. Cereal based diets, the largest source of energies (calories) for the rural people, are relatively low in vitamins and minerals which results in hidden hunger. In addition, poverty is a major factor that limits the access to nutritious foods e.g. meat, milk, fish, fruits, vegetables (Bouis et al., 2011a). About 800 million people in the world are chronically hunger (calorie deficiencies) (FAO et al., 2017) and more than 2 billion people are affected by hidden hunger (micronutrient deficiencies), the vast majority from developing countries (WHO, 2006; McGuire, 2015; Hodge, 2016). Based on the Disability-Adjusted Life Years (DALYs) data, Gödecke et al. (2018) have observed

Table 1. Essential micronutrients required for humans, livestock and crops †

Micronutrient	Humans	Livestock	Crops
Boron (B)	No	No	Yes
Cobalt (Co)	Yes	Yes	No
Copper (Cu)	Yes	Yes	Yes
Iron (Fe)	Yes	Yes	Yes
Manganese (Mn)	Yes	Yes	Yes
Molybdenum (Mo)	Yes	No	Yes
Zinc (Zn)	Yes	Yes	Yes
Fluorine (F)	Yes	No	No
Iodine (I)	Yes	Yes	No
Selenium (Se)	Yes	Yes	No
Chlorine (Cl)	No	No	Yes
Chromium (Cr)	Yes	No	No
Silicon (Si)	Yes	Yes	No
Nickel (Ni)	No	No	Yes

† Source: Bell and Dell (2008);

Table 2. Amount of essential micronutrients required for humans †

Element	RDA	RNI	UL	SUL
Fe (mg)	8.0-18.0	11.4	45.0	17.0
Zn (mg)	8.0-11.0	9.5	40.0	25.0
Mn (mg)	1.8-2.3	>1.4	11.0	4.0
Cu (mg)	0.9	1.2	10.0	10.0
I (µg)	150	140	1100	500
Se (µg)	55	75	400	450
Mo (µg)	45	50-400	2000	NS
Cr (µg)	25-35	>25	NS	NS
F (mg)	3-4	NS	10.0	NS
Si (mg)	NS	NS	NS	1500

† Source: White and Broadley (2005); NS = Non specified; RDA = Recommended daily allowance (US recommendation); RNI = Reference nutrient intake (UK recommendation) (Amount enough for at least 97% in a group); UL = Upper intake level (US recommendation); SUL= Safe upper level (UK recommendation)

that all country-level determinants have larger effects on the burden of chronic hunger (calorie deficiencies) than on the burden of hidden hunger (micronutrient deficiencies), and complementary micro-level interventions are required to end hidden hunger. Hidden Hunger Index (HHI) of different countries of south Asia and south-east Asia are shown in Table 3.

2.4 Micronutrient malnutrition in south Asia

The situation of Fe and Zn deficiency is worse in south and south-east Asia where high proportion of cereal crops, such as rice and wheat, is consumed as a staple food (Cakmak, 2008; Stein, 2009). Cereals contribute about 60% for Zn and 55% for Fe to the daily intake of these minerals by Bangladeshi people (Islam et al., 2014). Ahmed et al. (2016) has reviewed the micronutrient deficiencies among children and women in Bangladesh. The review states that as per National Micronutrients Status Survey report (2011-12), among the preschool-age children 20.5% are deficient in vitamin A, 44·5% in Zn and 10.7% in Fe. About 57% non-pregnant and non-lactating women are Zn deficient, and 25% women Fe deficient, and nearly 50% pregnant and lactating women are anaemic, induced by Fe deficiency. WHO (2007) estimates that in India about 27% population is suffering from Zn deficiency induced disorders which include poor immune system, diarrhea, poor physical and mental growth. Children are vulnerable to Zn deficiency which is the reason for 4.4% of the total child deaths in the world (Black, 2003).

Table 3. Hidden Hunger Index (HHI) and micronutrient deficiencies in south Asia and south-east Asia †

Region	Country	Deficiency prevalence (%)			
		HHI score	Zn ‡	Fe §	Vitamin A ¶
South Asia	Afghanistan	47.7	59.3	19	64.5
	India	48.3	47.9	34.7	62
	Pakistan	26.7	42	25.5	12.5
	Bangladesh	29.3	43	23.5	21.7
	Sri Lanka	22.3	19.2	12.6	35.3
	Nepal	35.3	49.3	24.2	32.3
	Bhuttan	33.3	37.5	40.3	22
	Maldives	30	31.9	48.9	9.4
South-East Asia	Indonesia	27.3	40.1	22.3	19.6
	Thailand	14.7	15.7	12.6	15.7
	Philippines	30.7	33.8	18.2	40.1
	Malaysia	11.7	15.6	16.2	3.5
	Singapore	NA	4.4	11.3	NA
	Vietnam	24	43.3	17.1	12
	Myanmar	36.3	40.6	31.6	36.7
	Cambodia	31	39.5	31	22.3
	Laos	38.7	47.6	24.1	44.7
	Brunei	NA	11.6	14.5	NA
	Timor-Leste	39	55.7	15.8	45.8

† Source: Muthayya et al. (2013); NA = Data not available, HHI score = [Stunting (%) + Anamia (%) + Low serum retinol (%)] / 3, three components equally weighted; ‡ Stunting as proxy for Zn;
§ Anemia as proxy for Fe; ¶ Low serum retinol, <0.7 µmol L^{-1}

Among the developing countries, Pakistan is recognized as one of the highest levels of child malnutrition country (Asim and Nawaz, 2018). In Asia, there are almost half of the total stunned children and two-thirds of all wasted children under the age of 5 years (UNICEF, 2015). Abeywickrama et al. (2018) from Sri Lanka reported an abundance of Fe, Zn, Ca, folate, and vitamin A deficiencies, with females being more vulnerable than males. Despite recent successes in economic growth, agricultural output and health care, the prevalence of micronutrient deficiencies is high in south Asia. Harding et al. (2017) have reviewed the situation using the metric of stunting (indicator of Zn deficiency). Pakistan has the highest national prevalence (44%) (AKU, 2011), followed by Afghanistan (41%) (Ministry of Public Health and UNICEF and Aga Khan University, 2014) and Nepal (41%) (MoHP, 2012), India (39%) (Raykar et al., 2015), Bangladesh (36%) (ICDDR,B, 2013) and Sri Lanka (13%) (Jayatissa et al., 2014). In Bangladesh 57% non-pregnant women and in Pakistan 41% women are Zn deficient. In south Asia, excepting Sri Lanka, about 40% children under 5 years are anemic, in Sri Lanka, this level is 20·0–39·9% (UNICEF et al., 2001). In India, Bangladesh and Nepal, the anaemia problem prevails more in rural areas than in urban. Iron deficiency causes about half of anemic populations in south Asia (Kassebaum et al., 2014).

2.5 Ways to address micronutrient malnutrition

Human micronutrient malnutrition can be addressed in four possible ways (Ritchie and Roser, 2020):

(a) Supplementation: Use of concentrated micronutrients in pill, powder or liquid form;

(b) Food fortification: Addition of micronutrients to food products during processing such as rice milling, wheat flours;

(c) Biofortification: Addition of micronutrients to food crops by breeding or agronomic method.

(d) Diet diversification: Consumption of micronutrient rich diet, e.g. fruits, vegetables, pulses etc.

In the past, nutrient supplementation, food fortification and diet diversification were largely used as means of reducing micronutrient deficiency (Mayer, 2005; Brown et al., 2007; Casey et al., 2009; Eneroth et al., 2010; Ritchie and Roser, 2020). However, these approaches had limited success (Ssemakula and Pfeiffer, 2011). Child mortality from diarrhoea and pneumonia reduced much in Bangladesh for use of 'baby zinc' tablet developed by ICDDR,B (Baqui, 2002; Brooks et al., 2005). However, fortification and supplementation programs can complement biofortification for better use by urban people, not by rural people.

3 Biofortification

There are two broad approaches of micronutrient biofortification in crops: breeding and agronomic. Breeding approach includes conventional breeding and genetic engineering (transgenic). Agronomic approach covers fertilizer management, variety screening and crop diversification.

3.1 Breeding method

Both conventional breeding and genetic engineering (transgenic) can play a good role to increase the Fe and Zn concentrations of edible parts of crops (Ghandilyan et al., 2006).

3.1.1 Conventional breeding method

The breeders generally give more attention to the development of crop varieties for yield improvement (Belford and Sedgley, 1991; Peng et al., 1999) and resistance to biotic (Datta, 2002; Pasalu et al., 2008) and abiotic stresses (Ashraf et al., 2012). Recently many crop scientists have paid considerable attention to the improvement of micronutrient density in the food crops (Zhang et al., 2012). For successful breeding for higher mineral content, exploration of genetic variability is essential and also knowledge about the genetics of the observed variation and genotype × environment interaction is important (Welch and Graham, 2004). As stated by Nair et al. (2013), the variation in mineral concentrations (0.03–0.06 g kg^{-1} for Fe, and 0.02–0.04 g kg^{-1} for Zn) among the mungbean genotypes renders the scope for mineral enrichment in the newly developed varieties. Reports are available about variation in Fe and Zn concentrations of wheat grain due to genetic variability (Rengel et al., 1999; Cakmak et al., 2002; Velu et al., 2011; Pant et al., 2020). The genetic variation in grain Fe and Zn concentrations among the cultivated varieties of cereals (e.g. wheat) is found generally low, but greater variation is often found in the wild relatives (Welch et al., 2005; Chhuneja et al., 2006; Pfeiffer and McClafferty, 2007; Cakmak, 2008; Tiwari et al., 2008). Wild accessions might have 2-fold higher grain Fe and Zn concentrations than the widely grown varieties for many cereals (White and Broadley, 2005). The CIMMYT breeding program has developed high-yielding bread wheat lines through hybridization and selection that contained 10-90% higher grain Zn and Fe concentrations than popular commercial varieties (Guzmán et al., 2014).

3.1.2 Transgenic (genetic engineering) method

Transgenic approach deals with improvement of mineral uptake from root zone, translocation to the shoot and accumulation in edible tissues, and also reducing the concentration of antinutrients and increasing the concentration of promoter substances (White and Broadley, 2005; Davies, 2007; Zhu et al., 2007). Limited works have been done on vegetable crops with respect to micronutrient biofortification. Modern biology technique (genetic engineering) can help vegetable breeders to incorporate candidate genes into elite cultivars for higher mineral content and thereby improving the mineral value (Gomathi et al., 2017). Bt brinjal (*Solanum melongena*) is the first genetically engineered crop in Bangladesh (Shelton et al., 2018).

During rice milling, more than 50% of the Zn could be lost and the remaining portion of Zn might not be fully available for intestinal absorption due to presence of antinutrient compounds e.g. phytates (Das et al., 2018). Thus it is suggested that biofortification programme should also aim at Zn partitioning more to seed endosperm. Garg et al. (2018) has given a good analysis about transgenic approach. When genetic diversity is not available, genetic transformation could be a better option. In this approach, once a useful gene is discovered, that can be utilized in multiple crops. Various genes from different sources have been utilized to enhance the level of vitamins, minerals, essential amino acids, and essential fatty acids in the food crops. Examples are phytoene synthase (PSY), carotene desaturase, and lycopene β-cyclase for vitamins, ferritin and nicotinamine synthase for minerals, albumin for essential amino acids, and $\Delta 6$ desaturase for essential fatty acids.

3.1.3 The 'HarvestPlus' programme

The HarvestPlus Challenge Programme on 'Biofortified Crops for Improved Human Nutrition' has been initiated in 2004 with the objective to develop cultivars of staple food crops with rich in Fe, Zn, and vitamin A (β-carotene). The Consultative Group on International Agricultural Research (CGIAR) has started this programme with financial support from the Bill and Melinda Gates Foundation, the World Bank, and USAID. It is an interdisciplinary alliance of research institutions and implementing agencies. The target crops include 7 food crops such as rice (*Oryza sativa* L.), wheat (*Triticum aestivum* L.), maize (*Zea mays* L.), cassava (*Manihot esculenta* Crantz), pearl millet (*Pennisetum americanum* Leeke), beans (*Phaseolus vulgaris* L.) and sweet potato (*Ipomoea batatas* L.). Those crops have been chosen based on the observation that those foods are consumed as staple foods by the world's poor. The HarvestPlus programme is going on in south Asia for rice Zn (target 28 mg g^{-1}) in Bangladesh and India, for wheat Zn (target 28 mg g^{-1}) (& Fe secondary) in India and Pakistan, and for lentil Fe (target 70 mg g^{-1}) (& Zn secondary) in Bangladesh, Nepal and India (HarvestPlus, 2014).

Success of biofortification programme depends on three factors, as outlined by Bouis et al. (2011b). The factors are: (i) the biofortified crop must be high yielding and profitable to the farmer, (ii) the biofortified crop must show as efficacious and effective in reducing micronutrient malnutrition of humans, and (iii) the biofortified crop must be acceptable to both farmers and consumers in the regions where people are afflicted by micronutrient deficiency. All these points are well taken in the HarvestPlus program (Hotz and McClafferty, 2007). Thus, the biofortified crop variety should be high yielding with high minerals content and acceptable to the people suffering from micronutrient malnutrition. For example, BRRI dhan62 (Zn enriched rice variety) has not been popularized among the farmers in Bangladeshi due to low yield potential (4.0-4.5 t ha^{-1}). However, the later varieties (BRRI dhan64, 72, 74 and 84) have addressed this problem.

3.1.4 Bioavailability of micronutrients

Micronutrient bioavailability refers to the proportion of a nutrient that is absorbed from the diet and used for normal body functions (Aggett, 2010). Bioavailability of a nutrient is regulated by some external and internal factors. External factors include food matrix and chemical form of the nutrient and internal factors are gender, age, life stage (e.g. pregnancy), etc. Not the whole amount of minerals present in plant foods is bioavailable to humans due to presence of antinutritional compounds that interfere with the absorption or utilization of the nutrients in humans (Welch and Graham, 1999). In general, seeds and grains of staple food crops contain very low bioavailable levels of Fe and Zn (i.e., about 5% of the total Fe and about 25% of the total Zn present in the seed is bioavailable). So far, phytic acid (myo-inositol-1,2,3,4,5,6-hexakisphosphate), fibres (e.g. cellulose), polyphenols (e.g. tannins), haemagglutinins (e.g. lectins) and heavy metals (e.g. Cd) are recognized as antinutritional compounds (Graham et al., 2001; Hurrell, 2004; Welch and Graham, 2004). Phytic acid or phytate can strongly bind divalent cations (e.g. Zn^{2+}) and thus limit the cation bioavailability, even in the digestive tract. On the contrary, phytate has positive function since it is a major storage form of seed phosphorus that needed for germination.

3.1.5 Mechanisms of Fe and Zn absorption

Plants possess two mechanisms for Fe acquisition from soil. In Strategy I (dicots and non-graminaceous monocots), the roots acidify the rhizosphere and release organic acids and phenolic compounds to increase Fe^{3+} concentrations in the soil solution. These compounds chelate Fe^{3+}, which is subsequently reduced to Fe^{2+} by ferric reductase enzymes in the plasma membrane of root epidermal cells (Wu et al., 2005; Mukherjee et al., 2005). In Strategy II (graminaceous monocots such as rice, corn and wheat), phytosiderophores (structural derivatives of mugineic acid) are released into the rhizosphere to chelate Fe^{3+}, and the Fe^{3+}–phytosiderophore complex is taken up by root cells (Roberts et al., 2004; Ishimaru et al., 2006). Concerning Zn acquisition, it is assumed that the most Zn is transported symplastically across the root to the xylem via the apoplast (White et al., 2002; Broadley et al., 2007). Zinc is taken up across the plasma membrane of root cells as Zn^{2+} or as a Zn–phytosiderophore complex (Suzuki et al., 2006; Broadley et al., 2007; Ismail et al., 2007). A number of 48 putative genes regulate the transport of Fe and Zn for accumulation in kernels (maize) which indicates that mineral accumulation in cereal grains is a complex polygenic process (Sharma and Chauhan, 2008; Maqbool and Beshir, 2018). The Zn and Fe concentrations in cereals is reported to be positively correlated (Jahiruddin and Islam, 2018). Chakraborti et al. (2009) has explained the correlation between kernel (maize) Zn and kernel Fe in terms of pleiotropic effects or linkage among the genes regulating these elements concentration.

3.2 Agronomic approach

Agronomic biofortification greatly concerns with fertilizer management to elevate the mineral concentrations in edible portions of crops (White and Broadley, 2009). For increasing the fertilizer use efficiency the 4R nutrient stewardship (right source, right rate, right time and right place) of fertilizer application is important (Johnston and Bruulsema, 2014). Zinc deficiency is pronounced in calcareous and wetland soils, and as crop maize and wetland rice are the most responsive to zinc fertilization (Jahiruddin, 2015). In situation, when availability of a nutrient in soil is low for fixation or any other reason and when mobility of a mineral within plant body is low, foliar spray of soluble inorganic fertilizers would be very helpful. It is reported that soil application combined with foliar spray is more effective in increasing micronutrient concentration in grains (Guo et al., 2016; Maqbool and Beshir, 2018). Foliar application of Fe in rice (Yuan et al., 2012) and wheat (Aciksoz et al., 2011), and foliar Zn in rice (Wei et al., 2012) and wheat (wen Yang et al., 2011) are reported to increase their concentration in grains. Foliar Zn application during early milk stage of rice could be the most effective way to elevate grain Zn concentration (Mabesa et al., 2013).

Besides fertilizer management, use of soil microbes, especially mycorrhizal fungi and plant growth promoting rhizobacteria (PGPR) such as *Bacillus*, *Pseudomonas* can play a good role for acquisition of immobile mineral elements from the root zones (Rengel et al., 1999; Mishra et al., 2011; Sharma et al., 2013). Thus, micronutrient fertilizers, organic manures and microbial biofertilizers need to be added to soil in an integrated way. Liming is also important for acid soils (pH<5.5) to reduce the toxicity of Al and some micronutrients (Fe, Zn and Mn). Crop varieties such as rice varieties may vary in yield potential and micronutrient density in their edible parts. They may differ in their capacity to absorb Fe and Zn from soil (Shivay et al., 2010; Jahiruddin and Islam, 2018). Thus, selection of a genotype which is high yielding and possesses comparatively higher efficiency to absorb and translocate micronutrients from roots to grains can be regarded as a good agronomic practice. Joy et al. (2015) in Africa reported 23, 7 and 19% increased Zn concentration in maize, rice and wheat grains due to soil application, and 30, 25 and 63% Zn increase for foliar spray in these crops, respectively.

Erosion and leaching loss of nutrients, liming of acid soils, and minimum use of micronutrient fertilizers and organic manure are the good reasons for micronutrient deficiencies in agricultural soils (Fageria et al., 2002). Positive influence of Zn fertilization is reported on Zn concentration of rice and maize grains, mungbean seeds, tuber (potato), curd (cauliflower) grown in alluvial soils of Bangladesh (Hossain et al., 2008; Sarker et al., 2019a,b). An increment of 4-8 µg g^{-1} Zn in wheat grain and 2-4 µg g^{-1} Zn in rice grain is possible through Zn fertilization (Jahiruddin and Islam, 2018). Farmers of south Asian countries commonly use N, P and K fertilizers; use of micronutrient fertilizers is limited (Jahiruddin, 2019). Positive information is also reported. Shukla et al. (2018) demonstrates that the extent of Zn deficiency in Indian soils is in declining trend and currently it is 36.5% Zn deficiency which shows farmers' awareness to apply Zn fertilizers.

Efficient management of N and Zn fertilizers would help enhance the grain Fe and Zn concentrations, as evidenced by positive correlation of seed Fe and Zn with N contents in several crops (Zhang et al., 2008; Cakmak et al., 2010; Kutman et al., 2010). In many cases, there is found inverse relationship between grain yield and grain Zn concentration (Garvin et al., 2006; McDonald et al., 2008). Information is also available that grain yield increases, along with a considerable increase in grain Zn concentration, as reported from Pakistan (Zou et al., 2012), China (Karim et al., 2012) and Turkey (Yilmaz et al., 1997). Siddika (2019) observed a synergistic relationship between N and Zn concentrations of rice.

3.3 Benefits and limitations of biofortification

There is an added benefit of agronomic biofortification that the micronutrient rich seeds of biofortified varieties would produce viable and vigorous seedlings and thus would improve disease resistance and growth characteristics, with giving yield benefits (Rengel and Graham, 1995; Graham and Welch, 1996; Cakmak, 2008). A great disadvantage is that agronomic biofortification gives short-term benefits and therefore, every time fertilizer application is necessary that would add an extra cost. Furthermore, fixation of Zn and Fe may occur in high pH soils that limit the capacity of biofortified crops to absorb them from soil. Low yield, interactions between genotype and environment, lack of sufficient genetic diversity for breeding program, consumer resistance and safety of genetically modified (GM) crops are the main weaknesses of genetic biofortification (Falk et al., 2002; Cakmak, 2008; Palmgren et al., 2008; Joshi et al., 2010). Moreover, adoption of biofortified varieties depends on the factors that they should perform higher yield, with higher stress tolerance and other qualities such as taste, color, and flavor (Wolson, 2007). Crops fortified with β-carotene (vitamin A) exhibit a deep yellow to orange color as seen in golden rice, orange-fleshed sweet potato, and yellow cassava (Pray et al., 2007; Ramaswami, 2007). On the contrary, Zn or Fe enriched varieties does not have such visible characteristics and this limits their acceptance by the consumers.

Breeding approach is a long-term process and needs tremendous efforts and time, requiring number of crossing and backcrossing activities over a number of years, and its success depends on the stability of the targeted micronutrient trait under various environmental conditions. Besides, the potential benefits of biofortification depend on the groups of people (men, women, children and elderly), amount of staple food(s) consumed, the prevalence of existing micronutrient deficiencies, and special needs for processes such as growth, pregnancy, and lactation (Hotz and McClafferty, 2007). Presently we are looking many successes of transgenic biofortification, e.g. lysine and tryptophan rich quality protein maize, vitamin A (β-carotene) rich orange sweet potato and vitamin A rich golden rice (Garg et al., 2018). However, the success rate and acceptability of genetic engineering technique (transgenic) appears to be much lower compared to conventional breeding. Furthermore, globally introduction of GMO food crops is a subject of debate and truly its consumption is very low. In breeding programs, interrupting the negative relationship between grain yield with Zn or Fe concentration is a challenging task for enhanced micronutrient density in cereal grains (Zhao and McGrath, 2009; Bouis and Welch, 2010; Waters and Sankaran, 2011). Research to develop a variety combining the qualities of high yield with high micronutrient concentration in grains would take fairly a long time. Processing of food grain is also important in the context of biofortification strategy. Minerals such as iron, zinc, and copper that are highest in the rice bran are lost during milling and polishing. This is not a problem for Se and S since they exist as maximum in the embryo (Gregorio et al., 2000). However, the extent of the loss is genotype dependent (Waters and Sankaran, 2011).

4 Sustainable strategies for micronutrient enrichment

When a soil is critically deficient in micronutrients, the benefits of biofortified varieties cannot be achieved. Thus, biofortification should be considered as an integrated approach in which both breeding and agronomic approaches are equally important for question of sustainability (Mubarak et al., 2015). In cultivation of micronutrient biofortified varieties, application of micronutrient fertilizers can be regarded as a sustainable strategy to boost the crop yield with higher mineral concentrations in edible parts (Bouis et al., 2003; Genc et al., 2005; White and Broadley, 2005; Graham et al., 2007; Pfeiffer and McClafferty, 2007). Concurrently, it is also needed to enhance the concentrations of 'promoter' substances such as ascorbate (vitamin C) which stimulates the absorption of mineral elements by the gut, and to lower the concentrations of 'antinutrients', such as phytate, which interferes with their absorption (White and Broadley, 2009). Agronomic biofortification is complementary to breeding approach. When the genotypes having higher grain minerals are developed, their cultivation should be properly fertilized with Fe and Zn (Prasad et al., 2014). Thus, neither breeding nor agronomic approach alone can solve the problem of micronutrient malnutrition adequately and sustainably. For an effective and sustainable strategy, agronomic biofortification needs to be complemented with breeding strategy for micronutrient enrichment of food crops.

5 Conclusions

A good progress has been made in research concerning mineral biofortification of food crops with a view to addressing micronutrient malnutrition in humans. The main tune of this effort is breeding strategy with transgenic approach supported by the HarvestPlus programme. Still there is a big challenge to clearly explain the molecular mechanisms and genetic behaviour of crops regarding Zn and Fe accumulation in grains. Development of farmers' acceptable varieties with high yield potential and high micronutrient characteristics still remains a great challenge. When a soil is highly deficient in Zn or Fe, the yield as well as nutrient concentration of the biofortified crops grown in that soil would not be satisfactory. Thus, integration of agronomic (fertilizer management) with breeding approach is required to achieve the goal of reducing micronutrient malnutrition.

Conflict of Interest

The author declares that there is no conflict of interests regarding the publication of this paper.

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