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Iron biofortification: a much-needed strategy for prevailing conditions of micronutrient malnutrition

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Abstract
Micronutrient-malnutrition is one of the most serious battle human beings are fighting. The so-called Hidden hunger is all because of micronutrient deficiencies. Iron deficiency anemia is affecting more people than any other prevailing disorder. However, iron-supplementation aggravate the infectious diseases and present policies of iron therapy carefully evaluate the pros and cons. In current review, we have evaluated the biofortification approaches for combating hidden hunger, in the light of medical and nutritional advancements. Enhancement of iron in edible plant parts is expected to improve nutrient status of human beings via crops. The density of minerals and vitamins in staple foods consumed by the poor can be raised using either traditional plant breeding or transgenic approaches, a process known as biofortification. Microbial iron biofortification is a valuable approach for human being especially in developing countries where poor people cannot afford to buy expensive supplementation. Moreover, prevailing condition of Covid-19 demands a fighting immune system and iron is likely to play vital role in improving human immune system.

Keywords
Micronutrient, malnutrition, biofortification, human health

Introduction

Micronutrients are considered to be of the highest significance to human beings. A lack of micronutrients has a significant detrimental effect on the health of a human being. According to Dommisch et al. (2018), micronutrients malnutrition is responsible for the mortality of 3 million children each year. Iron (Fe) insufficiency is the most common kind of micronutrient deficiency, affecting more than 2 billion people throughout the world, particularly in poor nations (Mayer et al., 2008). Anemia caused by a lack of iron can affect up to half of all pregnant women and up to forty percent of all pre-school-aged children. The human immune system relies heavily on iron to function properly (Vieth and Lane, 2014).

In order to successfully combat the viral infection caused by COVID-19 in its current state, a strong immune system is required. Iron deficiency anemia, often known as IDA, can severely impair both a person's physical development and their immune. The majority of nations struggle more with an inadequate intake of micronutrients than with insufficient amounts of calories. Anemia is caused by a number of factors, the most significant of which is the presence of malaria in regions where it is transmitted. Inadequate nutrition, the malaria infection itself, intestinal helminths, and HIV infection during pregnancy are among these risk factors. A lack of iron throughout the first few years of a person's existence has been linked to subpar brain development, according to a paper that was published

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not too long ago (Gromova et al., 2020).

Food fortification, pharmacological supplementation, and dietary diversity are three common approaches that are frequently employed to combat iron deficiency in both poor and wealthy nations. These prevalent tactics are hampered by socioeconomic circumstances, such as an insufficient amount to buy fortified foods and supplements, a lack of access to diverse meals, a lack of access to suitable agricultural infrastructure, and most crucially, an absence of long-term government policy. Another problem that arises is whether the general public would accept fortified foods due of changes in flavor and color (Thompson, 2007).

The World Health Organization recommends three methods for dealing with micronutrient deficits:

a. Enhanced nutritional status via the avoidance and correction of vitamin deficiencies;

b. Raising crop plants' iron levels;

c. Vaccination and other measures to prevent infection.

The biofortification of food crops is a viable, cost-effective, and long-term option. Biofortification has been used to increase the micronutrient content of potato, wheat, rice, beans, and maize (Sawicka et al., 2019) as part of the HarvestPlus program run by the Consultative Group on International Agricultural Research (CGIAR). It is crucial to have a deep understanding of the molecular mechanisms involved in nutrient intake and translocation. Iron consumption can be increased through food fortification, biofortification, and pharmaceutical supplementation. The World Health Organization (WHO) recognized in 2010 as a possible remedy for iron deficiency in malnourished people in developing nations. A correct line for iron supplementation is essential in nations where infectious illnesses are common. Iron-fortified foods include the NaFeEDTA-enhanced fish sauce consumed by Vietnamese ladies. It is possible to increase the iron content of food using a combination of agronomic fertilization and iron chelation, but this is not a widespread or sustainable practice in developing nations. The overuse of fertilizers has contributed to ecological problems. Iron-enriched food could be distributed to the world's undernourished population through a combination of conventional breeding and genetic engineering. These methods are being implemented in poor nations because of their low financial and ecological costs and their long-term viability. Even in low-income nations, biofortification is a practical way to increase the iron content of food). (Zulifqar et al., 2019).

Iron-Paradox

Plant loves to tkae iron in the form of ferrous Fe^{2+}. Iron-deficiency Anemia can be treated by increasing the amount of iron that is found in the body; however, there is some evidence that this may also stimulate the growth of infections. Iron needs can be easily satisfied to the optimal level in developed countries (Saldanha et al., 2007). In developing countries, on the other hand, where sickness is more prevalent and there is a higher risk of infection, it is more challenging to acquire iron supplements. Iron deficiency and folic acid concentrations may be improved by supplements; however, this may lead to accelerated neuro developments. It is possible that giving iron supplements to iron-sufficient youngsters or pregnant women who are suffering from infectious disorders like malaria could be hazardous to those individuals (Naito et al., 2021). The stimulation of pathogen growth that results from an excess of iron is the root cause of this problem.

Biofortification strategies (Velu et al., 2014)

Two of the most valuable strategies regarding biofortifying the iron contents for human being are:

(i). Lowering the concentration of antinutrients

(ii). Improving Fe in favorable iron absorbing compounds

The above-mentioned techniques are not equally important.

Lowering the concentration of antinutrients. Polyphenols and phytic acid are considered an important group of antinutrients as they reduce the iron absorption through making iron chelation. However, phytic acid also performs important biochemical functions. Phytate is an important reserve of Mg, K, Ca, Mn and Fe metals in seeds, either in the seed embryo or in the aleurone-cell. Phytate is a mixed salt of D-myo-inositol, commonly known as IP6 or InnsP6. No doubt, IP6 plays its part in mineral storage, it is also involved in cascade signaling initiated by drought resulting in stomatal closure. As a result, in ABA produces certain changes in IP6 in guard cells, which releases Ca+2 from endomembrane and triggers K+ inhibition rectifying channels (Bouis and Welch, 2010).

Improving Fe in favorable iron absorbing compounds. Genotypic variations are of utmost importance for a broad range of iron concentration in food crops.

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Fe concentration (mg/kg dry weight) in different crops like wheat (*Triticum spp.*), maize (*Zea mays*) and rice (*Oryza sativa*) ranges from 27-73, 10-63 and 6-24, respectively. Orphan crops Fe concentration also varied from different ranges like in pearl millet as well as in cassava roots, with ranges from 31.2-74.7 and 4-49 mg/kg dry weight, respectively (Coey and Sun, 1990).

Keeping in view the variations in ranges, iron-enriched food crops can be produced through focusing on different breeding techniques.

Higher Fe and Zn concentration have been recorded in *Triticum turgidum* ssp., a domesticated wheat progenitor, when compared with either drum or bread wheat cultivars. Scientists are in favor of fact that favorable traits can be excluded through domesticated processes. This fact is established by the ancestral gene identification form wild-wheat coding for a transcriptional factor (not functional in modern wheat verities) and which helps in improving Fe and Zn concentration in wheat along with improved sentences. The loss of such functional genes through domestication goes beyond the current review goals, it is of importance to reintroduce such genes through breeding approach to improve micronutrient contents in edible part of food crops. This is need of the hour to improve the nutritional status of food crops without compromising on other important attributes like agronomic and yield performance (Frossard et al., 2000).

The principal goal of various international groups like HarvestPlus is to improve the nutrient contents like Fe, Zn, Vitamin A) in food crops to overcome the prevailing micronutrient malnutrition through breeding and fortification techniques. HarvestPlus in addition is also focusing.

on dissemination of biofortified iron rich pearl and bean verities for less developed countries throughout the globe. AgroSalud (www.agrosalud.org) like Harvest Plus is supporting the distribution of Fe-Zn enriches rice and bean verities in undernourished areas especially in the Caribbean and Latin America.

An iron storage protein "Ferritin gene expression" is a possible transgenic approach to produce iron enrich food crops. Ferritins of eukaryotes consists of 24-subunits, assembled in a special structure which can bind or release iron on demand "a unique iron reserve". However, the ferritin gene mechanisms in human intestine is a mystery. One group of research believes that iron is being taken up by the enterocytes as ferritin is digested in the intestineas.

A recent analysis of iron absorption in non-anemic women revealed that intrinsically supplied ^{59}Fe as ferritin soybean was well absorbed, as the non-ferritin iron as iron sulphate ($^{59}FeSO_4$).

Rice iron concentration is found to be doubled after transforming with *Phaseolus vulgaris* and is found at highest iron level. Whenever, ferritin is overexpressed iron remains bioavailable in rice sedes (Zulifqar et al., 2019).

A notable increase of up to three-fold in rice seeds has also been reported from soybean ferritin under an endosperm specific promoter. Iron enrichment in rice is not only confined to ferrtitin genes, however, it also involves the iron regulation from rhizosphere, soil fertility, soil composition and transport of iron from roots to aerial plant parts. Further, overexpressing ferritin in transgenic lines represents a way to increase more iron concentration; like expression of nicotinamide synthase (NAs) and ferritin provides upto more than six-fold increase in iron

concentration in rice seeds. NA, an iron chelator is a vital component of iron homeostatic and assimilation. However, a possible drawback of ferritin gene over expression is in the field as iron concentration may depends on some other factors like soil fertility and soil compaction. More precisely, when growing crops in heavy metal contaminated soils, ferritin gene expression is at par as the metals are uptaken by the plants due to their favorable plant available forms. The actual heavy metals concentration resulted from ferritin gene has not been yet calculated. Therefore, it is not clear that restricting the ferritin expression to seeds can bypass the metals drawbacks (Bouis and Welch, 2010).

Conclusions

The major goal of scientific communities is to. completely eradicate the iron hidden hunger. A considerable approach considering the endemic-infections affecting more than 2 billion people around the globe is a rare need of the time. Supplementation is a one-time solution to micronutrient malnutrition. However, iron supplementation had a drawback of affecting the children exposed to malaria. This might be due to the fact that serum transferrin saturation might have been increased through supplementation which increase the iron availability to pathogens

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Now doubt, biofortified crops are a vital and safe source of fulfilling iron deficiencies, but the iron content in biofortified crops is still low than daily recommended iron uptake. The iron content in 200 g polished rice-seeds is 1.3-2.4 g, which is still much lower than the daily recommended uptake for 4-8 years children which is around 10 mg/kg (for details http://www.nutrisci. wisc.edu/NS623/ drivitasum.pdf). Therefore, the scientists are focusing on developing biofortified crops which will be a regular source of supplementing iron to the undernourished people (Lata-tenesaca et al., 2023).

But there is a strong need to conduct pilot-scale studies, in both infectious and non-infectious regions facing the problem of iron malnutrition. Rather to consider the whole population, one should pay attention to the individual having problem of iron deficiency and benefiting from the fortified crops, with enhanced iron contents. The iron-paradox depicts that a population facing the infectious endemic, the most important bottleneck for absorption of iron is the real poor-health conditions and reduction of iron absorption from diet. However, the research is lacking behind in terms of IP6 influence on iron deficiency anemia. The one benefit of IP6 on iron absorption is the fact it provides protection against certain cancer (Thompson, 2007). The regulatory framework for transgenic and breeding plants, which lags **significantly** behind scientific impetus, is a significant obstacle to the widespread adoption of biotechnology approaches. The fact that metabolic engineering plays a role in crop enhancement was demonstrated by the nomination of golden-rice as a viable source of vitamin A for human beings (Vélez-Bermúdez and Schmidt, 2023).

There is a significant gap between the biofortified crops and their systematic dissemination to the public community, which presents a significant challenge for researchers and a burden for members of the public community who could benefit from biofortification. The researchers are concentrating their efforts on the development of crop varieties that have the potential to boost the micronutrient content in crop plants and that have the potential to be an important source of delivering micronutrients.

Disclosure of potential conflicts of interests

There are no conflicts of interest of this study

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