Introduction

The world population that has micronutrient deficiencies can be estimated to be over 3 billion. This is common among women, infant, and children mostly in the third world countries (Mason and Garcia, 1993).

Micronutrient deficiency is known as “hidden hunger” and affect one in three people worldwide (FAO, 2013). Micronutrient deficiencies may lead to serious illnesses. For example, it could lead to poor growth, intellectual impairments, prenatal complications, and risk of morbidity and mortality (Bailey et al., 2015). Also, they aggravate infectious diseases including osteoporosis osteomalacia, thyroid deficiency, colorectal cancer, and cardiovascular diseases and thus greatly impact quality of life (Tulchinsky, 2010).

Deficiencies of Iron (Fe), Zinc (Zn), Folic acid, and β-carotene are global issues, but they are predominant in Asian, African, and Latin American countries (Tulchinsky 2010; Darnton-Hill et al., 2006).
Micronutrient deficiency affect women globally, potentially leading to intrauterine growth restriction, low birth weight, protein malnutrition, and chronic energy deficit (Ahmed et al., 2012). Deficiencies of Fe, I, Zn, and vitamin A, are common in Asia, Africa and Latin America which are responsible for about 12% of deaths globally among children under 5 years of age (Ahmed et al., 2012).

Enriched or fortified food crops could address micronutrient deficiencies and thus provide a sustainable solution to global malnutrition issues and health conditions caused by malnutrition (Welch, 2002). Peas (Pisum sativum L.), chickpeas (Cicer arietinum L.), lentils (Lens culinaris Medik.), common beans (Phaseolus vulgaris L.), mung beans (Vigna radiate L.) and Rice (Oryzae sativa) are examples of pulse crops grown globally (Duranti, 2006).

They are great sources of dietary proteins, complex carbohydrates, vitamins, and minerals required for human nutrition (Patterson et al., 2009; Roy et al., 2010; Ray et al., 2014; Diapari et al., 2014; Diapari et al., 2015; Jha et al., 2015). Pulse crops are common in everyday diets of people in many parts of the world since they are rich in proteins and amino acid carbohydrates (Duranti, 2006; Patterson et al., 2009; Messina, 1999).

Biofortification is a process of breeding nutrient into to crops to improve their nutritional contents. This procedure is cost-effective and sustainable in delivering micronutrients into crops. With the rise in malnourished people around the world especially in the third world countries, there is need to foster biofortification technology to meet the daily demands of nutrients. Many industrial fortified foods and food supplements that are readily available in developed countries are out reach for people in third world countries especially amongst low income people. Biofortified foods cannot deliver as high level of minerals and vitamins per day as food supplements or industrially fortified foods, but they can help to ensure bioavailability of micronutrients which is essential for healthy living (Bouis et al., 2011).

**Micronutrients**

These are essential nutrient that should be present in the every diet. These nutrients, although required in small amount are needed in the body to build immunity, Energy production, clotting and other functions. Some examples include: Zinc, Iron, Iodine, Selenium, Carotenoid and Vitamin A etc to mention a few.

**Function of micronutrients**

**Iron (Fe)**

Iron (Fe) is an indispensable nutrients and vital for various metabolic processes such as electron transport and deoxyribonucleic acid synthesis (Abbaspour et al., 2014). In humans, Fe is an essential part of hemoglobin; oxygen transport and enzymes involved in electron transfer and oxidation-reductions (Hurrell, 1997; McDowell, 2003). Iron serves as a carrier in the hemoglobin of oxygen (Oxyenated Hemoglobin) to deficient cells and tissues. Iron deficiency is predominant amongst micronutrient deficiencies and it is the major contributor of anemia that affect more than two billion people globally (WHO, 2001; 2008). It can cause weakness due to loss of energy, drowsiness, and poor pregnancy; premature births, low birth weight of babies, slow growth and development in infants, and poor cognitive skills (Bailey et al., 2015; Allen 2000; Lozof et al., 2008).
Zinc (Zn)

Zinc (Zn) is also an important mineral required by humans. It is involved in many biological functions, such as wound healing through its involvement in membrane signaling systems in cell growth and proliferation (Prasad, 1996; MacDonald, 2000), protecting cells from damage by quenching reactive oxygen species (Rostan, 2002; Prasad et al., 2004), and reducing risk of various cancerous diseases such as prostate and pancreatic cancer (Costello et al., 2017). Deficiency of Zn can lead to weak immune system, continuous infections, mental illness, retarded growth rate and fertility (Roohani et al., 2013).

Selenium (Se)

Selenium is an essential micronutrient which is required for growth and development. It protects the human body against infection, stress, and progressive cancer (Jansson, 1980; Rayman, 2005; Tinggi, 2008; Zeng, 2008). In humans, Se deficiency is associated with diseases, such as Keshan, Keshin-Beck, and myxedematous cretinism (Coppinger, 2001).

Iodine (I)

Iodine is the major constituent of the thyroid hormone. In humans, it is produced by the thyroid gland which is found around the neck region. The thyroid hormone secretes thyroxin and triiodothyronine both which are essential for growth and metabolism in humans. Deficiency of iodine causes hypothyroidism, goiter, cretinism, mental retardation, and retarded fertility and is accountable for prenatal death and infant mortality (Delange, 1994; WHO, 2007). Deficiency of iodine during pregnancy can impair brain development in offspring (Skeaf, 2011; Pearce et al., 2016). Deficiency of iodine is a global issues affecting both developed and under developed countries (Pearce et al., 2013; Cakmak et al., 2017; Gonzali et al., 2017). This could be as a result of low concentration of iron in the soils and cereal-based foods (Cakmak et al., 2017).

Carotenoids

Carotenoids are pigments produced by plants. They give the plant color. Crop foods are sources of carotenoids because humans and animals cannot synthesize carotenoids (Fraser and Bramley, 2004). There are different types of carotenoids that are of benefit to humans. Example include, Lutein and zeaxanthin which prevent age-related degeneration (Fraser and Bramley, 2004; Olmedilla et al., 2001). Lutein reduces the risk of cataracts and prevents cardiovascular disease (Moeller et al., 2000; Alves-Rodrigues, 2004). Vitamin A is important for sharp vision, bone developments, and cell division in mammals (Stephens et al., 1996). β-Cryptoxanthin initiates osteoblastic bone formation and inhibits osteoclastic bone resorption (Yamaguchi and Uchiyama, 2004), which makes an essential nutrient for bone formation. Carotenoids also have strong cancer-fighting properties (Tanaka et al., 2012) and protect cellular organelles from oxidative damage by scavenging free radicals generated during various metabolic processes (Iannone et al., 1998; Sujak et al., 1999). Carotenoids are considered as Fe absorption promoters and hence improve bioavailability of Fe from plant-based foods (Welch, 2002).

Folates

Folates are B9 vitamins and are cofactors in various metabolic functions such which includes nucleotide biosynthesis and amino acid metabolism in the human body (Bailey and Gregory, 1999; Scott et al., 2000), and
are therefore required for human growth and development. In plants, folates are essential for biosynthesis of molecules including lignin, alkaloids, and chlorophyll (Hanson and Roje, 2001). Humans depend on plant and/or animal-based food as their sources folates (Scott et al., 2000; Basset et al., 2005). Deficiency of folates is connected to various chronic diseases, such as neural tube defects (Geisel, 2003), impaired cognitive function (Ramos et al., 2005), Alzheimer’s disease (Seshadri et al., 2002), cardiovascular diseases (McCully, 2007), and certain types of cancers (Choi and Friso, 2005). Diets rich in folates are highly recommended during pregnancy as it reduces the risk of neural tube defects in newborns (Pitkin, 2007). Inadequate folate intake during pregnancy increases the risk of pre-term delivery and delay in fetal growth (Scholl and Johnsin, 2000).

**Different approach to improve availability of micronutrients in diets**

**Food supplements**

There are consumed inform of pills or solutions that contains different micronutrients. They are used when there are dietary deficiencies in the daily food consumed. Food supplements can be used as a short-term method to improve nutritional health and may be unsustainable for large populations. For example, folate levels in diets were achieved by the use of folic acid supplements (Blancquaert et al., 2013; Shohag et al., 2012; Hefni et al., 2010). Also, this method was successful with vitamin A and zinc supplementation (Black et al., 2008). Folic acid, iron, and zinc supplements have been helpful for children and pregnant women. However, this method is not cost-effective, especially for low-income consumers (Bailey et al., 2015; Wiltgren et al., 2015).

**Food fortification**

This is a process of adding essential nutrients, minerals and Vitamins into food to improve nutritional qualities and availability to low income consumers. This is done to selectively achieve nutrient availability with little or no health risk.

Food fortification with iron, ferrous sulfate, ferrous fumarate, ferric pyrophosphate, is usually accomplished through electrolytic iron powder compounds (WHO, 2006). Similarly, food folates level can be improved in diet with folic acid (Blancquaert et al., 2013; Hefni et al., 2010). Salt iodization was successfully achieved to reduce the occurrence of goiter (Gómez-Galera et al., 2010).

**Types of food fortification**

**Mass fortification**

This is the process of adding essential nutrient directly to consumables i.e Adding nutrient directly to food such as milk, cereals, oils and vegetable fats, milk, sugar, and condiments.

**Targeted fortification**

This is the process of adding sufficient amounts of essential micronutrients to provide large proportions of the daily needs through foods such as complementary foods for infants, foods for institutional programs such as those aimed at pre-school and school-aged children, and foods used under emergency situations.

**Market driven fortification**

This is a process by food manufacturing industries to increase the nutrient content and added value of a highly processed product with the purpose of attracting consumers and increasing sales.
Approach for food fortification

Mandatory and voluntary fortification

Mandatory fortification

Mandatory fortification occur when governments legally oblige food producers to fortify particular foods or categories of foods with specified micronutrients. Mandatory fortification, especially when supported by a properly resourced enforcement and information dissemination system, delivers a high level of certainty that the selected food(s) will be appropriately fortified and in constant supply.

Globally, mandatory regulations are most often applied to the fortification of food with micronutrients such as iodine, iron, vitamin A, and increasingly folic acid. Of these, the iodization of salt is probably the most widely adopted form of mandatory mass fortification (Allen et al., 2006).

Voluntary food fortification

Fortification is described as voluntary when a food manufacturer freely chooses to fortify particular foods in response to permission given in food law, or under special circumstances, is encouraged by government to do so.

Some fortified nutrients

Iron fortification

Iron fortification is important because iron is one of the essential micronutrients to human. In plants, there is an iron storage protein called ferritin (Theil, 1987) which is a large protein with 24-subunits, with increased ferroxidase activities and is capable of storing up to 4500 iron atoms in a non-toxic complex form (Andrews et al., 1992; Theil, 2003).

In soybean, the two types of ferritin proteins that are present are encoded by SoyferH1 and SoyferH2 ferritin genes (Kok, 2018). In human intestine absorption of iron from the soybean ferritin iron complex is achieved easily which is the reason soybean ferritin gene was considered to be the right gene for iron biofortification in rice (Theil, 2011).

Rice with high iron value is developed from molecular breeding and could be used as donor material in subsequent interbreeding programs for high iron local rice variety development. Vasconcelos et al., (2003) successful achieved high iron IR68144 rice variety by expressing soybean ferritin gene, which increased iron concentration in polished rice (Vasconcelos et al., 2003). Such interbreeding projects have a positive impact in developing countries which are one of the most consumers of rice grains to increase high iron rice varieties and help fight against micronutrient deficiencies.

Zinc fortification

Zinc deficiency can be alleviated by increasing dietary Zn intakes through supplements or by zinc biofortification of edible crops (White and Broadley, 2009). Crops can undergo biofortification through the application of Zn-fertilizers in the soil, which are then taken up by the plant. Alternatively, crop varieties have been developed which acquire more Zn from the soil and then collect it in the edible portions.

High concentrations of zinc can be achieved in roots and leaves with soil fertilizers and even with foliar zinc-fertilizers (Wei, 2012). However, zinc concentrations in fruits, seeds, and tubers are generally significantly lower. Plants generated through biotechnology can translocate zinc through the phloem and thus increase zinc concentrations to the edible portions of plant tissues.
Iodine fortification

There have been vast studies recorded on various methods such as foliar fertilization and application of salt in soil through irrigation water for biofortification of crops with iodine. The consumption of foods with low iodine concentration; grains, cereals is the major cause of iodine deficiency in humans (Gonzali et al., 2003; Cakmak et al., 2017; Fuge and Johnson, 2015). Compared to grain, biofortification of leafy vegetables can be easily achieved through translocation of the majority of iodine to xylem tissues, which is why majority of research is focused on iodine biofortification of vegetables instead of grains (Gonzali et al., 2003; Mackowiak and Grossl, 1999; Medrano-Macias et al., 2017).

Folic acid fortification

Folic acid is a monoglutamate synthetic compound, it is added to food to derive more chemically stable form than the natural vitamins (Blakley, 1969). Folic acid has been linked to many diseases including congenital abnormalities, which is why preventing folic acid deficiency is paramount. This can be achieved following 3 steps to improve folate status among target populations: pharmacological supplementation; which requires taking of folic acid tablets, fortification of staple foods with folic acid and the advice to increase intakes of natural folate food sources. Over the years, folic acid supplements have been generally accepted and it is use up till today, however, this drug is out of reach for rural dwellers with little income that are unlettered which is why folic acid fortification is considered to be the best approach to solving its deficiency.

Diet diversification/diet varieties

This is mostly carried out by household or by individuals to make available required nutrients for the body. It involves consuming different plant based food such as vegetables, fruits and whole grains. Dietary diversification also uses strategies at the household level, such as preparation of food that involves soaking, fermentation, and germination, as these enhance micronutrient content and bioavailability (Gibson and Hotz, 2001).

Fruits and Vegetable rich in nutrient promoters like; β- carotenoids, ascorbate when consumed would improves mineral uptake. For example, for iron improvement, foods rich in ascorbic acid is encouraged (Hurrell, 2002; WHO, 2004).

Microorganisms as growth enhancers

Several microorganisms that enable the growth and developments of plant is achieved through symbiotic relationships. They help in ensuring bioavailability of essential nutrients to plant and help in nutrient uptake. Examples includes: *Rhizobia, mycorrhizal fungi, actinomycetes, and diazotrophic bacteria* (FAO, 2019). Although these microbes are naturally present in the soil, their populations can be increased by seed inoculation or through agricultural management practices. Various plant growth-promoting microbes present in the soil including *Enterobacter, Bacillus, and Pseudomonas* can be used to increase the phytoavailability of micronutrients through the production of growth hormones, antibiotics, chitinases, and siderophores (Mahafee and Kloeper, 1994). Plant growth promoting microorganisms chelate iron through the production of siderophore compounds, solubilize phosphorus, and inhibit growth of pathogens (Panwar et al., 2012; Sreevidya et al., 2016), thus playing a significant role in soil fertility and iron fortification. Plant growth promoting microbes are usually present in soil compost and decomposing organic materials and...
provide an economical and harmless method for increasing crop production and improve environmental and soil health (Gopalakrishnan et al., 2016). Numerous studies have shown increased concentrations of iron, selenium, and zinc using microorganism inoculants through mycorrhizal associations (Rengel et al., 1999; Smith and Read, 2008; Cavagnaro, 2008).

Enhancement of nitrogen fixation, plant growth, and grain yield have been reported in legumes including chickpeas, soybeans and peas by colonization of Pseudomonas sp., Brevibacterium sp., Bacillus sp., Enterobacter sp., and Acinetobacter sp. in their roots and nodules (Tokala et al., 2002; Valverde et al., 2006; Minorsky, 2008; Soe et al., 2010; Gopalakrishnan et al., 2015).

Biofortification process

Biofortification is a process of improving nutritional profile of plant-based foods through agronomic interventions, genetic engineering, and plant breeding.

Agronomic approaches

Biofortification through agronomic approaches is achieved through direct application mineral fertilizers to the soil, foliar fertilization (White and Broadley, 2009), and soil bio-inoculation of beneficial microorganisms.

Fertilizer

These are inorganic substances containing essential minerals that are applied to the soil to improve or to increase the micronutrient in the soil and thus plant quality. The availability of minerals in the soil is often low which could be due to soil leeching or erosion; hence, to improve the concentration of beneficial minerals in food crops, the application of mineral fertilizers with high solubility and mobility of the minerals is required (White and Broadley, 2009). This method has been used by farmers to fortify plants with mineral elements, but not organic nutrients, such as vitamins, which are synthesized by the plant itself.

This method has been used to introduce Selenium, Iodine, and Zinc, due to their high mobility in the soil as well as in the plant tissues (White and Broadley, 2009; 2005; Dai et al., 2004; Hartikainen, 2005). For example, application of inorganic fertilizers containing sodium selenate increased Selenium concentration in various food items, fruits, vegetables, cereals, meat, dairy products, eggs, and fish in Finland (Eurola et al., 1989; 1991).

Also, application of fertilizers with sodium selenate proved to be an effective way to increase Selenium intake in the human population (Alfthan et al., 2015). This method has been used to enrich soil with Iodine and Zinc in China and Thailand (Winkler, 2011). However, Fe fertilization was not successful due to a low mobility of Fe in soil (Grusak, 1999).

The concentration of Zinc was increased in pea grains fields by soil application of Zinc fertilizer alone or combined form with foliar treatments. This method can be adopted for the biofortification of peas grains (Poblaciones et al., 2016). The fertilization approach for biofortification typically requires frequent applications, and this could be harmful to the environment because it would increase the availability of other minerals to soil (White and Broadley, 2009; Winkler, 2011; Hirschi, 2009). Furthermore, soil composition is location bound, mineral mobility, bioavailability are also constraints in execute this strategy (Frossard et al., 2000; Ismail et al., 2007).
Genetic engineering

Biofortification through genetic engineering is another alternative when variation in the desired traits is not available naturally in the available germ plasm. A specific micronutrient does not naturally exist in crops, and modifications cannot be achieved through conventional breeding (Mayer et al., 2008; Perez-Massot et al., 2013). Along with increasing the concentration of micronutrients, Genetic engineering can also be targeted simultaneously for removal of anti-nutrients or inclusion of promoters that enhances the bioavailability of micronutrients (White 2009; Garg, et al., 2018; Carvalho, 2013). This approach utilizes genes associated with various metabolic pathways operated in plants, and also genes from bacteria and other organisms (Christou and Twyman, 2004; Newell-McGlo, 2008).

Development of transgenic crops requires huge capital at the initial stage, but these transgenic crops through genetic modification can be a sustainable approach as a potential to target large populations, especially in developing countries (White, 2005; Hirschi, 2009; Heferon, 2016). Significant breakthrough has been recorded using this biofortification technique. For instance, enhanced accumulation of iron was noted in rice through expression of the iron-storage protein, ferritin (Goto et al., 2000; Vasconcelos et al., 2003). Genetically modified rice (golden rice) was developed to produce β-carotene (pro-vitamin-A) to combat vitamin-A deficiency (Paine et al., 2005). Recently, transgenic multivitamin corn was produced by simultaneous modification of three distinct metabolic pathways to increase the levels of three vitamins, i.e., β-carotene (169-fold), ascorbate (6-fold), and folate (2-fold), in the endosperm, and this could open the door to developing nutritionally complete cereals (Naqvi et al., 2009). Metabolic engineering was used to increase the folate concentration in tomato and rice (Blancquaert et al., 2013; 2014). Recently, targeted gene editing technologies using artificial nucleases, zinc finger nucleases (ZFNs), transcription nucleases (TALENs), and the clustered regularly interspaced short palindromic repeat (CRISPR)/CRISPR-associated protein 9 (Cas9) systems open the door to the possibility of precisely modifying genes of interest, and thus can be applied for crop improvement (Bortesi and Fischer, 2015; Jaganathan et al., 2018).

Plant breeding

In an attempt to provide micronutrients to plant based food, the use of fertilizers hasn’t given the most desired result in a long term. Its effectiveness, and sustainability which isn’t cost effective has given scientist the chance to explore the used of genetic engineering to produce genetic modified plants (GMO).

Genetically modified plants have desired traits; nutrients, and even in some cases traits to withstand adverse weather conditions without affecting outputs. This can be a technological approach for crop improvement; however, political views to GMOs in many countries, legal frame work to accept the commercialization of transgenic crops, along with expensive and extensive regulatory processes are the major hindrance of this method (Winkler, 2011; Inaba and Macer, 2004; Watanabe et al., 2005). For example, golden rice has been available since the early 2000s which has the potential to deliver required vitamin A needed for low income people, but unfortunately it has not been commercially introduced in any country to date due to risk factors involved in the approval processes (Wesseler et al., 2014; Bouis and Saltzman, 2017).
Some biofortified crops

Biofortified golden rice

Golden Rice, which is named due to its golden colour and its high β-carotene content, was generated using biotechnology to provide viable solutions to the deficiency of Vitamin A. This transgenic crop was engineered with two genes from different organisms (daffodil and the bacterium Erwinia uredovoa) which reconstitute the carotenoid biosynthetic pathway within the rice genome (Tang et al., 2009). The Golden Rice technology, known as GR2, utilizes genes from two distinct pro-vitamin A pathways, including the substitution of the phytoene synthesis gene from maize for the analogous daffodil gene used in GR1 rice (Tang et al., 2012; Shumskaya and Wurtzel, 2013).

Golden rice can produce β-carotene that would be up to 35 µg/g of dry rice (Tanumihardjo et al., 2010). In an experiment to determine the nutritional benefits and bioavailability potentials of GR2, 130–200 g of deuterium-labeled Golden rice grown hydroponically in heavy water expressing 0.99–1.53 mg β-carotene and was fed to human volunteers.

Blood samples were taken at 36 days and exhibited 0.34–0.94 µg retinol, indicating that β-carotene derived from Golden rice is effectively converted to vitamin A at a rate of 500–800 µg retinol per 100 g uncooked Golden rice, which is close to the recommended daily allowance for children (Tanumihardjo et al., 2010).

The vitamin A value of Golden rice, nontransformed spinach and β-carotene provided in oil to children were also compared, and the results of this study showed that the β-carotene derived from Golden rice was just as effective as pure β-carotene and in fact more effective than β-carotene provided from spinach in providing vitamin A to children (Haskell, 2012). Together, these results suggest that Golden rice could be used to alleviate Vitamin A deficiency amongst rice-consuming populations (Xudong et al., 2000). Golden Rice could be considered the first genetically engineered crop designed to combat malnutrition.

The advantage of a biofortified crop such as Golden Rice is that it could readily reach remote rural populations which have no access to food supplements (Van Loo-Bouwman et al., 2014; Murray-Kolb et al., 2002; De Steur et al., 2012). Genetic modified rice that expresses essential amino acids such as free lysine has also been developed using RNAi silencing-based technologies. De Steur et al., (2012) demonstrated that transgenic biofortified rice could be cost-effective in reducing folate deficiencies instead of investing in conventional supplementation programs. One of the short comings of biofortified rice is the presence of Phytic Acid.

This is known inhibitor of zinc absorption and other essential micronutrients like iron. It binds with zinc and iron to form an insoluble complex in the gastrointestinal walls that prevents mineral absorption. The presence of phytic acid in cereals such as wheat, corn and rice could have serious nutritional consequences (Brnić et al., 2014; Gao et al., 2013; Ali et al., 2013).

The application of recombinant microbial phytase helps to reduce the level of phytic acid in grain (Li et al., 2010). Several methods have been developed to lower the presence of phytic acid in rice and since microbial phytase has proven effective in lowering it and hence increase mineral availability and uptake.
Transgenic corn expressing phytase has been derived using *Aspergillus niger*. These transgenic varieties were found to be as efficient at lowering phytic acid levels as conventional corn that was supplemented with commercially used phytases (Muzhingi *et al*., 2011).

Recently, cereal mutants exhibiting a low phytic acid (lpa) phenotype have also been developed in rice, wheat and maize (Howe and Tanumihardjo, 2006).

**Biofortified maize and cassava**

Maize has also been genetically modified to provide essential micronutrients needed for a healthy life. Li *et al*., (2010) measured the triglycerol-rich lipoprotein proportion in blood from North American female volunteers who consumed biofortified maize porridge. In this case, the authors found a vitamin A equivalence value of β-carotene in biofortified maize to be 3.1-fold higher than in conventional white porridge maize (Mugode *et al*., 2014). A similar study using Zimbabwean men found biofortified yellow maize porridge provides an equivalence of 40%–50% of the US recommended Dietary Allowance of vitamin A (Jeong *et al*., 2008). Another study using Mongolian gerbils who were fed biofortified maize containing β-cryptoxanthin resulted in a more efficient bioconversion than the use of a β-carotene supplement (Jeong *et al*., 2008). These results show that biofortification of maize has increased the needed micronutrients through the use of biotechnology as an effective approach to solve micronutrient deficiencies. A vitamin fortified maize which expresses high amounts of β-carotene, ascorbate, and folate has been developed in the endosperm through metabolic engineering (Mugode *et al*., 2014). The transgenic kernels contained 169-fold the normal amount of β-carotene, 6-fold the normal amount of ascorbate, and double the normal amount of folate as conventionally-bred crops. Crops such as these can offer far more nutritionally complete meals for malnutrition in Africa (Jeong *et al*., 2008).

**Biofortified cassava**

Several projects have been enacted to enrich cassava to increase it functionality and usage. Cassava with high levels of β-carotene has been produced and fed to healthy volunteers in the form of porridge (Naqvi *et al*., 2009). Blood samples taken from these volunteers demonstrated that biofortified cassava increases β-carotene and retinyl palmitate TRL plasma concentrations (Naqvi *et al*., 2009). These indicate that, biofortified cassava can effectively combat the micronutrient deficiencies in sub-Saharan Africa. Cassava roots have shown reduced levels of the toxin cyanogens in roots, iron root uptake and protein accumulation in cassava could be enhanced (Sayre *et al*., 2011).

**Biofortified wheat**

Wheat has been genetically modified to increase its level of lysine, and essential amino acid. Biofortified wheat provides a better option for the fraction of populations who are gluten intolerant, and can also provide higher levels of micronutrients, such as iron and zinc, to those in developing countries who use wheat as a staple food (Gil-Humanes *et al*., 2014; Borrill *et al*., 2014; Hotz, 2009). Recently, wheat has been under studied to improve the presence of Zinc to help countries or communities that largely consume grain crops such as wheat. Zinc is known to be the leading causes of diseases in low-income countries. However, due to insufficient Zinc in the soil, Nitrogen management has enhanced the availability of
Zinc in soil and also increased its uptake by plant roots. Radiolabelled $^{65}$Zn has been shown to be taken up by plant roots, translocated to shoots and to accumulate in the wheat grain (Grillet et al., 2014; Cakmak, 2009). Erenoglu et al., (2011) demonstrated that by increasing the nitrogen content in soil would stimulate the root-to-shoot translocation of Zinc and enhance its accumulation in wheat grain, possibly by increasing the abundance of transporter proteins in the presence of nitrogen (Cakmak et al., 2010).

**Health implications of biofortification**

There have been numerous concerns about the consumption of biofortified crops majority due to misinformation or inadequate awareness. While Biofortified crops which have been nutritionally enhanced through biotechnology could clearly play a role in eradicating malnutrition for developing countries, a number of issues must still be addressed (Schubert, 2008). Prior to marketing they require the same regulatory approval, including an assessment of their safety, as is needed for single transformation events (Christer et al., 2011). In the European Union (EU), Genetically Modified (GM) maize and oilseed rape stacked events have already been evaluated with respect to their risks factor in the environment and for human or animal health (Siró et al., 2008). At least about three countries in Africa (South Africa, Burkina Faso and Sudan) have commercialized GM cotton and maize with great success, and several other African countries are undergoing field trials and taking steps toward commercializing GM foods. New GM crops that could help poor African farmers, such as insect resistant cowpea, are also under research and development (De Schrijvera et al., 2007). So far, the health implications of biofortified foods have been of grave importance. They have been able to replenish deficiencies of micronutrients in malnourished populace in sub-Saharan Africa. For example, the development and introduction of the biofortified orange sweet potato with β-carotene increased vitamin A intake among children and women in Mozambique (Hotz et al., 2012) and Uganda (Hotz et al., 2012), also maize biofortified with pro-vitamin A increased the concentration of vitamin A in children between the ages of 5-7 years in Zambia who consumed it for three months (Gannon et al., 2014). Similarly, serum ferritin and total body iron were improved in iron-deficient adolescent boys and girls from Maharashtra, India, who consumed biofortified pearl millet flat bread with iron for four months (Finkelstein et al., 2015). The vast majority of crops which have been approved for commercialization are pest resistance and herbicide tolerance crops (FAO, 2015). In the industrialized world, plants with improved fatty acid content, such as omega-3-Fatty Acid are now available (Butell et al., 2008).

**Biofortification and the future**

Biofortified crops have gained publicity in sub-Saharan Africa, example includes Orange Fleshed Sweet Potatoes, Cassava and Maize rich in carotenes as well as high-iron pearl millet beans (HarvestPlus, 2011). All crops were developed in the context of the HarvestPlus Challenge Program of the Consultative Group for International Agricultural Research (HarvestPlus, 2011). Also, there are over 150 biofortified varieties of crops which have been released in 30 countries, and are consumed by more than 20 million people in developing countries (Bouis et al., 2017).

Increased micronutrient density and high yields are prerequisites for effective biofortification, and these crops must be
adopted by farmers and accepted by the target population (Bouis et al., 2011). There are some major challenges facing the distribution and general acceptability of biofortified crops. They are: Building consumer capacity, introducing biofortified traits into public plant breeding programs and policies (Bouis et al., 2017).

Factors such as genetic diversity, the reduction of antinutrients (especially phytate and polyphenols), and increasing the concentration of promoters such as cysteine, lysine, methionine and ascorbic acid which enhance the absorption of essential minerals, are essential for the success of biofortification strategies (White and Broadley, 2009; Bouis, 2003).

Genetic variation in the plant gene pool, development time for desired trait, and the dependence on the phyto availability of the mineral nutrients in the soil are limitations for conventional breeding approach (Carvalho and Vasconcelo, 2013).

To make biofortification effective in solving malnutrition in Africa and beyond, focus should be driven to bioavailability of micronutrients to humans. This can be achieved by increasing the concentration of promoters that stimulate the absorption of minerals and by reducing the concentrations of antinutrients that interfere with absorption in humans (White and Broadley, 2009; Bouis, 2003). Some examples of such promoters include Vitamin E, vitamin D, vitamin C, choline, niacin, and provitamin A and stimulate the absorption of Selenium, Calcium Phosphorus, Iron, Zinc, methionine, and tryptophan (Brinch-Pedersen et al., 2007). Certain antinutrients including phytate and some polyphenols reduce the bioavailability of micronutrients in crops (White and Broadley, 2009; Bouis, 2003). Phytate is form of phosphorus stored in seed, is not digested by humans or monogastric animals (Warkentin et al., 2012). During digestion, it has the ability to bind to iron and zinc and thus restrict their absorption bracket (Liu et al., 2015). The concentration of phytate can be controlled by identifying low phytate lines by germplasm screening (Shewry and Ward, 2012), manipulating the biosynthesis of phytate via mutation of a myo-inositol kinase (MIK) gene (Shi et al., 2005), and over expressing phytase, a phytate degrading enzyme (Brinch-Pedersen et al., 2002).

Polyphenols is secondary metabolites which include flavonoids and proanthocyanidins (Vermeris et al., 2006) provides protection against various fungal pathogens (Lattanzio et al., 2006). They are natural sources of antioxidants in the human diet and are present in fruits, vegetables, cereals, and legumes (Manach et al., 2004; Scalbert et al., 2005).

Postharvest processing can play an important role in utilizing biofortified crops, as a significant amount of minerals from the diet can be lost by milling or polishing (Gregorio et al., 2000) and cooking. Therefore biofortified crops should be made in such a way to retain the micronutrient concentration in edible seeds and their absorption by the consumer after processing and cooking (Haas et al., 2005). Iodization of salt was not enough to overcome iodine deficiency due to several factors such as the unavailability of iodized salt for all households, the volatilization of iodine during cooking, and low consumption rate due to health issues (Cakmak et al., 2017; White and Broadley, 2009; 2000; Winger and Konig, 2008). Hence, further research is needed to identify traits that control uptake, mobilization, and retention of iodine in the plant, and these can be manipulated in plant breeding or using a genetic engineering approach during biofortification (Gonzali et al., 2017).
Micronutrients deficiencies is the causes of many diseases in Africa, it is popularly referred to as hidden hunger. Several interventions have been applied to curb the extent of this malnutrition. Biofortification through plant breeding have proven to be very effective in combating micronutrient deficiencies and it is generally accepted. Biofortification through genetic modification is another effective approach but health concerns by regulatory bodies have hindered the commercialization and public acceptance of this technology. Biofortification is also a cost effective approach for bioavailability of nutrients because it is one time investment as plant seedlings can be reproduced across the years for farmers during planting season. Also farmers sensitization, awareness, orientation and reorientation for acceptance for both farmers and the populace should be adopted as biofortification as proven to be very effective in making available micronutrients at all times.

Furthermore, research should be extended to determining the bio-safety, bio-hazard to human health and environments. Government policies should be adjusted to accommodate the research, developments and usage of Biofortified crops, through plant breeding and genetic engineering.

References

Adarme-Vega, T. C., Thomas-Hall, S.R., & Schenk, P.M. (2014). Towards sustainable sources for omega-3 fatty acids production. *Curr. Opin. Biotechnol.*, 26: 14–18.

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

Aldemir, S., Ates, D., Temel, H.Y., Yagmür, B., Alsaleh, A., Kahrıman, A., Özkan, H., Vandenbergh, A.; Abbaspour, N., Hurrell, R., & Kelishadi, R. (2014). Review on iron and its importance for human health. *J. Res. Med. Sci.*, 19: 164–174.

Alfthan, G., Eurola, M., & 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.

Ali, N., Paul, S., Gayen, D., Sarkar, S.N., Datta, K., & Datta, S.K. (2013). Development of low phytate rice by RNAi mediated seed-specific silencing of inositol 1,3,4,5,6-pentakisphosphate 2-kinase gene (IPK1). *PLoS One*, 8: 68-161.

Allen, L., de Benoist B., Dary O., & Hurrell R. (2006) Guidelines on food fortification with micronutrients. Geneva: World Health Organization and Food and Agriculture Organization of the United Nations. 19: 61-4.

Allen, L.H. (2000) Anemia and iron deficiency: Effects on pregnancy outcome. *Am. J. Clin. Nutr.* 71: 1280S–1284S.

Alves-Rodrigues, A., & Shao, A. (2004).The science behind lutein. *Toxicol. Lett.* 150: 57–83.

Andrews, S.C., Arosio, P., Bottke, W., Briat, J.F., Von Darl, M., Harrison, P.M., Lawler, J.P., Levi, S., Lobreaux, S., & Yewdall, S.J. (1992) Structure, function and evolution of ferritins. *J.Inorg. Biochem.*, 47: 116–174.

Apel, A. (2008). The costly benefits of opposing agricultural biotechnology. *New Biotechnol.* 27: 635–640.

Bailey, L.B., & Gregory, J. F. (1999). Folate metabolism and requirements. *J. Nutr.*, 129: 779–782.

Bailey, R.L., West, K.P., Jr. & Black, R.E. (2015). The epidemiology of global micronutrient deficiencies. *Ann. Nutr. Metab.*, 66: 2233.

Basset, G.J.C., Quinlivan, E.P., Gregory, J.F., III & Hanson, A.D. (2005). Folate synthesis and metabolism in plants and prospects for biofortification. *Crop Sci.*, 45: 449–453.

Bawa, A.S., & Anilakumar, K.R.(2013). Genetically modified foods: Safety, risks and public concerns—A review. *J. Food Sci. Technol.*, 50: 1035–1046.

Beebe, S., Gonzalez, A.V., & Rengifo, J. (2000). Research on trace minerals in the common bean. *FoodNutr. Bull.*, 21: 387–391.

Beyer, P. (2010) Golden Rice and “Golden” crops for human nutrition. *New Biotechnol.*, 27: 478–481.
Black, R.E., Allen, L.H., Bhutta, Z.A., Caulfield, L.E., de Onis, M., Ezzati, M., Mathers, C.; Rivera, J. (2008) Maternal and child under nutrition: Global and regional exposures and health consequences. *Lancet*, 371: 243–260.

Blair, M.W., Astudillo, C., Grusak, M., Graham, R., & Beebe, S. (2009). Inheritance of seed iron and zinc content in common bean (Phaseolus vulgaris L.). *Mol. Breed.*, 23: 197–207.

Blair, M.W., Astudillo, C., Rengifo, J., Beebe, S.E., & Graham, R. (2011). QTL for seed iron and zinc concentrations in a recombinant inbred line population of Andean common beans (Phaseolus vulgaris L.). *Theor. Appl. Genet.*, 122: 511–521.

Blair, M.W., Medina, J.I., Astudillo, C., Rengifo, J., Beebe, S.E., Machado, G., & Graham, R. (2010). QTL for seed iron and zinc concentrations in a recombinant inbred line population of Mesoamerican common beans (Phaseolus vulgaris L.). *Theor. Appl. Genet.*, 121: 1059–1070.

Blakley R. (1969) The biochemistry of folic acid and related pteridines. Amsterdam: North-Holland Publishing;, pp. 768

Blancquaert, D., De Steur, H., Gellynck, X., & Van Der Straeten, D. (2014). Present and future of folate biofortification of crop plants. *J. Exp. Bot.*, 65: 895–906.

Blancquaert, D., Storozhenko, S., Van Daele, J., Stove, C., Visser, R., Lambert, W., & 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.

Borrill, P., Connorton, J.M., Balk, J., Miller, A.J., Sanders, D., & Uauy, C. (2014). Biofortification of wheat grain with iron and zinc: Integrating novel genomic resources and knowledge from model crops Front. *Plant Sci.*, 5: 53, doi:10.3389/fpls.2014.00053.

Bortesi, L., & Fischer, R. (2015). The CRISPR/Cas9 system for plant genome editing and beyond. *Biotechnol. Adv.*, 33: 41–52.

Bouis, H.E. (2000). Enrichment of food staples through plant breeding: A new strategy for fighting micronutrient malnutrition. *Nutrition*, 16: 701–704.

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.

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

Bouis,H.E., & Saltzman,A. (2017). Improving nutrition through biofortification: A review of evidence from HarvestPlus, 2003 through 2016. *Glob. Food Sec.*, 12: 49–58.

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

Brinch-Pedersen, H., Sørensen, L.D., & Holm, P.B. (2002). Engineering crop plants: Getting a handle on phosphate. *Trends Plant Sci.*, 7: 118–125.

Brnič, M., Wegmüller, R., Zeder, C., Senti, G., & Hurrell, R.F. (2014). Influence of phytase, EDTA, and polyphenols on zinc absorption in adults from porridges fortified with zinc sulfate or zinc oxide. *J. Nutr.*, 144: 1467–1473.

Butelli, E., Titta, L., Giorgio, M., Mock, H.P., Matsos, A., Peterek, S., Schijlen, E.G., Hall, R.D., Bovy, A.G., Luo, J., Cathie, M., Robert, D.H., & Silke, P. (2008). Enrichment of tomato fruit with health-promoting anthocyanins by expression of select transcription factors. *Nat. Biotechnol.*, 26: 1301–1308.

Cakmak, I. (2009). Enrichment of fertilizers with zinc: An excellent investment for humanity and crop production in India. *J. Trace Elem. Med. Biol.*, 23: 281–289.

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

Cakmak, I., Prom-u-thai, C., Guilherme, L.R.G., Rashid, A., Hora, K., Yazici, A., Savasli, E., Kalayci, M., Tutus, Y., Phuphong, P., Rizwan, M., Martins, F.A.D., Dinali, S., &
Ozturk, L., (2017). Iodine biofortification of wheat, rice and maize through fertilizer strategy. Plant Soil, 418: 319–335.

Campion, B., Sparvoli, F., Doria, E., Tagliabue, G., Galasso, I., Fileppi, M., Bollini, R., & Nielsen, E. (2009). Isolation and characterization of anlpa (low phytic acid) mutant in common bean (Phaseolus vulgaris L.). Theor. Appl. Genet., 118: 1211–1221.

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

Casassus, B. (2012) Study linking GM maize to rat tumours is retracted: Nature News & Comment. Available online: http://www.nature.com/news/study-linkinggm-maizeto-rat-tumours-isretracted.1.14268 (accessed on 11 February 2015).

Cavagnaro, T.R. (2008) The role of arbuscular mycorrhizas in improving plant zinc nutrition under low soil zinc concentrations: A review. Plant Soil, 304: 315–325.

Choi, S.W., & Friso, S. (2005). Interactions between folate and aging for carcinogenesis. Clin. Chem. Lab. Med., 43: 1151–1157.

Christer Andersson, H., Arpaia, S., Bartsch, D., Casacuberta, J., Davies, H., du Jardin, P., Herman, L., Hendriksen, N., Kärenlampi, S., Kiss, J., Gjls K., Harry K., Antoine M., Herden, L., Hendriksen, N., Kärenlampi, S., Kiss, J., Gijs K., Harry K., Antoine M., Kaare, M., Joe, P., Annette, P., Jeremy S., Christoph T., Atte J.V.W., & Jean Micheal W. (2011). EFSA panel on Genetically Modified Organisms (GMO). EFSA J. 9: 2150, doi:10.2903/j.efsa.2011.2150.

Christou, P., & Twyman, R.M. (2004). The potential of genetically enhanced plants to address food insecurity. Nutr. Res. Rev., 17: 23–42.

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

Convention on Biological Diversity Biosafety Clearing House (2012). Guidance on Risk Assessment of Living Modified Organisms

Risk Assessment of Living Modified Plants with Stacked Genes or Traits. Available online:

https://bch.cbd.int/onlineconferences/guidanc edoc_ra_stackedgenes. shtml (accessed on 15 August 2014).

Cook, J. D. (2005) Diagnosis and management of iron-deficiency anaemia. Best Pract. Res. Clin. Haematol., 18: 319–332.

Coppinger, R.J., & Diamond, A.M. (2001). Selenium deficiency and human disease. In Selenium; Hatfield, D.L., Ed.; Springer: Boston, MA, USA, pp. 219–233.

Costello, L.C., & 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. ExpertOpin. Ther. Targets, 21: 51–66.

D’Introno, A., Paradiso, A., Scoditti, E., D’Amico, L., de Paolis, A., Carlucio, M. A., Nicoletti, I., DeGara, L., Santino, A., & Giovinazzo, G. (2009). Antioxidant and anti-inflammatory properties of tomato fruits synthesizing different amounts of stilbenes. Plant Biotechnol. J., 7: 422–429.

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

Darnton Hill, I. Bloem, M. Chopra, M. (2006) Achieving the millennium development goals through mainstreaming nutrition: Speaking with one voice. Public Health Nutr. 9: 537–539.

Davoodi-Semironi, A., Schreiber, M., Nalapalli, S., Verma, D., Singh, N.D., Banks, R.K., Chakrabarti, D., & Daniell, H. (2010) Chloroplast-derived vaccine antigens confer dual immunity against cholera and malaria by oral or injectable delivery. Plant Biotechnol. J., 8, 223–242.

De Schrijvera, A., Devosb, Y., van den Bulckeab, M., Cadotc, P., de Loosed, M., Reheulb, D., & Sneyers, M. (2007). Risk assessment of GM stacked events obtained from crosses between GM events Trends Food Sci. Technol., 18: 101–109.

De Steur, H.; Blancquaert, D.; Gellynck, X.; Ozturk, L., (2017). Iodine biofortification of wheat, rice and maize through fertilizer strategy. Plant Soil, 418: 319–335.

De Steur, H.; Blancquaert, D.; Gellynck, X.; Casassus, B. (2012) Study linking GM maize to rat tumours is retracted: Nature News & Comment. Available online: http://www.nature.com/news/study-linking-gm-maize-to-rat-tumours-isretracted.1.14268 (accessed on 11 February 2015).

Cavagnaro, T.R. (2008) The role of arbuscular mycorrhizas in improving plant zinc nutrition under low soil zinc concentrations: A review. Plant Soil, 304: 315–325.

Choi, S.W., & Friso, S. (2005). Interactions between folate and aging for carcinogenesis. Clin. Chem. Lab. Med., 43: 1151–1157.

Christer Andersson, H., Arpaia, S., Bartsch, D., Casacuberta, J., Davies, H., du Jardin, P., Herman, L., Hendriksen, N., Kärenlampi, S., Kiss, J., Gjls K., Harry K., Antoine M., Kaare, M., Joe, P., Annette, P., Jeremy S., Christoph T., Atte J.V.W., & Jean Micheal W. (2011). EFSA panel on Genetically Modified Organisms (GMO). EFSA J. 9: 2150, doi:10.2903/j.efsa.2011.2150.

Christou, P., & Twyman, R.M. (2004). The potential of genetically enhanced plants to address food insecurity. Nutr. Res. Rev., 17: 23–42.

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

Convention on Biological Diversity Biosafety Clearing House (2012). Guidance on Risk Assessment of Living Modified Organisms

Risk Assessment of Living Modified Plants with Stacked Genes or Traits. Available online:

https://bch.cbd.int/onlineconferences/guidanc edoc_ra_stackedgenes. shtml (accessed on 15 August 2014).

Cook, J. D. (2005) Diagnosis and management of iron-deficiency anaemia. Best Pract. Res. Clin. Haematol., 18: 319–332.

Coppinger, R.J., & Diamond, A.M. (2001). Selenium deficiency and human disease. In Selenium; Hatfield, D.L., Ed.; Springer: Boston, MA, USA, pp. 219–233.

Costello, L.C., & 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. ExpertOpin. Ther. Targets, 21: 51–66.

D’Introno, A., Paradiso, A., Scoditti, E., D’Amico, L., de Paolis, A., Carlucio, M. A., Nicoletti, I., DeGara, L., Santino, A., & Giovinazzo, G. (2009). Antioxidant and anti-inflammatory properties of tomato fruits synthesizing different amounts of stilbenes. Plant Biotechnol. J., 7: 422–429.

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

Darnton Hill, I. Bloem, M. Chopra, M. (2006) Achieving the millennium development goals through mainstreaming nutrition: Speaking with one voice. Public Health Nutr. 9: 537–539.

Davoodi-Semironi, A., Schreiber, M., Nalapalli, S., Verma, D., Singh, N.D., Banks, R.K., Chakrabarti, D., & Daniell, H. (2010) Chloroplast-derived vaccine antigens confer dual immunity against cholera and malaria by oral or injectable delivery. Plant Biotechnol. J., 8, 223–242.

De Schrijvera, A., Devosb, Y., van den Bulckeab, M., Cadotc, P., de Loosed, M., Reheulb, D., & Sneyers, M. (2007). Risk assessment of GM stacked events obtained from crosses between GM events Trends Food Sci. Technol., 18: 101–109.

De Steur, H.; Blancquaert, D.; Gellynck, X.; Lambert, W.; van der Straeten, D. (2012). Ex-ante evaluation of biotechnology innovations: The case of folate biofortified rice in China. Curr. Pharm. Biotechnol., 13:
2751–2760.

De Steur, H., Gellynck, X., Blancquaert, D., Lambert, W., van der Straeten, D., & Qaim, M. (2012) Potential impact and cost-effectiveness of multi-biofortified rice in China. New Biotechnol., 29: 432–442.

Delange, F (1994). The disorders induced by iodine deficiency. Thyroid, 4: 107–128.

Diapari, M.; Sindhu, A.; Bett, K.; Deokar, A.; Warkentin, T.D.; Tar’an, B. (2014). Genetic diversity and association mapping of iron and zinc concentrations in chickpea (CicerariatumumL.). Genome, 57:459–468.

Diapari, M., Sindhu, A., Warkentin, T. D., Bett, K., & Tar’an, B. (2015). Population structure and marker-trait association studies of iron, zinc and selenium concentrations in seed of field pea (Pisum sativum L.). Mol. Breed., 35: 30.

Duranti, M. (2006). Grain legume proteins and nutraceutical properties. Fitoterapia, 77: 67–82.

Erenoglu, E.B., Kutman, U.B., Ceylan, Y., Yildiz, B., & Cakmak, I. (2011). Improved nitrogen nutrition enhances root uptake, root-to-shoot translocation and remobilization of zinc ((65)Zn) in wheat. New Phytol., 189: 438–448.

Eurola, M., Ekholm, P., Ylinen, M., Koivistoinen, P., & Varo, P. (1989). Effects of selenium fertilization on the selenium content of selected Finnish fruits and vegetables. Acta Agric. Scand., 39: 345–350.

Eurola, M.H., Ekholm, P.I., Ylinen, M.E., Koivistoinen, P.E., & Varo, P.T. (1991). Selenium in Finnish foods after beginning the use of selenate-supplemented fertilisers. J. Sci. Food Agric., 56: 57–70.

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

FAO, (2013). The State of Food and Agriculture; Food and Agriculture Organization: Rome, Italy.

Finkelstein, J.L., Mehta, S., Udipi, S.A., Ghugre, P.S., Luna, S.V., Wenger, M.J., Murray-Kolb, L.E., Przybyszewski, E.M., & Haas, J.D. (2015). A randomized trial of iron-biofortified pearl millet in school children in India. J. Nutr., 145: 1576–1581.

Food and Agriculture Organization of the United Nations FAO GM Foods Platform, (2014) Available online: http://www.fao.org/food/food-safety-quality/gm-foods-platform/en/ (accessed on 15 August 2014).

Fraser, P.D. & Bramley, P.M. (2004). The biosynthesis and nutritional uses of carotenoids. Prog. Lipid Res., 43: 228–265.

Frossard, E., Bucher, M., Machler, F., Mozafar, A., & Hurrell, R. (2000). Potential for increasing the content and bioavailability of Fe, Zn and Ca in plants for human nutrition. J.Sci. FoodAgric., 80: 861–879.

Gannon, B., Kaliwile, C., Arscott, S.A., Schmaelzle, S., Chileshe, J., Kalungwana, N., Mosonda, M., Pixley, K., Masi, C., & Tanumihardjo, S.A. (2014). Biofortified orange maize is as efficacious 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.

Gao, C.Q., Ji, C., Zhao, L.H., Zhang, J.Y., & Ma, Q.G. (2013). Phytase transgenic corn in nutrition of laying hens: Residual phytase activity and phytate phosphorus content in the gastrointestinal tract. Poult. Sci., 92: 2923–2929.

Garcia-Casal, N., Layrisse, M., Solano, L., Baron, M.A., Arguello, F., Liovera, D., Ramírez, J., Leets, I., & Tropper, E. (1998). Vitamin A and beta carotene can improve non heme iron absorption from rice, wheat and corn by humans. J. Nutr., 128: 646–650.

Garcia-Casal,N., Leets,I., & Layrisse, M. (2000), Beta carotene and inhibitors of iron absorption modify iron uptake by Caco-2 cells. J. Nutr., 130: 5–9.

Garg, M., Sharma, N., Sharma, S., Kapoor, P., Kumar, A., Chunduri, V., & 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.

Gartland, K.M., Bruschi, F., Dundar, M., Gahan, P.B., Magni, V., & Akbarova, Y. (2013) Progress towards the “Golden Age” of biotechnology. Curr. Opin. Biotechnol., 24: S6–S13.

Geisel, J. (2003). Folic acid and neural tube
defects in pregnancy—A review. J. Perinat. Neonat. Nurs., 17: 268–279.

Ghosh, A., Hasim Reja, M., Nalia, A., Kanthal, S., Maji, S., Venugopalan, V., & Nath, R. (2019). Micronutrient biofortification in pulses: An agricultural approach. CJAST, 35: 1–12.

Gibson, R.S. & Hotz, C. (2001). Dietary diversification/modification strategies to enhance micronutrient content and bioavailability of diets in developing countries. Br. J. Nutr., 85: S159–S166.

Gil-Humanes, J., Pistón, F., Barro, F., & Rosell, C.M. (2014). The shutdown of celiac disease-related gliadin epitopes in bread wheat by RNAi provides flours with increased stability and better tolerance to over-mixing. PLoS One, 9: 91-931.

Giovinazzo, G., D’Amico, L., Paradiso, A., Bollini, R., Sparvoli, F., & DeGara, L. (2005) Antioxidant metabolite profiles in tomato fruit constitutively expressing the grapevine stilbene synthase gene. Plant Biotechnol. J., 3: 57–69.

Global Nutrition Report 2014. Actions and Accountability to Accelerate the World’s Progress on Nutrition. Available online: http://www.ifpri.org/sites/default/files/publications/ib85.pdf (accessed on 11 February 2015).

Gómez-Galera, S., Rojas, E., Sudhakar, D., Zhu, C., Pelacho, A.M., Capell, T., & Christou, P. (2010). Critical evaluation of strategies for mineral fortification of staple food crops. Transgenic Res. 19: 165–180.

Gonzali, S., Kiferle, C., & Perata, P. (2017). Iodine biofortification of crops: Agronomic biofortification, metabolic engineering and iodine bioavailability. Curr. Opin. Biotechnol. 44: 16–26.

Gopalakrishnan, S., Srinivas, V., Prakash, B., Sathya, A., & Vijayabharathi, R. (2015). Plant growth-promoting traits of Pseudomonas geniculata isolated from chickpea nodules. 3 Biotech, 5: 653–661.

Gopalakrishnan, S., Srinivas, V., Prakash, B., Sathya, A., & Vijayabharathi, R. (2015) Plant growth-promoting traits of Pseudomonas geniculata isolated from chickpea nodules. Biotech, 5: 653–661.

Gopalakrishnan, S., Vadlamudi, S., Samineni, S., & Sameer Kumar, C.V. (2016) Plant growth-promotion and biofortification of chickpea and pigeonpea through inoculation of biocontrol potential bacteria, isolated from organic soils. Springer plus, 5: 1882.

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

Gregorio, G.B., Senadhira, D., Htut, H., & Graham, R.D. (2000). Breeding for trace mineral density in rice. Food Nutr. Bull., 21: 382–386.

Grusak, M.A., & Della Penna, D. (1999) Improving the nutrient composition of plants to enhance human nutrition and health. Annu. Rev. Plant Physiol. Plant Mol. Biol., 50: 133–161.

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

Haas, J.D., Beard, J.L., Murray-Kolb, L.E., del Mundo, A.M., Felix, A., & Gregorio, G.B. (2005). Iron-biofortified rice improves the iron stores of non-anemic Filipino women. J. Nutr., 135: 2823–2830.

Haas, J.D., Beard, J.L., Murray-Kolb, L.E., del Mundo, A.M., Felix, A., & Gregorio, G.B. (2005) Iron-biofortified rice improves the iron stores of nonanemic Filipina women. J. Nutr., 135: 2823–2830.

Hanson, A.D., & Roje, S. (2001). One-carbon metabolism in higher plants. Annu. Rev. Plant Physiol. Plant Mol. Biol., 52: 119–137.

Hartikainen, H. (2005). Breeding for trace mineral density in rice. Food Nutr. Bull., 21: 382–386.

Hartikainen, H. (2005) Breeding for trace mineral density in rice. Food Nutr. Bull., 21: 382–386.

Haskell, M.J. (2012) The Challenge to reach nutritional adequacy for vitamin A: β-carotene bioavailability and conversion—Evidence in humans. Am. J. Clin. Nutr., 96:
adequate vitamin a status in Mongolian gerbils. J. Nutr., 136: 2562–2567.

Hurrell, R. F. (2002). How to ensure adequate iron absorption from iron-fortified food. Nutr. Rev., 60: S7–S15.

Hurrell, R. F.(1997). Bioavailability of iron. Eur. J. Clin. Nutr., 51: S4–S8.

Iannone, A., Rota, C., Bergamini, S., Tomasi, A., & Canfield, L.M. (1998). Antioxidant activity of carotenoids: An electron-spin resonance study on beta-carotene and lutein interaction with free radicals generated in a chemical system. J. Biochem. Mol. Toxicol., 12: 299–304.

Inaba, M., & Macer, D.(2004). Policy, regulation and attitudes towards agricultural biotechnology in Japan. J. Int. Biotechnol. Laws, 1: 45–53.

Ingrosso, I., Bonsegnia, S., de Domenico, S., Laddomada, B., Blando, F., Santino, A., & Giovinazzo, G. (2011). Over-expression of a grape stilbene synthase gene in tomato induces parthenocarpy and causes abnormal pollen development. Plant Physiol. Biochem., 49: 1092–1099.

ISAAA. (2015). Brief 46–2013: Executive Summary Global Status of Commercialized Biotech/GM Crops: 2013; ISAAA: Ithaca, NY, USA.

Islam, F.M.A., Basford, K.E., Jara, C., Redden, R.J., & Beebe, S.E. (2002). Seed compositional and disease resistance differences among gene pools in cultivated common bean. Genet. Resour. Crop Evol., 49: 285–293.

Ismail, A.M., Heuer, S., Thomson, M.J., & Wissuwa, M. (2007). Genetic and genomic approaches to develop rice germplasm for problem soils. Plant Mol. Biol., 65: 547–570.

Jaganathan, D., Ramasamy, K., Sellamuthu, G., Jayabalan, S., & Venkataraman,G. (2018). CRISPR for crop improvement: An update review. Front. Plant Sci., 9: 985.

Jansson, B. (1980). The role of selenium as a cancer-protecting trace element. Met. IonsBiol. Syst., 10: 281–311.

Jeong, J., & Guerinot, M. L. (2008). Biofortified and bioavailable: The gold standard for plant-based diets. Proc. Natl. Acad. Sci. USA, 105: 1777–1778.

Jha, A.B., Ashokkumar, K., Diapari, M.,

Hirschi, K.D. (2009). Nutrient biofortification of food crops. Annu. Rev. Nutr., 29: 401–421.

Hotz, C. (2014). The potential to improve zinc status through biofortification of staple food crops with zinc. Food Nutr. Bull. 2009, 30 (Suppl. 1), S172–S178.Grillet, L.; Mari, S.; Schmidt, W. Iron in seeds—Loading pathways and subcellular localization. Front. Plant Sci., 4: 535, doi:10.3389/fpls.2013.00535.

Hotz, C., Loechl, C., de Brauw, A., Eozenou, P., Gilligan, D., Moursi, M., Munhua, B., van Jaarsveld, P., Carriquiry, A., & Meenakshi, J.V. (2012). A large-scale intervention to introduce orange sweet potato in rural Mozambique increases vitamin A intakes among children and women. Br. J. Nutr., 108: 163–176.

Hotz, C., Loechl, C., Lubowa, A., Tumwine, J. K., Ndezei, G., NandutuMasawi, A., Baingana, R., Carriquiry, A., de Brauw, A., Meenakshi, J. V. & Gilligan, D.O. (2012). Introduction of β-carotene-rich orange sweet potato in rural Uganda results in increased vitamin A intakes among children and women and improved vitamin A status among children. J. Nutr., 142: 1871–1880.

Howe, J.A., & Tanumihardjo, S.A. (2006). Carotenoid-biofortified maize maintains
Ambrose, S.J., Zhang, H., Tar’an, B., Bett, K.E., Vandenberge, A., Warkentin, T.D., & Purves, R.W. (2015). Genetic diversity of folate profiles in seeds of common bean, lentil, chickpea and pea. J. Food Compos. Anal., 42: 134–140.

Jha, A.B., Purves, R.W., Elessawy, F.M., Zhang, H., Vandenberge, A., & Warkentin, T.D. (2019) Polyphenolic profile of seed components of white and purple flower pea lines. Crop Sci., 59: 2711–2719.

Jha, A.B., Tar’an, B., Diapari, M., & Warkentin, T.D. (2015) SNP variation within genes associated with amylose, total starch and crude protein concentration in field pea. Euphytica, 206: 459–471.

Khalid, S., Asghar, H.N., Akhtar, M.J., Aslam, A., & Zahir, Z.A. (2015). Biofortification of iron in chickpea by plant growth promoting rhizobacteria. Pak. J. Bot., 47: 1191–1194.

Kok, A.D., Yoon, L.L., Sekeli, R., Yeong, W.C., Yusof, Z.N.B., & Song, L.K. (2018) Iron biofortification of rice: Progress and prospects. In Rice Crop—Current Developments; Saha,F., Khan, Z.H., Iqbal, A., Eds.; Intech Open: London, UK, 3: 25–44.

La Frano, M.R., Woodhouse L.R., Burnett, D.J., & Burri, B.J. (2013). Biofortified cassava increases β-carotene and vitamin A concentrations in the TAG-rich plasma layer of American women. Br. J. Nutr., 110: 310–320.

Lai, H., He, J., Engle, M., Diamond, M.S., & Chen, Q. (2012) Robust production of virus-like particles and monoclonal antibodies with geminiviral replicon vectors in lettuce. Plant Biotechnol. J., 10: 95–104.

Lattanzio, V., Lattanzio, V.M.T., & Cardinali, A. (2006) Role of phenolics in the resistance mechanisms of plants against fungal pathogens and insects. In Phytochemistry: Advances in Research; Imperato, F., Ed.; Research Signpost: Kerala, India, pp. 23–67.

Leyva-Guerrero, E., Narayanan, N.N., Ihemere, U., & Sayre, R.T. (2012). Iron and protein biofortification of cassava: Lessons learned. Curr. Opin. Biotechnol., 23: 257–264.

Li, B., Liu, H., Zhang, Y., Kang, T., Zhang, L., Tong, J., Xiao, L., & Zhang, H. (2013). Constitutive expression of cell wall invertase genes increases grain yield and starch content in maize. Plant Biotechnol. J., 11: 1080–1091.

Li, S.S., Nugroho, A., Rocheford, T., & White, W.S. (2010) Vitamin A equivalence of the β-carotene in β-carotene-biofortified maize porridge consumed by women. Am. J. Clin. Nutr., 92: 1105–1112.

Liu, X., Glahn, R.P., Arganosa, G.C., & Warkentin, T. D. (2015). Iron bioavailability in low phytate pea. CropSci., 55: 320–330.

Lozof, B., Clark, K.M., Jing, Y., Armony-Sivan, R., Angelilli, M. L., & Jacobson, S.W. (2008). Dose-response relationships between iron deficiency with or without anemia and infant social-emotional behavior. J. Pediatr., 152: 696–702.

Lucca, P., Hurrel, R., & Potrykus, I. (2002). Genetic engineering approaches to improve the bioavailability and the level of iron in the rice grains. Theor. Appl. Genet., 102: 392–397.

MacDonald, R.S. (2000). The role of zinc in growth and cell proliferation. J. Nutr., 130: 1500S–1508S.

Mahafee, W.F., & 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, 122: 23–31.

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

Mason, J. B., & Garcia M. (1993) Micronutrient deficiency—the global situation. SCN News, 9:11–6.

Mayer, J. E., Pfeifer, W.H., & Bouis, P. (2008). Biofortified crops to alleviate micronutrient malnutrition. Curr. Opin. Plant Biol. 11: 166–170.

McCully, K.S. (2007). Homocysteine, vitamins, and vascular disease prevention. Am. J. Clin. Nutr., 86: 1563S–1568S.

McDowell, L.R. (2003). Minerals in Animal and Human Nutrition, 2nd ed.; Elsevier Science: Amsterdam, The Netherlands, p. 660.

McMillan, T. (2014). In push to snare low income shoppers, Whole Foods to put cigarette-like
warnings on GMO foods. Available online: http://geneticliteracyproject.org/2014/11/21/nn-push-to-snare-low-income-shoppers-wholefoods-to-put-cigarette-like-warnings-on-gmo-foods/ (accessed on 11 February 2015).

Messina, M. J. (1999). Legumes and soybeans: Overview of their nutritional profiles and health effects. *Am. J. Clin. Nutr.*, 70: 439S–450S.

Minorsky, P. V. (2008) On the inside. *Plant Physiol.*, 146: 323–324.

Moeller, S. M., Jacques, P.F., & Blumberg, J.B. (2000). The potential role of dietary xanthophylls in cataract and age-related macular degeneration. *J. Am. Coll. Nutr.*, 19: 522S–527S.

Moghissi, A.A., Pei, S., & Liu, Y. (2015). Golden rice: Scientific, regulatory and public information processes of a genetically modified organism. *Crit. Rev. Biotechnol.*, 21: 1–7.

Moretti, D., Biebinger, R., Bruins, M.J., Hoeft, B., & Kraemer, K. (2014). Bioavailability of iron, zinc, folic acid, and vitamin A from fortified maize. *Ann. N. Y. Acad. Sci.*, 1312: 54–65.

Mugode, L., Há, B., Kaunda, A., Sikombe, T., Phiri, S., Mutale, R., Davis, C., Tanumihardjo, S., & de Moura, F.F. (2014). Carotenoid retention of biofortified provitamin a maize (Zea mays L.) after Zambian traditional methods of milling, cooking and storage. *J. Agric. Food Chem.*, 62: 6317–6325.

Murray-Kolb, L.E., Takaiwa, F., Goto, F., Yoshihara, T., Theil, E.C., & Beard, J.L. (2002). Transgenic rice is a source of iron for iron-depleted rats. *J. Nutr.*, 132: 957–960.

Muzhingi, T., Gadaga, T.H., Siwela, A.H., Grusak, M.A., Russell, R.M., & Tang, G. (2011). Yellow maize with high β-carotene is an effective source of vitamin A in healthy Zimbabwean men. *Am. J. Clin. Nutr.*, 94: 510–519.

Naqvi, S., Zhu, C., Farre, G., Ramessar, K., Bassie, L., Breitenbach, J., Perez Conesa, D., Ros, G., Sandmann, G., Capell, T., & Christou, P. (2009). Transgenic multivitamin corn through biofortification of endosperm with three vitamins representing three distinct metabolic pathways. *Proc. Natl. Acad. Sci. USA*, 106: 7762–7767.

Nayyar, H., Kaur, S., Singh, S., & Upadhyaya, H.D. (2006). Differential sensitivity of Desi (small-seeded) and Kabuli (large-seeded) chickpea genotypes to water stress during seed filling: Effects on accumulation of seed reserves and yield. *J. Sci. Food Agric.*, 86: 2076–2082.

Nemeth, A. (2010). GM Wheat Means Hope for Celiac Sufferers. Available online: http://www.foodsafetynews.com/2010/01/genetically-modified-foods-are-becoming-1/ (accessed on 15 August 2014).

Newell-McGloughlin, M. (2008). Nutrionally improved agricultural crops. *Plant Physiol.*, 147: 939–953.

Olmedilla, B., Granado, F., Blanco, I., Vaquero, M., & Cajigal, C. (2001) Lutein in patients with cataracts and age-related macular degeneration: A long-term supplementation study. *J.Sci. Food Agric.*, 81: 904–909.

Paine, J.A., Shipton, C.A., Chaggar, S., Howells, R.M., Kennedy, M.J., Vernon, G., Wright, S.Y., Hinchlife, E., Adams, J.L., Silverstone, A.L., & Drake R. (2005). Improving the nutritional value of Golden Rice through increased pro-vitamin A content. *Nat. Biotecnol.*, 23: 482–487.

Pandey, A., Misra, P., Khan, M.P., Swarnkar, G., Tewari, M.C., Bhamhani, S., Trivedi, R., Chattopadhyay, N., & Trivedi, P.K. (2014). Co-expression of Arabidopsis transcription factor, AtMYB12, and soybean isoflavone synthase, GmIFS1, genes in tobacco leads to enhanced biosynthesis of isoflavones and flavonols resulting in osteoprotective activity. *Plant Biotechnol. J.*, 12: 69–80.

Panthar, Q.A., Othman, R., Rahman, Z.A., Meon, S., & Ismail, M.R. Isolation and characterization of phosphate-solubilizing bacteria from aerobic rice. Afr. J. Biotecnol. 2012, 11, 2711–2719. 123.

Panzeri, D., Cassani, E., Doria, E., Tagliabue, G., Forti, L., Campion, B., Bollini, R., Brearley, C.A., Pihu, R., Nielsen, E., & Spavolli, F. (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.
Patterson, C.A., Maskus, H, & Dupasquier, C. (2009). Pulse crops for health. *Cereals Food World*, 54: 108–113.

Pearce, E.N., Andersson, M., & Zimmermann, M.B. (2013). Global iodine nutrition: Where do we stand in 2013? *Thyroid*, 23: 523–528.

Pearce, E.N., Lazarus, J.H., Moreno-Reyes, R., & Zimmermann, M.B. (2016). Consequences of iodine deficiency and excess in pregnant women: An overview of current knowns and unknowns. *Am. J. Clin. Nutr.*, 104: 918S–923S.

Pellegrino, E., & Bedini, S. (2014). Enhancing ecosystem services in sustainable agriculture: Biofertilization and biofortification of chickpea (*Cicer arietinum* L.) by arbuscular mycorrhizal fungi. *Soil Biol. Biochem.*, 68: 429–439.

Perez-Massot, E., Banakar, R., Gomez-Galera, S., Zorrilla-Lopez, U., Sanahuja, G., Arjo, G., Miralpeix, B., Vamvaka, E., Farré, G., Rivera, S.M., Berman, J., Sabalza, M., Yuan, D., Bai, C., Basse, L., Twyman, R.M., Capell, T., Christou, P., & Zhu C., (2013). The contribution of transgenic plants to better health through improved nutrition: Opportunities and constraints. *Genes Nutr.*, 8: 29–41.

Petry, N., Egli, I., Campion, B., Nielsen, E., & Hurrell, R. (2013) Genetic reduction of phytate in common bean (*Phaseolus vulgaris* L.) seeds increases iron absorption in young women. *J. Nutr.*, 143: 1219–1224.

Pfeifer, W.H., & McClaferty, B. (2007). HarvestPlus: Breeding crops for better nutrition. *CropSci.*, 47: S88–S100.

Pillay, K., Siwela, M., Derera, J., & Veldman, F.J. (2014). Provitamin A carotenoids in biofortified maize and their retention during processing and preparation of South African maize foods. *J. Food Sci. Technol.*, 51: 634–644.

Pitkin, R.M. (2007). Folate and neural tube defects. *Am. J. Clin. Nutr.*, 85: 2855–288S.

Poblaciones, M.J., & Rengel, Z. (2016). Soil and foliar zinc biofortification in field pea (*Pisum sativum* L.). Grain accumulation and bioavailability in raw and cooked grains. *Food Chem.*, 212: 427–433.

Poblaciones, M.J., Rodrigo, S., Santamaria, O., Chen, Y., & McGrath, S.P. (2014). Selenium accumulation and speciation in biofortified chickpea (*Cicer arietinum* L.) under Mediterranean conditions. *J. Sci. Food Agric.*, 94: 1101–1106.

Poblaciones, M.J., Rodrigo, S., Santamaria, O., Chen, Y., & McGrath, S.P. Agronomic selenium biofortification in Triticum durum under Mediterranean conditions: From grain to cooked pasta. *Food Chem.* 2014, 146, 378–384.

Potrykus, I. (2010). Lessons from the “Humanitarian Golden Rice” project: Regulation prevents development of public good genetically engineered crop products. *New Biotechnol.*, 27: 466–472.

Potrykus, I. (2010). Regulation must be revolutionized. *Nature*, 466: 561.

Potrykus, I. (2010). The private sector’s role in public sector genetically engineered crop projects. *New Biotechnol.*, 27: 578–581.

Prasad, A.S. (1996). Zinc deficiency in women, infants, and children. *J.Am. Coll. Nutr.*, 15: 113–120.

Prasad, A.S., Bao, B., Beck, F.W., Kucuk, O., & Sarkar, F.H. (2004). Antioxidant effect of zinc in humans. *FreeRadic. Biol. Med.*, 37: 1182–1190.

Ramos, M.I., Allen, L.H., Mungas, D.M., Jagust, W.J., Haan, M.N., Green, R., & Miller, J.W. (2005). Low folate status is associated with impaired cognitive function and dementia in the Sacramento Area Latino Study on Aging. *Am. J. Clin. Nutr.*, 82: 1346–1352.

Rao, C.K. (2008). Causes of Death of Cattle and Sheep in the Telengana Region of Andhra Pradesh in India; Foundation for Biotechnology Awareness and Education: Bangalore, India.

Ray, H., Bett, K.E., Tar’an, B., Vandenberg, A., Thavarajah, D., & Warkentin, T. (2014). Mineral micronutrient content of cultivars of field pea, chickpea, common bean, and lentil grown in Saskatchewan, *Canada. Crop Sci.*, 54: 1698–1708.

Rayman, M.P. (2005). Selenium in cancer prevention: A review of the evidence and mechanism of action. *Proc. Nutr. Soc.*, 64: 527–542.

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

Richter, L.J., Thanavala, Y., Arntzen, C.J., & Mason, H.S. (2000). Production of hepatitis B surface antigen in transgenic plants for oral immunization. *Nat. Biotechnol.*, 18: 1167–1171.

Rodrigo, S., Santamaría, O., Chen, Y., McGrath, S.P., & Poblanos, M.J. (2014). Selenium speciation in malt, wort, and beer made from selenium-biofortified two-rowed barley grain. *J. Agric. Food Chem.*, 62: 5948–5953.

Roohani, N., Hurrell, R., Kelishadi, R., & Schulin, R. (2013). 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., & Pinnell, S.R. (2002). Evidence supporting zinc as an important antioxidant for skin. *Int. J. Dermatol.*, 41: 606–611.

Roy, F., Boye, J.I., & Simpson, B.K. (2010). Bioactive proteins and peptides in pulse crops: Pea, chickpea and lentil. *Food Res. Int.*, 43: 432–442.

Ruiz-López, N., Haslam, R.P., Napier, J.A., & Sayanova, O. (2014). Successful high-level accumulation of fish oil omega-3 long-chain polyunsaturated fatty acids in a transgenic oilseed crop. *Plant J.*, 77: 198–208.

Ruiz-López, N.I., Haslam, R.P., Venegas-Calérón, M., Li, T., Bauer, J., Napier, J.A., & Sayanova, O. (2012). Enhancing the accumulation of omega-3 long chain polyunsaturated fatty acids in transgenic Arabidopsis thaliana via iterative metabolic engineering and genetic crossing. *Transgenic Res.*, 21: 1233–1243.

Sarker, A., El-Askhar, F., Uddin, M.J., Million, E., Yadav, N.K., Dahan, R., & Wolfgang, P. (2007). Lentil improvement for nutritional security in the developing world. Presented at the ASA-CSSA-SSSA International Annual Meeting, New Orleans, LA, USA, 4–8 November 2007.

Sathya, A., Vijayabharati, R., Srinivas, V., & Gopalakrishnan, S. (2013). Plant growth-promoting action-bacteria on chickpea seed mineral density: An upcoming complementary tool for sustainable biofortification strategy. *3 Biotech*, 6: 138.

Sayre, R., Beeching, J.R., Cahoon, E.B., Egesi, C., Fauquet, C., Fellman, J., Fregene, M., Gruissem, W., Mallowa, S., Manary, M.; Maziya-Dixon, B., Mhbanaso, A., Schachtman, D.P., Siritunga, D., Tarloy, N., Vandershuren, H., & Zhang, P. (2011). The BioCassava plus program: Biofortification of cassava for sub-Saharan Africa. *Annu. Rev. Plant Biol.* 62: 251–272.

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

Scholl, T.O., & Johnson, W.G. (2000). Folic acid: Influence on the outcome of pregnancy. *Am. J. Clin. Nutr.*, 71: 1295S–1303S.

Schubert, D.R. (2008). The problem with nutritionally enhanced plants. *J. Med. Food*, 11: 601–605, doi:10.1089/jmf.2008.0094.

Scott, J., R’beill’e, F., & Fletcher, J. (2000). Folic acid and folate: The feasibility for nutritional enhancement in plant foods. *J. Sci. Food Agric.*, 80: 795–824.

Seshadri, S., Beiser, A., Selhub, J., Jacques, P.F., Rosenberg, I.H., D’Agostino, R.B., Wilson, P.W.F., & Wolf, P.A. (2002). Plasma homocysteine as a risk factor for dementia and Alzheimer’s disease. *N. Engl. J. Med.*, 346: 476–483.

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

Shi, J., Wang, H., Hazebroek, J., Ertl, D.S., & 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.

Shohag, M.J.I., Wei, Y., & Yang, X. (2012). Changes of folate and other potential health promoting phytochemicals in legume seeds as affected by germination. *J. Agric. Food Chem.*, 60: 9137–9143.

Shumskaya, M., & Wurtzel E.T. (2013). The carotenoid biosynthetic pathway: Thinking in all dimensions. *Plant Sci.*, 208: 58–63.

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

Siró, I., Kápolna, E., Kápolna, B., & Lugasi, A.
(2008). Author information Functional food. Product development, marketing and consumer acceptance - A review. Appetite, 51: 456–467.

Skeaff, S.A. (2011). Iodine deficiency in pregnancy: The effect on neurodevelopment in the child. Nutrients, 3: 265–273.

Smith, S.E., & Read, D.J. Mycorrhizal Symbiosis, 3rd ed.; Elsevier: London, UK. 2007. 127.

Soe, K.M., Bhromsiri, A., & Karladee, D. (2010) Effects of selected endophytic actinomycetes (Streptomyces sp.) and Brady rhizobia from Myanmar on growth, nodulation, nitrogen fixation and yield of different soybean varieties. CMU J. Nat. Sci., 9: 95–109.

Soe, K.M., Bhromsiri, A., & Karladee, D. (2010). Effects of selected endophytic actinomycetes (Streptomyces sp.) and Bradyrhizobia from Myanmar on growth, nodulation, nitrogen fixation and yield of different soybean varieties. CMU J. Nat. Sci., 9: 95–109.

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

Stephens, D., Jackson, P.L., & Gutierrez, Y. (1996). Subclinical vitamin A deficiency: A potentially unrecognized problem in the United States. Pediatr. Nurs., 22: 377–389.

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

Sujak, A., Gabielska, J., Grudzinski, W., Borc, R., Mazurek, P., & Gruszczki, W.I. (1999). Lutein and zeaxanthin as protectors of lipid membranes against oxidative damage: The structural aspects. Arch. Biochem. Biophys., 371: 301–307.

Sutherlin, E. (2013). Could Congress finally end the GMO labeling war. The Genetic Literacy Project; The City University of New York: New York, NY, USA.

Talano, M. A., Oller, A.L., González, P.S., Agostini, E. (2012). Hairy roots, their multiple applications and recent patents. Recent Pat. Biotechnol., 6: 115–133.

Tamura, T., & Picciano, M.F. (2006). Folate and human reproduction. Am. J.Clin. Nutr., 83: 993–1016.

Tanaka, T., Shnimizu, M., & Moriwaki, H. (2012). Cancer chemoprevention by carotenoids. Molecules, 17: 3202–3242.

Tang, G., Hu, Y., Yin, S.A., Wang, Y., Dallal, G.E., Grusak, M.A., & Russell, R.M. (2012). β-Carotene in Golden Rice is as good as β-carotene in oil at providing vitamin A to children. Am. J. Clin. Nutr., 96: 658–664.

Tang, G., Qin, J., Dolnikowski, G.G., Russell, R.M., & Grusak, M.A. (2009). Golden Rice is an effective source of vitamin A. Am. J. Clin. Nutr., 89: 1776–1783.

Tang, M., He, X., Luo, Y., Ma, L., Tang, X., & Huang, K. (2013). Nutritional assessment of transgenic lysine-rich maize compared with conventional quality protein maize. J. Sci. Food Agric., 93: 1049–1054.

Tanumihardjo, S.A., Palacios, N., & Pixley, K.V. (2010). Provitamin a carotenoid bioavailability: What really matters? Int. J. Vitam. Nutr. Res., 80: 336–350.

Theil, E. (1987) Ferritin: Structure, gene regulation, and cellular function in animals, plants and microorganisms. Annu. Rev. Biochem., 56: 289–315.

Theil, E.C. (2003) Ferritin: At the crossroads of iron and oxygen metabolism. J. Nutr., 133: 1549–1553.

Theil, E.C. (2011) Iron homeostasis and nutritional iron deficiency. J. Nutr. 141: 724S–728S.

Tinggi, U. (2008). Selenium: Its role as antioxidant in human health. Environ. Health Prev. Med., 13: 102–108.

Tokala, R.K., Strap, J.L., Jung, C.M., Crawford, D.L., Salove, M.H., Deobald, L.A., Bailey, J.F., & Morra, M.J. (2002) Novel plant-microbe rhizosphere interaction involving Streptomyces lydicus WYEC108 and the pea plant (Pisum sativum). Appl. Environ. Microbiol., 68: 2161–2171.

Tong, Z., Xie, C., Ma, L., Liu, L., Jin, Y., Dong, J., & Wangm, T. (2014). Co-expression of bacterial aspartate kinase and adenylylsulfate reductase genes substantially increases sulfur amino acid levels in transgenic alfalfa (Medicago sativa L.). PLoS One, 9: e88–310.

Trijatmiko, K.R., Dueñas, C., Tsakirpaloglu, N., Torrizo, L., Arines, F.M., Adeva, C., Balindong, J., Oliva, N., Saposap, M.V., Borrero, J., Rey, J., Francisco, P., Nelson, A., Nakanishi, H., Lombi, E., Tako, E., Glahn, 269
R.P., Stangoulis, J., Chadha-Mohanty, P., Johnson, A.A.T., Tohme, J., Barry, G., & Slamet-Loedin, I.H. (2016). Biofortified indica rice attains iron and zinc nutrition dietary targets in the field. *Sci. Rep.*, 6: 19792.

Tsakirpaloglou, N., Mallikarjuna Swamy, B.P., Acuin, C., & Slamet-Loedin, I.H. (2019) Biofortified Zn and Fe rice: Potential contribution for dietary mineral and human health. In *Nutritional Quality Improvement in Plants*. Concepts and Strategies in Plant Sciences; Jaiwal, P., Chhillar, A., Chaudhary, D., Jaiwal, R., Eds.; Springer: Cham, Switzerland, pp. 1–24.

Tulchinsky, T. H. (2010). Micronutrient deficiency conditions: Global health issues. *Public Health Rev.*, 32: 243.

Valverde, A., Burgos, A., Fiscella, T., Rivas, R., Velazquez, E., Rodriguez-Barrueco, C., Cervantes, E., Chamber, M., & Igual, J.M. (2006). Differential effects of co-inoculations with *Pseudomonas jessenii* PS06 (a phosphate-solubilizing bacterium) and *Mesorhizobium ciceri* C-2/2 strains on the growth and seed yield of chickpea under greenhouse and field conditions. *Plant Soil*, 287: 43–50.

Van Loo-Bouwman, C.A., Naber, T.H., & Schaafsma, G. (2014). A review of vitamin A equivalency of β-carotene in various food matrices for human consumption. *Br. J. Nutr.*, 111: 2153–2166, doi:10.1017/S0007114514001166.

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

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

Vermeris, W., & Nicholson, R. (2006). Phenolic Compound Biochemistry; Springer: Dordrecht, The Netherlands.

Wallock, L.M., Tamura, T., Mayr, C.A., Johnston, K.E., Ames, B.N., & Jacob, R.A. (2001) Low seminal plasma folate concentrations are associated with low sperm density and count in male smokers and nonsmokers. *Fertil. Steril.* 75: 252–259.

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

Watanabe, K.N., Sasa, Y., Suda, E., Chen, C.H., Inaba, M., & Kikuchi, A. (2005). Global political, economic, social and technological issues on transgenic crops-review. *Plant Biotechnol. J.*, 22: 515–522.

Waters, B.M., & Grусak, M.A. (2008). Quantitative trait locus mapping for seed mineral concentrations in two Arabidopsis thaliana recombinant inbred populations. *NewPhytol.*, 179: 1033–1047.

Welch, R.M. (2002). Breeding strategies for biofortified staple plant foods to reduce micronutrient malnutrition globally. *J. Nutr.*, 132: 495S–499S.

Welch, R.M., & Graham, R.D. (2005). Agriculture: The real nexus for enhancing bioavailable micronutrients in food crops. *J. Trace Elem. Med. Biol.*, 18: 299–307.

Wesseler, J., & Zilberman, D. (2014). The economic power of the Golden Rice opposition. *Environ. Dev. Econ.*, 19: 724–742.

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

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

Wilson, S.A., & Roberts, S.C. (2014). Metabolic engineering approaches for production of biochemicals in food and medicinal plants. *Curr. Opin. Biotechnol.*, 26: 174–182.
Wiltgren, A.R., Booth, A.O., Kaur, G., Cicerale, S., Lacy, K.E., Thorpe, M.G., Keast, R.S., & Riddell, L.J. (2015). Micronutrient supplement use and diet quality in university students. *Nutrients*, 7: 1094–1107.

Winger, R., Konig, J., & House, D. (2008) Technological issues associated with iodine fortification of foods. *Trends Food Sci. Technol.*, 19: 94–101.

Winkler, J. T. (2011). Biofortification: Improving the nutritional quality of staple crops. In Access Not Excess; Pasternak, C., Ed.; Smith-Gordon Publishing: St Ives, UK, pp. 100–112.

World Health Organization. (2008). Worldwide Prevalence of Anaemia 1993–2005: WHO Global Database on Anaemia; de Benoist, B., McLean, E., Egli, I., Cogswell, M., Eds.; WHO: Geneva, Switzerland.

World Health Organization. (2007). Iodine Deficiency in Europe: A Continuing Public Health Problem; Andersson, M., de Benoist, B., Darnton-Hill, I., Eds.; WHO: Geneva, Switzerland.

World Health Organization. (2007): 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.

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

World Health Organization and Food and Agriculture Organization. (2004) Vitamin and Mineral Requirements in Human Nutrition, 2nd ed.; WHO: Geneva, Switzerland.

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

Xudong, Y., al-Babili, S., Klöti, A., Zhang, J., Lucca, P., Beyer, P., & Potrykus, I. (2000). Engineering the provitamin A (b-carotene) biosynthetic pathway into carotenoid-free rice endosperm. *Science*, 287: 303–305.

Yamaguchi, M., & Uchiyama, S. (2004). beta-Cryptoxanthin stimulates bone formation and inhibits bone resorption in tissue culture in vitro. *Mol. Cell. Biochem.*, 258: 137–144.

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

Zhang, Y., Xu, X., Zhou, X., Chen, R., Yang, P., Meng, Q., Meng, K., Luo, H., Yuan, J., Yao, B., & Wei, Z. (2013). Over expression of an acidic endo-β-1,3-1,4-glucanase in transgenic maize seed for direct utilization in animal feed. *PLoS One*, 8: 81-993.

**How to cite this article:**

Iyabo Christianah Oladipo and Olatayo Shamsudeen Ishola. 2020. Biofortification and Human Health. *Int.J.Curr.Microbiol.App.Sci.* 9(07): 247-271.

doi: https://doi.org/10.20546/ijcmas.2020.907.028