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BIO-FORTIFICATION; FUTURE CHALLENGES TOWARD NUTRITIONAL SECURITY : MINI REVIEW

Barnali Roy
Department of Botany, Kanchrapara College, Kanchrapara, North 24 Pgs., West Bengal.
E-Mail : barnaliroy_barnali@yahoo.com

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ABSTRACT

Nutritional deficiency which increasing tremendously during the last two decades creates micronutrients malnutrition is a very common problem especially for women and children in the developing countries. The hidden hunger which is due to malnutrition affecting one in the three people globally. Several efforts like dietary diversification, food supplementation and food fortification have been taken to overcome micronutrients malnutrition of which bio-fortification is a very promising sustainable approach to reduce the micronutrients malnutrition. The bioavailability of micronutrients provides a very promising effect under bio-fortification. In bio-fortification, apart from the agronomic approach, and plant breeding approach, genetic engineering technology is very useful to increase the micronutrients in the food crops. The bio-fortified crop varieties provide the adequate nutrients to the target people in the developing countries. The bio-fortification which is an innovative crop-based strategy brings big challenge towards nutritional security.

Keywords : Micronutrients malnutrition, bio-fortification, agronomic approach, genetic engineering, plant breeding

Introduction

The micronutrient deficiency affecting a major part of the world's population in the developing countries (Stein, 2010) where billions of individuals continuously facing the problems of malnutrition as they intake staple food crops (White and Broadly, 2005; Thavarajah and Thavarajah, 2012; Graham *et al*., 2007) which do not contain sufficient mineral and vitamins for proper human growth. The deficiencies of micronutrients like Fe, I, Zn and vitamin A are very high in Africa and Asia and this deficiency leads to about 12% death of children under 5 years of age worldwide (Ahmed *et al*., 2012). The hidden hunger which is due to malnutrition affecting one in three people globally (FAO, 2013). Actually hidden hunger is due to deficiency in iron and zinc that causes in low immunity, rigidity, fatigue, muscle weakness and ultimately leads to death of human population (Stein, 2010 and Wintergerest, 2007). There are about 800 million undernourished people worldwide (FAO, 2017). The undernourishment of pregnant mother is a major health issue which generally leads to intrauterine growth restriction, low birth weight, protein energy mal nutrition and chronic energy deficit (Ahmed *et al*., 2012). The micronutrients deficiencies mainly noticed among the 1/3 to ½ of the world population where the intake of bioavailable micronutrients is very low that does not meet the nutritional demand of human beings (Allen *et al*., 2006). In fact the malnourished children below 5 years of age cannot grow properly and the pregnant women facing the various illness due to malnutrition (Alanis *et al*., 2006). Indeed there are about 49 nutritional components which are very essential for human growth. Among the various nutritional components, the deficiency of Zinc and iron affecting more than two billion people globally (Sramkova *et al*., 2009). It is noticed that Zinc deficiency around 40%, Fe deficiency around 5% and Selenium deficiency near about 28%, Ca deficiency near about 54% people of Asian and African countries (De Valenca *et al*., 2017).

Regarding these aspects various strategies have been taken to minimize the malnutrition in different parts of the world such as mineral supplementation, dietary diversification and food fortification programme etc (Welch and Graham 2004a; White and Broadly 2005). But these are not crop based technique. Bio-fortification, a crop based technique is becoming popular to reduce the micronutrient mal - nutrition throughout the world (Meenakashi *et al*., 2010).

Nutrients deficiency and its impact

The undernourishment of pregnant mother affecting near about 50 % of the world's population which generally leads to intrauterine growth restriction, low birth weight, protein-energy malnutrition and chronic energy deficit is due to micronutrient deficiency (Ahmed *et al*., 2012).

Among the various micronutrients Fe and Zn deficiencies are widespread among the people in different parts of the world. Iron deficiency causes anemia that affecting two billion people worldwide (WHO 2001; Yang *et al*., 2007). The maternal mortality which is related with iron deficiency is near about 5% and this acute deficiency leads to death of young women at the time of childbirth (Meenakshi *et al*., 2010). Zinc which protects the cells from oxidative damage (Rosan *et al*., 2002; Prasad *et al*., 2004) can overcome the chances of prostrate and pancreatic cancers (Costello *et al*., 2017). The deficiency of Zinc shows mental illness, decrease infertility and weak immune system that affecting women during pregnancy (Roohani *et al*., 2013). Actually one third of the world's population affected by zinc deficiency (Muller and Krawinkle, 2005) that results in diseases and death of human being in developing countries (White and Broadly, 2009). The vitamin A deficiency is another problem specially for low income group of people in developing countries which affecting near about 125 million preschool-aged children and 7 million pregnant women. Iodine deficiency which is a major health problem in developed countries can causes mental retardation, goiter hyperthyroidism and low fertility (WHO, 2007). About 20% of world population suffering from iodine deficiency and during pregnancy iodine disorder results in to mentally impaired babies (Bruno *et al*., 2008; Hetzel *et al*., 2004).

Selenium is another important essential micronutrient and selenium deficiency also observed in different parts of the world. The deficiency of selenium creates several complications like epilepsy, oxidative stress-related conditions, infertility, low immunity in human body (Rayman 2012; Zeng and Combs, 2008; Whanger 2004).

So the problem of micronutrient deficiency is very challenging health issue and much attention should be given to ensure the nutritional security of undernourished people.

Strategies for Improvement of Essential Nutrients

About two third of the world population suffering from malnutrition as they do not intake micronutrient-rich foods and this deficiency can be overcome through dietary diversification, food supplementation and food fortification program (White and Broadly, 2009). Dietary diversification which involves the consumption of a variety of healthy fruits, vegetables and different grains is related with several factors like affordability, dietary habits and accessibility of the poor people. Food supplement is a short-term method for the betterment of nutritional status and may not be applicable for huge population. Actually food supplements are micronutrients which can be taken in the form of powder, pills and in the form of solution in that cases daily diet does not meet the essential nutrient in such cases the use of folic acid supplements can be applied to increase the folate level in dietary plate (Blanequaert *et al*., 2013; Hefni *et al*., 2010). Folic acid, iron and zinc supplements is very useful for children and pregnant women and this method is not cost effective (Bailey *et al*. 2015; Wiltgrenet *et al*., 2015). Though supplementation for folic acid, zinc and iron is low cost effective but it needs proper medical consultancy and adequate educational programmes (Stoltzfus, 2011).

Food fortification is the improvement of the nutritional quality of foods by the addition of vitamins and minerals. Iron, ferrous sulfate, ferrous fumerate, ferric pyrophosphate and electrolytic iron powder compounds are generally applied for food fortification (World Health Organization, 2006). Various food assistance programmes have been developed by the World Food Programmes (WFP) where pre-cooked and milled cereals and fortified pulses can minimize the unhealthiness due to malnutrition.

Bio-fortification

Among the various strategies taken for improvement of nutritional qualities, bio-fortification is popularly known as an alternative low cost sustainable technique for poor people (Nestel *et al*., 2006). Bio-fortification is most feasible approach to deliver micronutrients to the people who are generally used to inadequate intake of essential micronutrients in daily diet (Bouis and Saltzman, 2017). Actually food crops being low in micronutrient content as the cultivation of high-yielding varieties require high quantity of micronutrients that reduces the soil micronutrient level in various parts of the world (Fageria and Baligar 2008). The bioavailability of micronutrients provides a very promising effect underbio-fortification. The level of micronutrient content in food crops as well as the bioavailability of micronutrient level both are essential to overcome the micronutrient specially in developing countries for large population (Sperotto *et al*., 2012). Besides this the mechanisms of adaptation of micronutrient stress by plant and the pathway of translocation of micronutrient from soil to plant body has been well understood for successful bio-fortification programme (Khush *et al*., 2012). Several approaches have been taken in bio-fortification programme like agronomic approach, genetic engineering and breeding approach.

Agronomic Approach

It is short-term and sustainable technique applied for bio-fortification (Cakmak, 2008). Agronomic bio-fortification approach involves micronutrient uptake from the surrounding soil and translocation into edible parts of the plant body. Actually the high yielding crop varieties causes the depletion of soil native micronutrient level that results low micronutrient density in food crops causing micronutrient malnutrition. Basically, at micronutrient-deficient soil, application of micronutrient fertilizer is found more effective for crop plants. It has been shown that both productivity and micronutrient density of grains has been increased after the use of fertilizers enriched with Zinc in wheat (Hu *et al*., 2003), rice (Lie *et al*., 2003). The application of mineral fertilizers to the soil is required due to low phyto-availability of minerals in the soil (White and Broadley, 2009). The application of foliar fertilization gives better result than the application in soil in case of wheat (Cakmak *et al*., 2010a). The application of zinc as a foliar fertilizer in wheat shows the improvement of zinc concentration of wheat grain by 2-3 folds (Cakmak *et al*., 2010 b; Cakmak 2008). The use of zinc- based fertilizers can minimize the phytic acid concentration which causes the improvement of bioavailability of zinc at the dietary plate (Cakmak *et al*., 2010b; Erdal *et al*., 2002). The iron availability and its mobility in calcerous soil is limited and in that case the application of iron fertilizer is not so effective and due to this reasons foliar application of iron based fertilizer is recommended (Cakmak, 2008). Recent research findings shows that there is a relationship between iron and nitrogen concentration of grain and the transport mechanism of nitrogen and iron in food crops is controlled by the plant's genetic system (Waters *et al*., 2009).

The application of mineral fertilizer enriched with Se. I and Zn was successful because these elements having high mobility (Dai *et al*., 2004; HartiKainen, 2005; White and Broadley, 2005). The application of fertilizers enriched with sodium selenite is very significant to improve Se in take in the human body (Alfthan *et al*., 2015). Foliar fertilization is applicable where mineral elements are not present sufficiently in the soil or not easily available to the plant tissues (Garg *et al*., 2018). It was noticed by Shivay *et al*. (2015) that there is a link between Zn uptake and the yield of chickpeas after the foliar application of Zn. It was observed that Se concentration has been increased after the foliar application of Se fertilizers in the seeds of peas and lentils (Smrkolj *et al*., 2006; Rahman *et al*., 2015). The use of beneficial soil micro-organisms is another approach of biofortification.

Use of Micro-organisms

The presence of beneficial soil microorganisms with symbiotic association in plant roots provides the production of plant growth hormones and enhances the availability of mineral nutrients (FAO, 2019). The soil micro-organisms like *Bacillus*, *Pseudomonas* applied to promote the phyto-availability of micronutrients used mainly as seed inoculants. These micro-organisms promote the plant growth through the production of antibiotics, chitinases siderophore and growth hormones (Mahaffee, 1994). The use of plant growth promoting micro-organisms in iron fortification is very useful that can chelate iron though the generation of siderophore compounds and solubilize phosphorus and prevent the growth of plant pathogens (Panhwar *et al*., 2012; Sreevidya *et al*., 2016). The concentration of Fe, Se, and Zn have been increased after the application of the microorganism inoculants with mycorrhizal approach (Rengel *et al*., 1999; Smith and Read, 2007; Cavagnoro, 2008).

The use of intercropping of cereals with appropriate dicot plant can play a vital role to increase the iron and zinc penetration through root interactions (Huang *et al*., 2012; Kamal *et al*., 2000; Zuo *et al*., 2004; Inal *et al*., 2007). There are some limitations in agronomic bio-fortification where existing variability of micronutrient availability and creates micronutrient deficiency in plant roots (Yang *et al*., 2007).

Genetic Engineering Technology

The modification of plant genetic construction is possible through the application of genetic engineering technology that can induce the synthesis of minerals and vitamins and inhibit the synthesis of anti-nutrient components (Bouis *et al*., 2003; Raboy, 2002; Tucker, 2003). The genetic engineering has been applied for bio-fortification when a specific micronutrient not found in crops and where modifications is not possible through traditional breeding (Mayer *et al*., 2008; Periz *et al*., 2013). The fully sequenced genomes in several crops is now available through genetic engineering. With the progress of genetic engineering specific antinutrients can be removed or promoters can be included that can promote the bioavailability of micronutrients (Garg *et al*., 2018; Carvallo and Vasconceles, 2013). Recently genetic engineering technology has been applied for the improvement of nutritional profile in the pulse crops. It has been shown that the concentration of amino acid methionine become higher in transgenic bean through the expression of a methionine-rich storage albumin obtained from Brazil nut (Aragao *et al*., 1999). To reduce the micronutrient deficiency of large population specially in developing countries the application of transgenic technique has been developed in rice where the Fe accumulation can be induced through the iron storage protein ferritin (Gele *et al*., 2000; Vasconcelos *et al*., 2003). The golden rice that was developed by genetic engineering is consumed to overcome vitamin A deficiency (Paine *et al*., 2005) among the people. It was reported the folate concentration is being increased in rice and tomato by metabolic engineering (Blancquaert *et al*., 2013 and Blancquaert *et al*., 2014). The genetic engineering technique has been applied to increase folate concentration more than 100 times via over expression of Arabidopsis thaliana pterin in rice (Storozhenko *et al*., 2007). It is reported that the CRISR / Cas 9 and TALENs technologies are exploited to develop mutant lines for the genes that are associated in small RNA processing in case of *Glycine max* and *Medicago truncatuta* also (Curtin *et al*., 2018).

Breeding Approach

It is easy and low-cost effective technique for bio-fortification programme. There is genotypic variation among the staple food crops regarding micronutrient concentration (Graham *et al*., 2007) and so that to utilize this existing genotypic variation among the food crops is the main target in breeding technique (Zapata-Caldas *et al*., 2009). The Consultative group on International Agricultural Research (CGIAR) centre started the “Harvest Plus” programme in which the main target is to increase the concentration and bioavailability of zinc and iron in widely used staple food crops through breeding (Bouis, 2002; Pfeiffer and McClafferty, 2007). As the variation in iron and zinc conc. has been noticed among the food crops in such case selective breeding is recommended to increase the level of micronutrient (Tiwari *et al*., 2009). The Harvest Plus Programme was developed in 2003 to take initiative of micronutrient deficiencies in major food crops of common beans, maize, sweet potatoes, pearl millet, cassava, rice in Asian and African countries (Bouis and Welch, 2010). The rural people actually prefer the conventional plant breeding approaches as the commercially marketed fortified foods are not easily available to the large populations of remote areas (Bouis, 2003). The iron and zinc level may vary in rice grain (Khush *et al*., 2012) and the considerable variation in iron conc. have been noticed among rice, wheat and maize also (White and Broadly, 2005). Several research initiatives have been taken to increase the contents of micronutrient, vitamin A, tryptophan and lysine among the food crops throughout the world (Pfeiffer and McClafferty, 2007) among which appropriate breeding technique might be the best bio-fortification tool.

Current Status of Bio-fortified Crops

As the nutrient deficiency is a big problematic issue in developing countries where near about 150 bio-fortified varieties of 10 crops had been developed that are consumed by more than 20 million people (Bouis and Saltzman, 2017). It has been reported that the intake of Fe bio-fortified beans can increase the hemoglobin level and body iron in iron-depleted women in Rwanda (Haas *et al*., 2017). Bio-fortified maize can increase the concentration of vitamin A that had been shown among 5-7 years old child after the intake of bio-fortified maize in Zambia (Gannon *et al*., 2004). Several varieties of bio-fortified lentils enriched with iron and Zinc have been released by the International Centre for Agricultural Research in Dry Areas (ICARDA) of various zones and Harvest Plus also released 10 Fe- bio-fortified bean varieties. Harvest Plus works with public and private organization for the production and delivery of bio-fortified crops (Bouis and Saltzman, 2017).

Key factors for the success of Bio-fortification

Till date the bio-fortification programme is in the phase of research. Proper knowledge is required regarding the bioavailability of micronutrients within the food crops and their distribution in plant body (Smith *et al*., 2016). The genetic diversity in the germplasms, the low level of antinutrients and the high level of promoter substances such as amino acids and ascorbic acid that can induce the absorption of essential minerals (Bouis, 2003) which are the major criteria for the success of bio-fortification. In the conventional breeding programs there are some limitations like low genetic variations, long time for generating desired cultivars and the dependency on phytoavilability of mineral nutrients of the soil which can overcome by the use of soil with high variation in micronutrient concentration and the use of available wild germplasms (White and Broadly 2009; Garg *et al*., 2018; Carvalho and Vasconcelos, 2013). Genetic diversity is very useful to enhance the micronutrient status by the use of conventional and modern breeding practices. Actually, the magnitude of success of bio-fortified crops depends on the acceptance of bio-fortified varieties by the undernourished people.

Future Challenges

The current bio-fortification methodology is a major challenging issue to reduce the deficiency of micronutrient malnutrition. The basic understanding regarding the micronutrient acquisition and their transport through the soil-plant system and the safety issues of bio-fortified crops should be analyzed in detailed. The knowledge of bioavailability of micronutrient among the food crops and the mineral distribution pattern in plant body needs to be explored. The bioavailability of micronutrients at high concentration is required for success in bio-fortification which is possible through the increasing concentration of promoter substances that enhance the absorption of minerals and lowering the concentration of antinutrients (White and Broadly, 2009). The absorption of Se, Ca, P, Fe, Zn, methionine and tryptophan can be enhanced by the promoter substances like vitamin E, vitamin D, vitamin C, provitamin A, choline as well as niacin (Brinch-Pedersen *et al*., 2007). The antinutrient phytate present in the seed (Warkentin *et al*., 2012) may be bind with iron and zinc and prevent their absorption in human body (Liu *et al*., 2015). The low phytate lines can be obtained through the germplasm screening (Shewry & Word, 2012) or manipulation of biosynthesis of phytate through the mutation of a myo-inositol kinase (MIK) gene (Shi *et al*., 2005). It has been reported that the low phytate lines have been generated that may enhance the mineral absorption in pulse crop by lowering the phytate concentration (Campion *et al*., 2009; Panzeri *et al*., 2011; Shunmugam *et al*., Commielli *et al*., 2018). It was thought earlier that polyphenols which can inhibit the Fe bioavailability in human are secondary metabolites and present in cereals, legumes and also in various fruits (Manach *et al*., 2004; Scalbert *et al*., 2005). Recently it has been reported that among polyphenols four polyphenols enhance Fe uptake which can be used in future breeding programme (Hart *et al*., 2018). About 30 polyphenols have been identified by Jha *et al*., 2019 in a recombinant inbred line population derived through the crossing between CDC Amarillo and CDC Dakota pea cultivars.

The bio-fortification technique have been applied to some major crops but it should be applied in future on all the crops which are indirectly or directly related with micronutrient deficiencies and for these interdisciplinary research team should conduct the experiments to eliminate the micronutrient malnutrition.

Conclusion

Bio-fortified crops provide essential micronutrients which are very essential for proper human growth. Malnutrition is a major health issue in the underdeveloped and developing countries. Essential intervention is needed for delivering bio-fortified crops to target people. Proper awareness among the people regarding the health benefits of bio-fortified crops is required to overcome the micronutrient malnutrition. The bio-fortification strategy brings great promise towards nutritional security.

References

Ahmed, T.; Hossain, M. and Sanin, K.I. (2012). Global burden of maternal and child undernutrition and micronutrient deficiencies. *Ann. Nutr. Metab*., 61: 8–17. [CrossRef]

Alanis-guzman, Maria Guadalupe, Carlos Amaya-guerra, Sergio O Serna Sald (2006). Soyabean fortification and enrichment of regular and quality protein maize tortillasaffects brain development and maze performance of rats. 161–68.

Alfthan, G.; Eurola, M. and Ekholm, P. (2015). Effects of nationwide addition of selenium to fertilizers on foods, and animal and human health in Finland: From deficiency to optimal selenium status of the population. *J. Trace Elem. Med. Biol*., 31: 42–147. [CrossRef]

Allen, L.D.; de Benoist, B.; Dary, O. and Hurrell, R.E. (2006). Guidelines on food fortification with micronutrients. Geneva: World Health Organization/ Food and Agriculture Organization; 2006.

Aragao, F.J.L.; Barros, L.M.G.; De Sousa, M.V.; Grossi de Sa, M.F.; Almeida, E.R.P.; Gander, E.S. and Rech, E.L. (1999). Expression of a methionine-rich storage albumin from the Brazil nut (*Bertholletia excelsa* H.B.K., Lecythidaceae) in transgenic bean plants (*Phaseolus vulgaris* L., Fabaceae). *Genet. Mol. Biol*., 22: 445–449. [CrossRef]

Bailey, R.L.; West, K.P., Jr. and Black, R.E. (2015). The epidemiology of global micronutrient deficiencies. *Ann. Nutr. Metab*. 66: 2233. [CrossRef] [PubMed]

Blancquaert, D.; De Steur, H.; Gellynck, X. and Van Der Straeten, D. (2014). Present and future of folatebiofortification of crop plants. *J. Exp. Bot*. 65: 895–906. [CrossRef] [PubMed]

Blancquaert, D.; Storozhenko, S.; Van Daele, J.; Stove, C.; Visser, R.; Lambert, W. and Van Der Straeten, D. (2013). Enhancing pterin and paraaminobenzoate content is not sufficient to successfully biofortify potato tubers and Arabidopsis thaliana plants with folate. *J. Exp. Bot*., 64: 3899–3909. [CrossRef]

Bouis, H.E. (2002). Plant breeding: A new tool for fighting micronutrient malnutrition. *J. Nutr.* 132: 491S–494S.[CrossRef]

Bouis, H.E. (2003). Micronutrient fortification of plants through plant breeding: Can it improve nutrition in man at low cost? *Proc. Nutr. Soc*., 62: 403–411. [CrossRef] [PubMed]

Bouis, H.E. and Saltzman, A. (2017). Improving nutrition through biofortification: A review of evidence from Harvest Plus, 2003 through 2016. *Glob. Food Sec*. 12: 49–58. [CrossRef]

Bouis, H.E. and Welch, R.M. (2010). Biofortification-A sustainable agricultural strategy for reducing micronutrient malnutrition in the global south. *Crop Sci*., 50: S20–S32. [CrossRef]

Brinch-Pedersen, H.; Borg, S.; Tauris, B. and Holm, P.B. (2007). Molecular genetic approaches to increasing mineral availability and vitamin content of cereals. *J. Cereal Sci.*, 46: 308–326. [CrossRef]

Bruno, D.B.; Erin, M. and Maria, A. *et al*. (2008). Iodine deficiency in 2007: global progress since 2003. *Food Nutr Bull.,* 29: 195-202

Cakmak, I. (2008). Enrichment of cereal grains with zinc: agronomic or genetic biofortification? *Plant Soil,* 302: 1–17.

Cakmak, I.; Kalayci, M.; Kaya, Y.; Torun, A.A.; Aydin, N.; Wang, Y.; Arisoy, Z.; Erdem, H.; Yazici, A.; Gokmen, O.; Ozturk, L. and Horst, W.J. (2010a). Biofortification and localization of zinc in wheat grain. *J Agric Food Chem.,* 58: 9092–9102.

Cakmak, I.; Pfeiffer, W.H. and McClafferty, B. (2010b). Biofortification of durum wheat with zinc and iron. *Cereal Chem.,* 87: 10–20.

Campion, B.; Sparvoli, F.; Doria, E.; Tagliabue, G.; Galasso, I.; Fileppi, M.; Bollini, R. and Nielsen, E. (2009). Isolation and characterisation of an lpa (low phytic acid) mutant in common bean (*Phaseolus vulgaris* L.). Theor. Appl. Genet., 118: 1211–1221. [CrossRef]

Carvalho, S.M.P. and Vasconcelos, M.W. (2013). Producing more with less: Strategies and novel technologies for plant-based food biofortification. *Food Res. Int*., 54: 961–971. [CrossRef]

Cavagnaro, T.R. (2008). The role of *Arbuscularmy corrhizas* in improving plant zinc nutrition under low soil zinc concentrations: A review. *Plant Soil*, 304: 315–325. [CrossRef]

Cominelli, E.; Confalonieri, M.; Carlessi, M.; Cortinovis, G.; Daminati, M.G.; Porch, T.G.; Losa, A. and Sparvoli, F. (2018). Phytic acid transport in *Phaseolus vulgaris*: A new low phytic acid mutant in the PvMRP1 gene and study of the PvMRP spromoters in two different plant systems. *Plant Sci*., 270: 1–12. [CrossRef]

Costello, L.C. and Franklin, R.B. (2017). Decreased zinc in the development and progression of malignancy: An important common relationship and potential for prevention and treatment of carcinomas. *Expert Opin. Ther. Targets*, 21: 51–66. [CrossRef]

Curtin, S.J.; Xiong, Y.; Michno, J.M.; Campbell, B.W.; Stec, A.O.; Cˇ ermák, T.; Starker, C.; Voytas, D.F.; Eamens, A.L.; Stupar, R.M. (2018). CRISPR/Cas9 and TALENs generate heritable mutations for genes involved in small RNA processing of Glycine max and *Medicago truncatula*. *Plant Biotechnol. J*. 16: 1125–1137. [CrossRef]

Dai, J.L.; Zhu, Y.G.; Zhang, M. and Huang, M.Z. (2004). Selecting iodine-enriched vegetables and the residual effect of iodate application to soil. *Biol. Trace Elem. Res*., 101: 265–276. [CrossRef]

De Valença, A.W.; Bake, A.; Brouwer, I.D.; Giller, K.E. (2017). Agronomic biofortification of crops to fight hidden hunger in Sub-Saharan Africa. *Global Food Security.,* 12: 8–14.

Erdal, I.; Yilmaz, A.; Taban, S.; Eker, S.; Torun, B. and Cakmak, I. (2002). Phytic acid and phosphorus concentrations in seeds of wheat cultivars grown with and without zinc fertilization. *J Plant Nutr.,* 25: 113–127.

Fageria, N.K. and Baligar, V.C. (2008). Ameliorating soil acidity of tropical Oxisols by liming for sustainable crop production. *Adv Agron*., 99: 345–399.

FAO (2019). The Plant Production and Protection Division (AGP). Soil Biological Management with Beneficial Microorganisms; FAO: Rome, Italy, 2019.

FAO, IFAD, UNICEF, WHO. The state of food security and nutrition in the World: Building Resilience for Peace and Food Insecurity. FAO, Rome; 2017.

Gannon, B.; Kaliwile, C.; Arscott, S.A.; Schmaelzle, S.; Chileshe, J.; Kalungwana, N.; Mosonda, M.; Pixley, K.; Masi, C. and Tanumihardjo, S.A. (2014). Biofortified orange maize is as edacious as a vitamin A supplement in Zambian children even in the presence of high liver reserves of vitamin A: A community-based, randomized placebo-controlled trial. *Am. J. Clin. Nutr*. 100: 1541–1550. [CrossRef] [PubMed]

Garg, M.; Sharma, N.; Sharma, S.; Kapoor, P.; Kumar, A.; Chunduri, V. and Arora, P. (2018). Biofortified crops generated by breeding, agronomy, and transgenic approaches are improving lives of millions of people around the world. *Front. Nutr*., 5: 12. [CrossRef] [PubMed]

Goto, F.; Yoshihara, T. and Saiki, H. (2000). Iron accumulation and enhanced growth in transgenic lettuce plants expressing the iron-binding protein ferritin. *Theor. Appl. Genet*. 100: 658–664. [CrossRef]

Graham, R.D.; Welch, R.M.; Saunders, D.A.; Ortiz-Monasterio, I.; Bouis, H.E.; Bonierbale, M.; de Haan, S.; Burgos, G.; Thiele, G.; Liria, R.; Meisner, C.A.; Beebe, S.E.; Potts, M.J.; Kadian, M.; Hobbs, P.R.; Gupta, R.K. and Twomlow, S. (2007). Nutritious subsistence food systems. *Adv. Agron*., 92: 1–74.

Haas, J.; Luna, S.V.; Lung'aho, M.G.; Ngabo, F.;Wenger, M.; Murray-Kolb, L.; Beebe, S.; Gahutu, J. and Egli, I. (2017). Consuming iron biofortified beans significantly improved iron status in Rwandan women after 18 weeks. *J. Nutr.,* 146: 1586–1592. [CrossRef]

Hart, J.J.; Tako, E.; Kochian, L.V.; Glahn, R.P. (2015). Identification of black bean (*Phaseolus vulgaris* L.) polyphenols that inhibit and promote iron uptake by Caco-2 cells. *J. Agric. Food Chem*., 63: 5950–5956. [CrossRef]

Hartikainen, H. (2005). Biogeochemistry of selenium and its impact on food chain quality and human health. *J. Trace Elem. Med. Biol.*, 18: 309–318. [CrossRef]

Hefni, M.; Öhrvik, V.; Tabekha, M.M. and Witthöft, C. (2010). Folate content in foods commonly consumed in Egypt. *Food Chem.* 121: 540–545. [CrossRef]

Hetzel, B.S.; Delange, F.; Dunn, J.T.; Ling, J.; Venkatesh, M. and Pandav, C.S. (2004). Towards the global elimination of brain damage due to iodine deficiency-a global program for human development with a model applicable to a variety of health, social and environmental problems. Oxford University Press, New Delhi, pp 10-12.

Hu, Y.X.; Qu, C.G. and Yu, J.N. (2003). Zn and Fe fertilizers' effects on wheat's output. *Chin Germplasm*, 2: 25–28.

Huang, Y.; Yuan, L. and Yin, X. (2012). Biofortification to struggle against iron deficiency. In: Yuan L, Yin X (eds) Phytoremediation and biofortification-two sides of one coin. Springer, Netherlands, pp 59–74

Inal, A.; Gunes, A.; Zhang, F.S. *et al* (2007). Peanut/maize intercropping induced changes in rhizosphere and nutrient concentrations in shoots. *Plant Physiol Biochem*., 45: 350–356.

Jha, A.B.; Purves, R.W.; E-Elessawy, F.M.; Zhang, H.; Vandenberg, A. and Warkentin, T.D. (2019). Polyphenollic propfile of seed components of white and purple flower pea lines. *Crop Sci.*, 59: 2711-2719.

Kamal, K.; Hagagg, L. and Awad, F. (2000). Improved Fe and Zn acquisition by guava seedlings grown in calcareous soils intercropped with graminaceous species. *J Plant Nutr*., 23: 2071–2080.

Khush, G.S.; Lee, S.; Cho, J.I. and Jeon, J.S. (2012). Biofortification of crops for reducing malnutrition. *Plant Biotechnol Rep.,* 6: 195–202.

Li, Z.G.; Ye, Z.Q.; Fang, Y.Y. and Yang, X.E. (2003). Effects of Zn supply levels on growth and Zn accumulation and distribution. *China Rice Sci.,* 17: 61–66.

Liu, X.; Glahn, R.P.; Arganosa, G.C. and Warkentin, T.D. (2015). Iron bioavailability in low phytate pea. Crop Sci., 55: 320–330. [CrossRef]

Mahaffee, W.F. and Kloepper, J.W. (1994). Applications of plant growth-promoting rhizobacteria in sustainable agriculture. In Soil Biota: Management in Sustainable Farming Systems; Pankhurst, C.E., Doube, B.M., Gupta, V.V.S.R., Grace, P.R., Eds.; CSIRO: Melbourne, Australia, 23–31.

Manach, C.; Scalbert, A.; Morand, C.; Rémésy, C. and Jimenez, L. (2004). Polyphenols: Food sources and bioavailability. *Am. J. Clin. Nutr*., 79: 727–747. [CrossRef]

Mayer, J.E.; Pfeier, W.H. and Bouis, P. (2008). Biofortified crops to alleviate micronutrient malnutrition. *Curr. Opin.Plant Biol.* 11: 166–170. [CrossRef] [PubMed]

Meenakshi, J.V.; Johnson, N.L.; Manyong, V.M. *et al.* (2010). How cost-effective is biofortification in combating micronutrient malnutrition? An ex ante assessment. *World Dev*, 38(1):64–75. doi:http:// dx.doi.org/ 10. 1016/j.worlddev.2009.03.014

Muller, O. and Krawinkle, M. (2005). Malnutrition and health in developing countries. *Can Med Assoc J*.,173: 279–286.

Nestel, P.; Bouis, H.E.; Meenakshi, J.V. and Pfeiffer, W. (2006). Biofortification of staple food crops. *J. Nutr.* 136: 1064–1067. [CrossRef]

Paine, J.A.; Shipton, C.A.; Chaggar, S.; Howells, R.M.; Kennedy, M.J.; Vernon, G.; Wright, S.Y.; Hinchlie, E.; Adams, J.L.; Silverstone, A.L. *et al*. (2005). Improving the nutritional value of Golden Rice through increased pro-vitamin A content. *Nat. Biotechnol.* 23: 482–487. [CrossRef] [PubMed]

Panhwar, Q.A.; Othman, R.; Rahman, Z.A.; Meon, S.; Ismail, M.R. (2012). Isolation and characterization of phosphate-solubilizing bacteria from aerobic rice. *Afr. J. Biotechnol*., 11: 2711–2719.

Panzeri, D.; Cassani, E.; Doria, E.; Tagliabue, G.; Forti, L.; Campion, B.; Bollini, R.; Brearley, C.A.; Pilu, R. and Nielsen, E. (2011). A defective ABC transporter of the MRP family, responsible for the bean lpa1 mutation, affects the regulation of the phytic acid pathway, reduces seed myo-inositol and alters ABA sensitivity. New Phytol. 191: 70–83. [CrossRef] [PubMed]

Perez-Massot, E.; Banakar, R.; Gomez-Galera, S.; Zorrilla-Lopez, U.; Sanahuja, G.; Arjo, G.; Miralpeix, B.;Vamvaka, E.; Farré, G.; Rivera, S.M. (2013). The contribution of transgenic plants to better health through improved nutrition: Opportunities and constraints. *Genes Nutr.* 8: 29–41. [CrossRef] [PubMed]

Pfeiffer, W.H. and McClafferty, B. (2007). Harvest Plus: breeding crops for better nutrition. *Crop Sci*., 47(Suppl 3): S88

Prasad, A.S.; Bao, B.; Beck, F.W.; Kucuk, O. and Sarkar, F.H. (2004). Antioxidant effect of zinc in humans. *Free Radic. Biol. Med.* 37: 1182–1190. [CrossRef]

Raboy, V. (2002). Progress in breeding low phytate crops. *J. Nutr.,* 132: 503S–505S.

Rahman, M.M.; Erskine, W.; Materne, M.A.; McMurray, L.M.; Thavarajah, P.; Thavarajah, D. and Siddique, K.H.M. (2015). Enhancing selenium concentration in lentil (*Lens culinaris* sub sp. culinaris) through foliar application. *J. Agric. Sci*., 153: 656–665.

Rayman, M.P. (2012). Selenium and human health. *Lancet,* 379: 1256–1268.

Rengel, Z.; Batten, G.D. and Crowley, D.D. (1999). Agronomic approaches for improving the micronutrient density in edible portions of field crops. *Field Crop. Res*., 60: 27–40. [CrossRef]

Roohani, N.; Hurrell, R.; Kelishadi, R.; Schulin, R. Zinc and its importance for human health: An integrative review. *J. Res. Med. Sci*., 18: 144–157.

Rostan, E.F.; DeBuys, H.V.; Madey, D.L. and Pinnell, S.R. (2002). Evidence supporting zinc as an important antioxidant for skin. *Int. J. Dermatol*., 41: 606–611. [CrossRef]

Scalbert, A.; Manach, C.; Morand, C. and Remesy, C. (2005). Dietary polyphenols and the prevention of diseases. *Crit. Rev. Food Sci. Nutr*., 45: 287–306. [CrossRef]

Shewry, P.R. and Ward, J.L. (2012). Exploiting genetic variation to improve wheat composition for the prevention of chronic diseases. *Food Energy Secur.* 1: 47–60. [CrossRef]

Shi, J.; Wang, H.; Hazebroek, J.; Ertl, D.S. and Harp, T. (2005). The maize low-phytic acid 3 encodes a myo-inositol kinase that plays a role in phytic acid biosynthesis in developing seeds. *Plant J*., 42: 708–719. [CrossRef] [PubMed]

Shivay, Y.S.; Prasad, R. and Pal, M. (2015). Effects of source and method of zinc application on yield, zinc biofortification of grain, and Zn uptake and use efficiency in chickpea (*Cicer arietinum* L.). Commun. *Soil Sci. Plant Anal*., 46: 2191–2200. [CrossRef]

Shunmugam, A.S.K.; Bock, C.; Arganosa, G.C.; Georges, F.; Gray, G.R. and Warkentin, T.D. (2015). Accumulation of phosphorus-containing compounds in developing seeds of low-phytate pea (*Pisum sativum* L.) mutants. *Plants Sci*., 4: 1–26. [CrossRef]

Smith, S.E. and Read, D.J. (2007). Mycorrhizal Symbiosis, 3rd ed.; Elsevier: London, UK.

Smrkolj, P.; Germ, M.; Kreft, I.; Stibilj, V. (2006). Respiratory potential and Se compounds in pea (*Pisum sativum* L.) plants grown from Se-enriched seeds. *J. Exp. Bot*. 57: 3595–3600. [CrossRef]

Sperotto, R.A.; Ricachenevsky, F.K.; Waldow, V.D.A. and Fett, J.P. (2012). Iron biofortification in rice: it's a long way to the top. *Plant Sci*., 190: 24–39.

Šramková, Zuzana, EditaGregová, Ernest Šturdík (2009). Chemical composition and nutritional quality of wheat grain. *Acta Chimica Slovaca*. 2(1): 115–138.

Sreevidya, M.; Gopalakrishnan, S.; Kudapa, H.; Varshney, R.K. (2016). Exploring PGP actinomycetes from vermicompost and rhizosphere soil for yield enhancement in chickpea. *Braz. J. Microbiol.*, 47: 85–95. [CrossRef]

Stein, A.J. (2010). Global impact of human mineral malnutrition. *Plant Soil,* 335: 133–154.

Stoltzfus, R.J. (2011). Iron interventions for women and children in low-income countries. *J. Nutr*., 141: 756S–762S. [CrossRef] [PubMed]

Storozhenko, S.; De Brouwer, V.; Volckaert, M.; Navarrete, O.; Blancquaert, D.; Zhang, G.F.; Lambert, W. and Van Der Straeten, D. (2007). Folate fortification of rice by metabolic engineering. Nat. Biotechnol. 25: 1277–1279. [CrossRef] [PubMed]

Thavarajah, D. and Thavarajah, P. (2012). Evaluation of chickpea (*Cicer arietinum* L.) micronutrient composition: biofortification opportunities to combat global micronutrient malnutrition. *Food Res Int.,* 49: 99–104.

Tiwari, V.K.; Rawat, N. and Chhuneja, P. *et al* (2009). Mapping of quantitative trait loci for grain iron and zinc concentration in diploid A genome wheat. *J Hered*, 100: 771–776.

Tucker, G. (2003). Nutritional enhancement of plants. *Curr Opin Biotechnol*., 14: 221–225.

Vasconcelos, M.; Datta, K.; Oliva, N.; Khalekuzzaman, M.; Torrizo, L.; Krishnan, S.; Oliveira, M.; Goto, F. and Datta, S.K. (2003). Enhanced iron and zinc accumulation in transgenic rice with the ferritin gene. *Plant Sci*. 164: 371–378. [CrossRef]

Warkentin, T.D.; Delgerjav, O.; Arganosa, G.; Rehman, A.U.; Bett, K.E.; Anbessa, Y.; Rossnagel, B. and Raboy, V. (2012). Development and characterization of low-phytate pea. Crop Sci., 52: 74–78. [CrossRef]

Waters, B.M.; Uauy, C. and Dubcovsky, J. *et al.* (2009). Wheat (*Triticum aestivum*) proteins regulate the translocation of iron, zinc, and nitrogen compounds from vegetative tissues to grain. *J Exp Bot.,* 60: 4263–4274.

Welch, R.; Robin M. and Graham, D. (2004). Breeding for micronutrients in staple food crops from a human nutrition perspective, 55(396): 353–364.

Whanger, P.D. (2004). Selenium and its relationships to cancer: an update. *British J Nutr*., 91: 11–18.

White, P.J. and Broadley, M.R. (2005). Biofortifying crops with essential mineral elements. *Trends Plant Sci.,* 10: 586–593.

White, P.J. and Broadley, M.R. (2009). Biofortification of crops with seven mineral elements often lacking in human diets-Iron, zinc, copper, calcium, magnesium, selenium and iodine. *New Phytologist*. 182: 49–84.

Wiltgren, A.R.; Booth, A.O.; Kaur, G.; Cicerale, S.; Lacy, K.E.; Thorpe, M.G.; Keast, R.S. and Riddell, L.J. (2015). Micronutrient supplement use and diet quality in university students. *Nutrients,* 7: 1094–1107. [CrossRef]

Wintergerst, E.S.; Maggini, S. and Hornig, D.H. (2007). Contribution of selected vitamins and trace elements to immune function. *Ann. Nutr. Metab*., 51: 301-323.

World Health Organization (2001). Iron Deficiency Anaemia: Assessment, Prevention and Control, a Guide for Programme Managers; WHO: Geneva, Switzerland.

World Health Organization and Food and Agriculture Organization of the United Nations. Guidelines on Food Fortification with Micronutrients; Allen, L., de Benoist, B., Dary, O., Hurrell, R., Eds.; WHO: Geneva, Switzerland, 2006.

World Health Organization; United Nations Children's Fund; International Council for the Control of Iodine Deficiency Disorders. Assessment of iodine deficiency disorders and monitoring their elimination. In A Guide for Programme Managers, 3rd ed.; World Health Organization: Geneva, Switzerland, 2007.

Yang, X.E.; Chen, W.R. and Feng, Y. (2007). Improving human micronutrient nutrition through biofortification in the soil–plant system: China as a case study. *Environ Geochem Health,* 29: 413–428.

Yang, X.E.; Chen, W.R. and Feng, Y. (2007). Improving human micronutrient nutrition through biofortification in the soil–plant system: China as a case study. Environ Geochem Health, 29: 413–428.

Zapata-Caldas, E.; Hyman, G.; Pachon, H.; Monserrate, F.A. and Varela, L.V. (2009). identifying candidate sites for crop biofortification in Latin America: case studies in Colombia, Nicaragua and Bolivia. *Int J Health Geogr,* 8: 29.

Zeng, H. and Combs, G.F. (2008). Selenium as an anticancer nutrient: roles in cell proliferation and tumor cell invasion. *J Nutr Biochem*., 19: 1–7.

Zuo, Y.M.; Liu, Y.X.; Zhang, F.S. and Christie, P. (2004). A study on the improvement in iron nutrition of peanut by intercropping maize on nitrogen fixation at early stages of growth peanut on calcareous soil. *Soil Sci Plant Nutr*., 50(7): 1071–10.