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REVIEW PAPER

BIOFORTIFICATION AND THE INVOLVED MODERN APPROACHES

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Abstract

Being responsible for severe social and health issues, micronutrient malnutrition gives rise to serious apprehension throughout the world. Nutrition is the key factor in any strategy designed to reduce the burden of diseases globally. More than 3 billion people around the world suffer from micronutrient deficiency due to the consumption of poor-quality food. The green revolution fulfilled the need for greater yield, but the quality of the developed crops suffered. Today, poor people predominantly are suffering from micronutrient malnutrition as they cannot afford dietary supplementation due to poverty. Brain development and other body mechanisms and functions are critically affected due to the consumption of Zn and Fe deficient diet. Hence, the production of biofortified food crops is the need of time to solve the problem of micronutrient deficiency on a sustainable basis. Biofortification of commonly used food crops will offer the simplest solution to complex nutritional disorders. So, experimentation and testing should be done at both national and international levels to improve food quality and quantity. This review discusses different biofortification strategies that are employed to counteract several nutrient deficiencies. The role of several international agencies in this direction has also been discussed. This may help researchers to have an overview of the approaches in which more advancement is required. We emphasize that more efforts to modify the existing genomes using molecular techniques can open new pathways in the field of biofortification.

Keywords: agriculture, biofortification, hidden hunger, malnutrition, wheat.

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INTRODUCTION

Good nutrition is the key to good health (Magni et al. 2017), and it is heavily dependent on sustainable agriculture (WHO 2018). The quest for quality food has risen from the fact that the world's population is increasing constantly (United Nations 2017), and is expected to be 9.8 billion by the end of 2050 (Kaneda et al. 2015). Unfortunately, for producing more food, the quality factor has been ignored. Nowadays, undernourishment is a significant problem (Webb et al. 2018). Micronutrient deficiencies causing various nutritional disorders have become a global issue (Haddad et al. 2016) and have gained significant attention from scientists from almost all the sectors, including health, nutrition, economic, tourism, and agriculture sector (Feng et al. 2019). These deficiencies are prevalent due to regular inadequacies in diets, or dependence of people on a single staple food crop, especially on cereals (Datta, Vitolins 2016). These food insecurities are more challenging in developing and under-developed countries (Pérez-Escamilla 2017) mainly due to poor lifestyle and diets (Gakidou et al. 2017). To overcome endemic nutritional diseases, commonly used food crops are fortified or some other supplement measures are taken into account (Bouis et al. 2017).

The addition of missing nutrients to target food to counteract their deficiency is called fortification (Bouis et al. 2011). Although fortification of staple food crops is the need of the hour, it is rather expensive, mostly available in urban areas (Bouis, Welch 2010) and is hardly affordable by poor populations (Gilligan 2012). Supplementation and fortification can only work best in centralized urban areas, where infrastructure is good enough to support such programs. However, supplementation can easily lead to overdosing and may cause diseases (Pérez-Massot et al. 2013). Additionally, there are concerns regarding technologicy, costs and safety considerations (Sharma et al. 2017). The biofortification of food crops is a promising solution (Connorton, Balk 2019) as it is strongly related to the improvement in food production systems (Rani et al. 2018).

For human health disorders, prophylactic measures are much better than numerous rounds of remedial measures. There is an exigent requisite for the attainment of goals set in the public health sphere, both nationally and internationally, and relevant policies should be implemented, especially in developing countries. Hence, this review will mainly focus on Zn and Fe deficiency symptoms in plants and humans, health problems created by hidden hunger, and the role of modern agriculture to produce the quality crops for reducing the problem of malnutrition.

BARRIERS FOR THE ACCUMULATION OF MICRONUTRIENTS IN PLANTS

One of major obstacles to biofortification is the lack of knowledge about the loading of minerals to seeds, and uncertainties about the genes and pathways to target for modifications (Waters, Sankaran 2011). Additionally, climate change has resulted in significant reduction in nutrients accumulated in plants (Milius 2017).

There are several barriers that need to be overcome for the enhanced accumulation of more micronutrients in the edible portion of plants (Figure 1). These are controlled by homeostasis, which has an important role in the regulation of metal absorption, translocation, and redistribution in the plant body (Kulcheski et al. 2015).

The rhizosphere creates one of the biggest barriers. Essentially, soil is the main supplier of micronutrients to plants and hence their bioavailability is influenced by various soil and environmental factors (Rawat et al. 2019).

Plant roots uptake nutrients from the soil and transport them to aerial plant parts. Before entering the plants, these nutrients have to pass through the concentric layers of epidermis, root cortex, and endodermis. Differentiation of endodermis and its developmental plasticity functions as barriers to nutrient translocation in plants (Barberon 2017).

Absorption mechanisms (i.e. ion channels and transporters) present in the plasma membrane of root cells also act as a barrier for the movement of nutrients to plants. If they are not active and specific, then they hinder

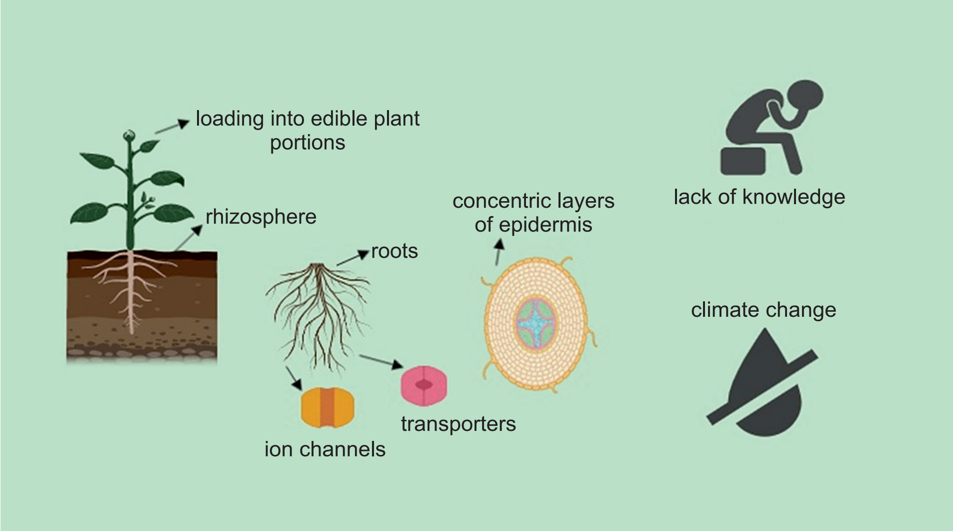

Fig. 1. Barriers to the accumulation of micronutrients in edible plant parts

the entrance of micronutrients into the apoplasm of root cells, and thus their translocation to the plants is reduced (Hosmani et al. 2013, Kamiya et al. 2015, Doblas et al. 2017, Li et al. 2017).

ENRICHING CROPS WITH VITAMINS AND NUTRACEUTICALS

Vitamin and nutritional deficiencies can be treated by biofortifying local varieties of food crops, and this solution can greatly reduce the burden of vitamin deficiencies. Thus, the demand for biofortified foods supplemented with various vitamins, such as A, C, E and phytochemicals called nutraceuticals, has increased to a significant extent due to their importance in preventing diseases and malnutrition (Lobo et al. 2010). For biofortification of food crops with vitamins and nutraceuticals, various methods are being used, such as agronomical methods, conventional breeding, and transgenic techniques (Levine et al. 1995, Chen et al. 2003, Storozhenko et al. 2007, Zhu et al. 2007, Aluru et al. 2008, Cong et al. 2009, Wang et al. 2014, Blancquaert et al. 2015, Decourcelle et al. 2015,). Selection, introduction, and hybridization are the most popular methods in conventional breeding used for the development of nutraceuticals in food crops. Conventional breeding relies on the presence of variation in vitamins in the germplasm that is sexually compatible (Strobbe, Van Der Straeten 2017). Various researchers have identified the nutraceutical sources, and have transferred them in high yielding cultivars by using traditional breeding methods. In traditional methods, intrinsic properties of specific food crops are used, but this approach takes a relatively long time. Due to some technical disadvantages in conventional breeding methods, transgenic approaches are now being widely used for the bioaccumulation of nutraceuticals in food crops. Transgenic approaches are rapid and have direct applicability for elite cultivars. This technique helps the transfer of desired genes responsible for delivering nutraceuticals to the edible portion of food crops (Garg et al. 2018). Metabolic engineering by utilizing the GM technology helps to introduce multiple desired genes that in turn directly influence the metabolism of a plant towards greater accumulation of elements. This technology is not dependent on the gene sources based on sexual compatibility, and the genetic elements from the diversified pools can also be utilized.

ENRICHING CROPS WITH IODINE AND SELENIUM

Selenium is a microelement that is required in smaller amounts, but it can easily reach the toxicity level. Almost 15% population across the globe is affected by the selenium deficiency in foods. Currently, the trend to biofortify crops with Se is less strong than Zn and Fe biofortification. As cereals and vegetables are widely consumed on a daily basis throughout the world, biofortification of these crops with Se and other micronutrients can offer a great contribution to the alleviation of these deficiencies. Soil fertilization with Se is considered an important aspect of increasing the Se content (Chen et al. 2002, Fang et al. 2008, Ros et al. 2016). In Finland, the addition of Se in fertilizers has been manadatory since 1984, and at present all fertilizers in that country are supplied with 10 mg S kg^{-1} (White et al. 2007). Additionally, transgenic approaches have been successful in enhancing the bioaccumulation of Se in edible plant parts (LeDuc et al. 2004). However, it is extremely important to prevent toxicity levels of Se in food crops, as slightly elevated concentrations in a human body can evoke various problems.

In many countries worldwide, iodine deficiency is a serious concern for human health. Although Sub-Saharan African and South Asian countries are mostly suffering from the lower intake of iodine, this problem also exists in developed countries, including Australia, the USA, and Europe. About 2 billion people are affected by iodine deficiency. Iodine can be supplied to edible parts of plants by foliar or soil application. In addition to the fertilizer's application, iodine biofortification can also be achieved by transgenic approaches as an alternative, where the genome analysis, metabolomics, whole-genome sequencing, and DNA sequencing techniques are employed (Landini et al. 2012, Smoleń et al. 2014). Both Se and I are required for maintaining the thyroid health; thus, biofortification is worthwhile our attention as a solution to this problem (Smoleń et al. 2014, 2016).

ROLE OF MODERN AGRICULTURE

At present, it is agreed that researchers in the fields of nutrition and agriculture should work together to make the greatest impact to reduce malnutrition (Dubock 2017). Continued improvement in nutritional quality and yield of agricultural crops will constitute a basic step towards nutritional and food security for the growing world population (Goicoechea, Antolín 2017).

Earlier, the green revolution has significantly increased the production of grain crops, but it has also contributed to a greater proportion of undernourished people all over the world (Smoleń et al. 2016). An increase in yield has caused a dilution effect, with lower levels of mineral nutrients in grains (Shewry et al. 2016).

However, there have been significant advances in the past few years, owing to modern agricultural techniques, regarding yield improvement and

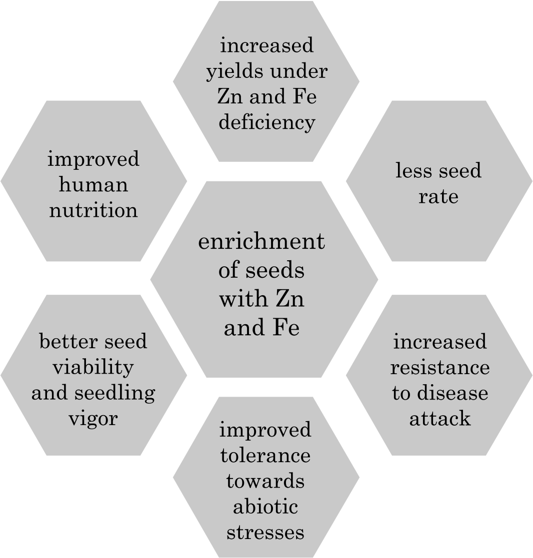

Fig. 2. Benefits of using Zn and Fe enriched seeds

crop quality (Shah, Wu 2019). There is great potential to mitigate the widespread problem of Fe and Zn deficiency in human beings by improving the Fe and Zn content in grains (Phattarakul et al. 2012) – Figure 2.

By using modern agricultural practices, biofortified seeds have been produced, which are more useful for crop production, are more resistant to stresses and diseases, and produce more uniform yields (Ros et al. 2016). The economic situation is critical for the fortification of foods during the processing steps; however, it is difficult and even unnecessary for large rural populations to consume processed foods. Moreover, it should be taken into account that most of developing countries lack viable food processing industries and proper product distribution channels, which is a consequence of economic shortages and the unwillingness of authorities towards this aspect.

Based on the above considerations, it can be concluded that a long-term solution for large rural populations may include ensuring their access to diversified diet. Thus, the alternative biofortification approach is much promising because it targets mainly economically disadvantageous large rural populations of the developing world. To date, biofortified food crops have been successfully used in different parts of the world (Haas et al. 2005, Garg et al. 2018).

BIOFORTIFICATION BY APPLICATION OF PLANT GROWTH PROMOTING RHIZOBACTERIA

Complex microbial community is developed when plants are grown under field conditions (Lundberg et al. 2012). A well-regulated and structural community of microorganisms in the soil is always associated with plants (Smith et al. 2017). Bacteria are the basic elements and have a strong association with all plant structures (Berg et al. 2015). Plants exert beneficial effects on rhizobacteria by producing root exudates of many compositions (Zhang et al. 2017). The use of plant growth-promoting rhizobacteria is an important bio-revolution to increase the bioavailability of nutrients to the plants (Timmusk et al. 2017).

Soils with dynamic ecologies of microbes and more organic matter have low requirements for fertilizers than the soils which are conventionally managed (Bender et al. 2016). Interactions between plants and microbes have a direct role in the improvement of plant nutrition by increasing the solubility and bioavailability of plant nutrients and thus, improves the nutrient contents in edible plant portions (Manikandan, Subramanian 2016).

Many microbial strains have been reported to increase the solubility and bioavailability of Zn and Fe with special reference to the improvement in plant yield and quality in various crops (Saha et al. 2016).

Micronutrient bioavailability in the soil is greatly affected by the soil physio-chemical characteristics, which can be modified by the plant microbial interactions (Ray, Banik 2016). Inoculation with a combination of strains results in better effects than inoculation with individual rhizobacterial strain. Additionally, the application of Zn solubilizing PGPR also increases the production of siderophores, solubilization of phosphorus, nitrogen fixation, tolerance against diseases (Andreote, Silva 2017) and protection against abiotic and biotic stresses (Othman et al. 2017).

BIOFORTIFICATION BY GENETIC MODIFICATION APPROACH

The transgenic approach is a promising technique for the production of biofortified crops (Bouis et al. 2017) and novel genetic information is directly introduced into the plant genome. It is a better alternative to develop biofortified crops when there is no genetic variation in the nutritional contents of genotypes (Brinch-Pedersen et al. 2007).

Especially when a specific micronutrient is not naturally present in the crop, then the transgenic approach is one of the effective feasible options for the genetic fortification of that crop with particular nutrient

(Pérez-Massot et al. 2013). Gene functions are identified and characterized and then they are utilized to engineer the plant`s metabolism to reduce anti-nutrients factors and to increase the concentration of promoter substances and to increase the concentration of micronutrients by making them more bio-available (Christou, Twyman 2004).

Additionally, genetic modifications can be used to target the redistribution of micronutrients in between the tissues to increase their concentration in the edible parts of the plant. Even selected pathways can be reconstructed to improve the efficiency of specific biochemical processes in the edible parts (Hefferon 2016).

Though the transgenic approach involves more efforts, investment and time, but in the long turn, this is one of the most sustainable approaches (Hefferon 2016). Transgenic wheat, rice (Trijatmiko et al. 2016) barley, maize, sorghum, legumes and pulses, common beans, lupines, vegetables, oilseeds, fruits and even, transgenic fodder have been produced (Garg et al. 2018).

Crops are genetically modified after breeding to improve the absorption capacity and nutritional status of the grains (Bouis et al. 2003). Modern advancement in the discipline of plant breeding has become the root cause to reduce the malnutrition caused by the lack of genetic diversity in micronutrients (Trijatmiko et al. 2016). QTL mapping for seed mineral concentrations also serves as a master regulator for the fulfillment of seed micronutrient demands. The manipulation of such regulators could be used to ideally accomplish all the steps at the same time (Li et al. 2018).

BIOFORTIFICATION BY AGRONOMIC PRACTICES

Biofortification is a long journey from soil to grains (Hefferon 2015). In the food chain, plants are an initial link, so enhanced uptake of minerals from soil to plant parts is essential for the achievement of biofortification (Basu 2016).

By growing high yielding varieties, the micronutrient content of crops becomes decreased due to more intensive mining of nutrients from the soil. So, the replenishment of nutrients by fertilizer application and by management practices is essential (Jones, de-Brauw 2015). Therefore, successful biofortification is strongly dependent on the external application of micronutrients to the soil-plant system (Dimkpa, Bindraban 2016).

Application of Zn and Fe fertilizers is a useful and quick solution to produce biofortified food crops, and this approach can be easily implemented in developing countries (Cakmak, Kutman 2018). Mostly Zn deficiency in wheat is due to the shortage of soil moisture because of irregular and scanty rainfalls, so moisture levels shouod be adjusted properly (Karim, Rahman 2015).

The type of fertilizer, method of application, packaging, and plant developmental stages at which fertilizer is applied are also important (Jones, de-Brauw 2015). Additionally, the cropping system, intercropping, and crop rotations increase the crop yield and improve quality (Zuo et al. 2000). Biofortification can be achieved by seed treatment and by foliar application of fertilizers (Rehman et al. 2016).

Micronutrients can also be applied along with the soil amendment substances to increase crop yield and nutritional quality (Vanlauwe et al. 2015). Fertilizers along with organic matter significantly improve micronutrient content in soil and their bioavailability (Thilakarathna, Raizada 2015). The application of Zn fertilizer along with green manure has improved grain Zn content and yield of Basmati rice in India (Pooniy, Shivay 2013). Foliar application is a useful agronomic biofortification strategy that provides mineral fertilizers in the most appropriate, phyto-available form (Lawson et al. 2015). However, it is not a feasible approach in windy and rainy areas (García-Bañuelos et al. 2014).

There is not a single approach that could invariable produce superior results, hence an integrated micronutrient management system and supply chain approach as a whole are required to meet the demand of attaining higher Fe and Zn content in edible portions of plants (Zhang et al. 2017).

BIOFORTIFICATION USING NANOTECHNOLOGY

Nanotechnology is a field offering numerous scientific applications. Among several advancements in technology, nanotechnology seems to be a promising direction in agriculture (Elemike et al. 2019). The formulation of fertilizers has a strong impact on the bioavailability of micronutrients. Depending on the type and size of applied fertilizers, there can be neutral, positive or negative interactions, thus affecting the nutrient use efficiency and the yield (Thakur et al. 2018).

The micronutrient use efficiency of commercial fertilizers ranges between just 2.5% to 5%. This is due to their relative stabilization in soil, less intensive penetration into the leaf surface, and low mobility within plant parts. Conventional fertilizers are unable to synchronize the release of micronutrients from plant fertilizing sources (Table 1).

By decreasing the particle size of applied fertilizers, more nutrients can be be uptaken by plant roots, as there are more reaction sites, in addition to which nanoparticles are in a continuous state of motion called “the Brownian motion” (Jiang et al. 2018). Thus, biofortification through nanotechnology offers opportunities for boosting agricultural productivity and enhancing food quality as well as nutritional value in an eco-friendly manner.

Table 1

RDA Values for Fe, Zn, I and Se in Human Beings

Age	Male/Female			
	Fe (mg)	Zn (mg)	Iodine (mcg)	Selenium (µg)
Birth to 6 months	0.27/0.27	-	110/110	-
7-12 months	11/11	3/3	130/130	-
1-3 years	7/7	3/3	90/90	20/20
4-8 years	10/10	5/5	90/90	30/30
9-13 years	8/8	8/8	120/120	40/40
14-18 years	11/15	11/9	150/150	55/55
19-50 years	8/18	11/8	150/150	-
51 plus years	8/8	11/8	150/150	-

HARVEST PLUS AND OTHER INTERNATIONAL ORGANIZATIONS WORKING FOR BIOFORTIFICATION

HarvestPlus is a leader in its global efforts to develop and disseminate quality staple food crops. It is an interdisciplinary program active in over 40 countries and carried out in collaboration with both public and private sectors, including such organizations as the International Center for Tropical Agriculture (CIAT), International Rice Research Institute (IRRI), National Agricultural Research and Extension Systems – NARES ANDERSSON et al. 2017. Consultative Group on International Agriculture Research (CGIAR) and the World Health Organization have included the programs in their main goals to develop high yielding and nutritional rich biofortified crops. Collaborative international interdisciplinary efforts are required to solve the problem of malnutrition (PLUS 2012). To reduce the travel cost, significant global and regional meetings could be organized as satellite-boradcast meetings, which will also serve as an outreach component.

CONCLUSIONS

Currently, a direct pathway towards better nutrition is needed to generate considerable economic benefits. Biofortification is a lasting and self-sustaining solution. There is a dire need to ensure food security, ensuring nutritional advocacy and responding to dietary recommendations. Thus, multi-faceted plans should be implemented to address the problem of malnutrition in a synchronized manner. The persistent burden of malnutrition should be submitted to intensive research by dedicated scientists from many disciplines. Policy-makers and researchers should define appropriate approaches to strove towards food security and balanced nutrition. The research community needs to focus on biofortification with special concern to demand-driven innovations. By using modern and advanced technologies, it is possible to serve communities sensibly, ensuring optimism owing to dynamically achieved results that can be successfully transformed into reality.

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