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Varun Sharma
School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Bhupendra Mathpal
Assistant Professor, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Iron deficiency: A global issue and its possible remedies

Varun Sharma and Bhupendra Mathpal

Abstract

Iron (Fe) is one of the essential element required by plants to do various metabolic and respiration processes. The deficiency of Fe is becoming a very important global issue in the present day world due to various factors such as such as non-uniform concentration in soil, soil pH, less organic matter, soil moisture content and interaction of Fe with other nutrients. After the absorption, translocation and uneven distribution of Fe inside the plant body is another problem. Most of the absorbed Fe get accumulated in straw part and makes the grains deficient of it. As more than 50% of world's population depends on plant based foods mainly cereals so a large proportion of humans are suffering from Fe deficiency. Various strategies like dietary diversification, supplementation and food fortification can be used to alleviate the Fe deficiency in human population. Whereas, biofortification through breeding, genetic engineering and agronomic approaches are the principle ways to improve the Fe content in grains of crop plants.

Keywords: Iron deficiency, uptake, translocation, biofortification, grains

Introduction

The word heavy metal refers to the element which has high specific gravity (Farlex 2005) [1]. Because of characteristic features of Fe it can also be considered as heavy metal. Out of 90 elements which occur naturally, fifty three are heavy metals (Weast 1984) [2]. Iron (Fe) is required by every plant for its normal growth. Even bacteria itself requires Fe for its optimum growth but is also one of the essential element which is required for the formation, growth and functioning of the symbiosis (O'Hara 2001) [3]. Only 5 percent of earth's crust constitutes Fe (Mengel and Kirkby 1987) [4] but still it is present in unavailable form which causes Fe deficiency in many plants and causes symptoms such as interveinal chlorosis and reduction in the productivity of plants (Jeong and Guerinot 2009) [5].

Bioavailability of Fe can be improved by increasing the number of promoter compounds (Bouis, 2003) [6]. Various experiments conducted have shown that in humans the Fe absorption is regulated by only one amino acid and that is cysteine (Glahn and Campen 1997) [7]. So, if the cysteine residue of the crop can be improved we are able to have the better Fe availability. Overexpressing zinc (Zn) transporter in barley increased the Fe content. ß-carotene also helps in improving the bioavailability of Fe (Lucca *et al.* 2006) [8]. The balance of Fe is very important for RBCs production, its deficiency may result cell death of the blood cells (Le and Richardson 2002) [9]. It is very important for humans as blood in our body requires Fe to transport oxygen to different body parts. Its deficiency in humans can cause anemia (Miller 2013) [10]. Various organisms have evolved to control Fe homeostasis which protects them from toxicity of Fe due to high concentration (Hentze *et al.* 2004) [11]. A study of various people from a rural area showed the low Fe status at 21.5% in school going children of age group 6 to 15 (Rahman *et al.* 2003) [12].

Status of iron in soil

Iron (Fe) is a type of metal which is always ready to gain or lose electrons (Romheld and Marschner 1990) [13]. Due to this characteristic feature it is required by plants as it acts as essential nutrient and at the same time it is also helping in making oxygen reactive species which is toxic (Halliwell and gutteridge 1984) [14]. Under aerobic conditions it is very less soluble in water despite the fact that it is abundantly present in the soil. Rice is the only cereal that can be grown for extended periods in the flooded soil (Samaranayake *et al.* 2012) [15]. As the availability of the oxygen present in the soil decreases the Fe present in the soil gets reduced from ferric (Fe^{3+}) to ferrous (Fe^{2+}). Therefore, at a point when the soil is submerged or the condition of the soil is flooded the concentration of Fe ion increases in the soil (Becker and Asch 2005) [16].

Corresponding Author:
Bhupendra Mathpal
Assistant Professor, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

We all know that Fe is present in abundance in the soil but still plants are not able to utilize it properly because it is mostly available in the form of Fe^{3+} compounds (Chen and Barak 1992) [17]. Other thing making this condition even worse is that 30 percent of the total soil which is cultivable is calcareous soil having high pH (Nozoye *et al.* 2011) [18]. Therefore plants have found a way by which they can uptake Fe from the soil and also can translocate it from soil to the stem and then to is grains (Bashir *et al.* 2011) [19]. It is done through a mechanism in which the plants of gramineae family secrete small molecules which are called mugineic acid family phytosiderophores (MAs) which help in solubilizing Fe (Takagi 1976) [20].

The Fe concentration decreases with every increase in pH of soil and the minimum solubility is from 7.5 to 8.5 (Lindsay and Schwab 1982) [21]. The predominance of ferrous (Fe^{2+}) and ferric (Fe^{3+}) forms of Fe present in the soil are determined by soil pH, status of aeration in the soil, plant adaptations and reactions with organic matter (Morghan and Mascagni 1991) [22]. Some plants excrete hydrogen ion (H^+) from their roots to cope up with the low availability of Fe in the soil which helps in lowering the pH at root interface and also helps in increasing the Fe solubility from its hydroxides (Schulte 2004) [23]. The movement of Fe from soil to the roots of the plant is aided by Fe chelates, but these chelates are never absorbed to a particular extent. The equilibrium in terms of chemical relationships helps in telling the availability as well as solubility of Fe in soil (Lindsay and Schwab 1982) [21].

Status of iron in plants

Iron (Fe) is one of the essential elements which is required by every plant or animal because of its very important role in day to day processes such as photosynthesis (Kobayashi and Nishizawa 2012) [24]. Even after abundance in nature its biological activity is low because of the formation of highly insoluble Fe compounds at normal or neutral pH. It helps in maintaining the structure of chloroplast and also plays a very vital role in the synthesis of chlorophyll. (Fernandez *et al.* 2011) [25]. The Fe present in the soil dictates the yield distribution as well as nutritional value of the plant. Low uptake of Fe causes various problems such as the growth of the plant gets retarded and interveinal chlorosis. Iron (Fe) is required for plants to defeat the regularly limited accessibility of soil Fe by procedures that expansion its versatility and confine its take-up when present in abundance. (Schmidt *et al.* 2020) [26].

Iron (Fe) is one of the most important micronutrient as it is involved in various processes i.e. synthesis of DNA, photosynthesis process and respiration process (Kobayashi and Nishizawa 2012) [24]. Various metabolic pathways are started by Fe and it acts as an essential component in various enzymes for example cytochromes of the electron transport chain (Rout and Sahoo 2015) [27]. Large part of Fe is present in leaf is in chloroplast with a little amount in cytoplasm and some other organelles as well (Terry and Low 1982) [28]. Iron (Fe) present in the plant is in heme and non-heme form. Nearly 9 percent of the total Fe present in the leaf is in the form of heme whereas 19 percent is in non heme form. 63 percent is in Fe protein and rest of the Fe is present in the form of ferritin (Miller *et al.* 1995) [29]. Crop growth ratio, leaf area index, chlorophyll density and roots per plant are affected by high Fe level and its split application. Application of required quantity of Fe increases the height and biomass of the plant. Its application to crops like wheat helps in improving the benefit cost ratio (Majeed *et al.* 2020) [30].

Uptake and translocation of iron

Low concentration of Fe in the rhizosphere has forced the plants to adapt with new strategies to take up Fe (Ishimaru 2006) [31]. First type of strategy involves the release of positive charge ions (H^+) into soil to bring down the pH of the soil, the ferric ion chelate reductases production takes place and three genes for ferric ion chelate reductases have been isolated from Arabidopsis (Robinson *et al.* 1999) [32]. Second type of strategy involves the synthesizing of mugineic acid (MAs) from the roots of the plants which help in mixing the ferric ions in the soil (Kobayashi and Nishizawa 2012) [24]. There has been identification of nine different types of MAs till date which are produced from S-adenosyl-L-methionine. The production of mugineic acids are secreted twice daily with more of the production in the morning. The root cells which are having low concentration of Fe are seen to be swollen in the very morning but they tend to reduce the swelling the evening (Bashir *et al.* 2011) [19].

The genes are taken from Barley and other graminaceous crops which are responsible for the synthesis of mugineic acids (Feng *et al.* 1999) [33]. If anyhow the concentration of Fe becomes low these genes help in increasing the secretion as well as production of MAs. The Fe^{3+}-MAs transporter helps in taking up Fe^{3+}-MAs complexes (Kobayashi and Nishizawa 2012) [24]. The translocation of Fe inside the body of the plant is directed with suitable chelating molecules and by controlling the ferrous and ferric redox states (Hell and Stephan 2003) [34]. The translocation of Fe in plants is having different parts for example transport in tissue of roots radially, loading and unloading in xylem, transfer to phloem, transportation inside the plant, movement towards the site where the demand is more (Kim and Guerinot 2007) [35]. Citrate, nicotianamine (NA) and mugineic acids (MAs) are the main chelators present inside the plant body (Kakei *et al.* 2009) [36].

As we know that rice is a strategy II plant, which is having 18 YSL members. Various research and experiments show that the long distance transportation of NA- chelated Fe and Mn to large distances is due to the OsYSL-2 (Koike *et al.* 2004) [37]. The absorption through roots and the transport of Fe inside the plant is due to OsYSL-15 which also transports deoxymugineic acids (Inoue *et al.*, 2009) [38]. The chelating and transportation of Fe in xylem sap is thought to be due to presence of citrate. An actual form of Fe-citrate complex was identified in xylem sap of tomato as a tri-Fe (III) tri-citrate complex (Rellan-Alvarez *et al.* 2010) [39].

Factors affecting iron availability

(i) Concentration in soil

Iron (Fe) present in all soils makes up about 5% by weight of total earth’s crust (Fanning *et al.* 1989) [40]. Among different types of soil ultisols and oxisols contain maximum content of Fe. Iron (Fe) containing primary silicate minerals are olivine, augite, hornblende and biotite. The most common soil iron oxide minerals are goethite (α-FeOOH), lepidocrocite (r-FeOOH), hematite (α-Fe_2O_3), maghemite (r-Fe_2O_3), ferrihydrite ($HFe_5O_8.4H_2O$) and magnetite (Fe_3O_4) (Schulte 2004) [23].

(ii) Soil pH

Optimum Fe concentration required by most of the plants is 10^{-8} M (Manthey *et al.* 1994) [41]. The hydrogen ion is removed from the water with the increase in pH which further gives various hydrolysis products (Hem and Cropper 1962) [42]. If we take a soil solution having pH 8 and that solution is in equilibrium with Fe gives an Fe concentration of 10^{-10} M hence, pH plays a very important role in finding out the solubility of Fe, which is very low in the soils having pH range 7.5 to 8.5 i.e. calcareous soil (Katyal and Vlek 1985) [43]. The oxidized insoluble form of Fe i.e. Fe^{3+} is not readily available to plants is found under anaerobic condition i.e. without the presence of oxygen (Kobayashi and Nishizawa 2012) [24].

(iii) Organic matter

Soil organic matter is largely controlled by the climate and the environment and it in turn affects the availability of most of the plant nutrients (Santos *et al.* 2019) [44]. The release of aliphatic acids, phenols, phenolic acids and component of stable humus such as humic and fulvuic acid help in chelation of Fe and making it more available to plants (Zanin *et al.* 2019) [45]. In addition siderophores produced by soil bacteria and fungi help to chelate Fe and make it more available to plants (Stevenson 1991) [46]. Many reports showed that Fe^{2+} concentration can be increased by the application of rice straw for about 4 weeks of submergence. Similarly application of organic manures to rice fields increased Fe concentration uptake in rice and it is also reported that their regular addition was best way to avoid Fe deficiency (Mishra *et al.* 1996) [47].

(iv) Soil moisture content

Submergence condition of soil create reduced conditions which leads to the conversion of Fe^{3+} to Fe^{2+} and makes iron available to crop plants. Rice nurseries sown during hot summer months showed Fe deficiency which can be easily overcome by frequent irrigation (Mahender *et al.* 2019) [48]. Flooding and Compaction are the two main causes of poor soil aeration and its low oxygen level. Depending on other soil conditions it can affect Fe availability to plants (Abuarab *et al.* 2019) [49]. When microbial activity and root growth are limited due to low temperature of soil in early growing season the deficiency of Fe takes place. As the soil warm, microbial activity and root proliferation increases, allowing plants to absorb more Fe. Some Fe oxides and hydroxides are convert into more soluble ferrous form if in acid soils the oxygen supply is decreased due to microbial activity (Mishra *et al.* 1996) [47]. The lowland rice yield is highly reduced by Fe toxicity. The uptake of other essential nutrients is also adversely affected by the presence of Fe^{2+} in the rhizosphere in high concentration (Fageria *et al.* 2008) [50], (Ethan *et al.* 2011) [51].

(v) Interaction of iron with other nutrients

Most of the plant nutrients interact negatively with Fe except potassium (K) (Caliskan and Caliskan 2017) [52]. Potassium (K) helps in maximum utilization of Fe in tomato and soybean cultivars were unable to respond to Fe deficiency stress in the presence of K in nutrient solution (Jolly *et al.* 1988) [53]. Increased uptake of NO_3^- nitrogen was reported to reduce Fe uptake. Similarly high soil phosphorus (P) levels were also found to decrease Fe uptake and the possible mechanism include immobilization of soil Fe, inhibition of Fe absorption by roots and Fe transport from roots to shoot and inactivation of plant Fe (Elliot and Lauchli 1985) [54]. Other studies have found that Fe increased manganese (Mn) concentrations in soybean shoots (Izaguirre and Sinclair 2005) [55] and in soybean leaves, whereas in Indian mustard Mn concentration was reduced (Hamlin and Barker 2008) [56]; (Ai-Qing *et al.* 2011) [57].

Zinc-iron interaction

The interaction among Zn and Fe is also complex like P-Zn interaction. It has been earlier shown that Zn interferes with Fe uptake and translocation while Fe inhibits the Zn translocation at high Zn concentrations (Alloway 2008) [58]. Infact three mechanisms have been put forward documenting an antagonistic relationship between the two elements which are exhibiting a competition with each other for the uptake site. (Kabata-Pendias 2001) [59] or an interference in xylem unloading (Alloway 2008) [58]. There are many other reports which also showed antagonism between Zn and Fe. In an experiment when Zn was supplied at a rate of 10 mg L^{-1} wheat Fe concentration was found to be reduced by an average of 8% (Zhao *et al.* 2011) [60].

Strategies of iron enrichment

Dietary diversification

There are two forms of dietary Fe i.e. heme and non heme Fe. Non vegetarian food products such as meat, fish provide us with heme Fe which is easily absorbed whereas non heme Fe is difficult to absorb and is provided by vegetables and cereals (Lauren and Christopher 2015) [61].

Supplementation

Various form of dietary supplements for Fe are used nowadays, these include multivitamin and multimineral tablets which contain good amount of Fe. Ferrous salts such as ferrous sulfate, ferrous gluconate and Ferric salts such as ferric sulfate, ferric citrate are commonly used Fe supplements (Murray *et al.* 2010) [62].

Food fortification

Food fortification refers to increasing the amount of any micronutrient to improve and sustain Fe nutrition on permanent basis (Bauernfeind and Lachance 1991) [63]. In various countries like South Africa, Thailand different food s such as sugar, curry powder are used with NaFe EDTA for Fe fortification (Ballot *et al.* 1989) [64]. Iron (Fe) compounds such as ferrous sulfate, ferric iron pyrophosphates are mixed in milk and is available in various countries (Bothwell and MacPhail 1992) [65].

Biofortification

Biofortification is the process in which with the help of biotechnology or plant breeding, the concentration of micronutrients can be increased in the edible parts of the plant (Riaz *et al.* 2020) [66]. Various other approaches such as the use of fertilizers having optimum quantity of micronutrients or by manipulating the nutrient contents of foods by enhancing the micronutrient bioavailability (Nestel *et al.* 2006) [67]. This process is said to be the best and the most cost effective way to remove micronutrient starvation in the rural areas where this problem is prevailing very largely (Mayer *et al.* 2008 [68]; Waters and Sankaran 2011) [69].

Breeding approaches

For Zn and Fe, due to optimum genotypic variations in the germplasm of most of the cereal crops, breeding can be done to get higher concentration of these micronutrients in the edible parts of the crop (White and Broadley 2009) [70]. The concentration of Fe and Zn in the grain of any crop is affected due to the remobilization of these micronutrients from leaves and translocation to grain (Wang *et al.* 2018) [71]. Latest studies have concluded that both grain protein content and the concentrations of Fe and Zn in grain of emmer wheat is affected by grain protein content B1 (Gpc-B1). (Distelfeld *et al.* 2007 [72]; and Uauy *et al.* 2006) [73].

In an experiment conducted, three different groups of Fe genes were attached to the chromosomes 7, 8 and 9 of rice crop having 19-30% varied Fe content (Tiwari *et al.* 2009) [74]. Similarly three major QTL for the concentration of Fe and Zn in the grains of *Triticum durum* and *T. dicoccoides* RIL population were also reported (Peleg *et al.* 2007) [72] where the QTL for Zn and Fe was in the same marker interval as reported previously on chromosome 7A by Tiwari *et al.* (2009) [74] in wheat RIL population. Genes for high concentration of Fe and Zn in the grain is due to chromosomes 2 and 7 of wild wheats-*Aegilops kotschyi*, *Ae. peregrina* and *Ae. longissima* (Tiwari *et al.* 2010) [75].

Genetic engineering approaches

Various transgenic practices are also being practiced nowadays. One of such examples is the use of recombinant human lactoferrin (rHLF) in rice crop which results in the production of the HLF protein content of about half percent of the grain weight and a two times increase in the concentration of Fe in the grain (Nandi *et al.* 2002) [76]. HLF is one of the major proteins having high-affinity for Fe binding and also regulates the absorption of Fe is found in the human milk (Rosa *et al.* 2017) [77]. As the ferrous sulfate is having the bioavailability of Fe to humans, same type of bioavailability of Fe is found in the recombinant HLF protein produced in the transgenic rice (Lonnerdal and Bryant 2006) [78]. One of the other examples is also the endosperm- specific expression of the soybean ferritin gene in rice leading to two to three times increase in the concentration of Fe in the grain. Iron (Fe) which is present in plant ferritin is as bioavailable to humans as ferrous sulfate (Qu *et al.* 2005) [79].

Phytate is responsible for decreasing the bioavailability of Fe and Zn. It is present in the aleurone layer as well as seed's embryo cell. Reduction of phytate content is possible but it drastically affects the yield as well as germination of the seed (Brinch-Pedersen *et al.* 2007) [80]. An alternative method can be adopted in which a phytase gene (PhyA) is expressed from microorganisms (e.g. *Aspergillus niger* or *Aspergillus fumigatus*) in the endosperm of cereal grain (Brinch-Pedersen *et al.* 2006) [81].

Agronomic approaches

Use of various industrial by products in the field application such as low grade pyrite based mining residue and Fe dust from the steel industry can be done. Application of inorganic fertilizers such as $FeSO_4.7H_2O$ through fertigation (Chen and Shenker 2005) [82]. Management of soil is also one of the important aspects in Fe enrichment. It is seen that anaerobic microsites were formed by the maintenance of soil which helped in increasing the Fe availability (Wallace and Wallace 1992) [83]. Foliar application of $FeSO_4$ also helps in providing Fe to the plant. It was noted that solution was absorbed by the hydrophilic pores through the cuticle (Marschner 1995) [84].

Conclusion

Although Fe is abundant in soil but still its deficiency is a serious problem worldwide. Plants adopt various mechanisms to absorb the nutrients from soil in which secretion of phytosiderophores is a very unique strategy. Many efforts have been done to enrich the crop plants with micronutrients but still there is a need to do more in this area. A combination of agronomic, breeding and genetic engineering approaches can be effective to improve the uptake, translocation and further remobilization into the grains.

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