Chapter 4

Vegetal Sources of Iron

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Additional information is available at the end of the chapter

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Abstract

Iron deficiency anemia is a global public health problem. According to the World Health Organization, anemia affects 1620 million of people worldwide, which corresponds to 28% of the population. Fifty percent of the anemia cases are attributed to low iron intake. Among the main sources of iron from vegetable origin are legumes, such as beans, lentils, soybeans, lupin, some vegetables such as spinach, and some dehydrated fruits. Non-hemic iron is mainly from legumes and is the most important source of this mineral in the diet of developing countries' population, but its bioavailability is very variable. Consequently, the fortification of foods with high and cheap iron sources is a practical way to prevent its deficiency. Some studies have shown that the roots of some legumes, especially nitrogen fixers, accumulate a significant amount of iron mainly in the nodule proteins. The purpose of this chapter is to present the current knowledge of novel sources of plant-based hemic iron with a high bioavailability to be used in food fortification.

Keywords: plants, iron, anemia, fortification

1. Introduction

Iron deficiency affects an important part of the human population; it is the most common nutritional disorder and causes approximately 50% of anemia cases. The groups most likely to have iron deficiency and iron deficiency anemia are infants, young children, adolescents, premenopausal women, and especially pregnant women. The recommended iron intake depends on the individual's health status, age, and sex. However, some sociodemographic factors such as race or ethnicity, socioeconomic status, eating habits, etc. have an influence on the risk of developing anemia. Iron deficiency and iron deficiency anemia have undesirable physiological consequences especially in children, having an impact on cognitive performance and growth [1].

This pathology decreases the amount of oxygen transported to the muscles, which affects people's physical capacity and work performance. It generates a decrease in the immune system response and therefore an increased risk of contracting infections. Iron deficiency also disrupts the digestive system functioning. During pregnancy, iron deficiency anemia increases the perinatal risk of both mothers and children and can lead to an increase in infant mortality. From the biochemical point of view, it has been observed that it affects the metabolism of some neurotransmitters, thyroid hormones, and the activity of some iron-dependent enzymes. Due to the great impact of iron deficiency and iron deficiency anemia on human health and its high incidence, international organizations led by the World Health Organization have developed a series of programs to avoid this problem [2].

In developed countries, iron deficiency is usually a consequence of absorption disorders, loss of blood, or the intake of a restricted diet (vegan diet). Foods present different forms of iron that differ in their bioavailability, depending to the source. Hemic iron is present mainly in animal proteins such as hemoglobin and myoglobin, which has a higher bioavailability; these proteins are present in meat, fish, and shellfish [3].

Non-hemic iron is present in different chemical forms, which significantly affects its absorption. This type of iron is present in both organic and inorganic forms. The most common sources of non-hemic iron present in foods are low-molecular-weight compounds such as ferric citrate, phosphate, phytate, oxalate, and hydroxide and high-molecular-weight compounds such as ferritin, lactoferrin, and leghemoglobin. The best sources of non-hemic iron are seeds, grains, nuts, and the green leaves of vegetables [3, 4].

Likewise, the absorption of iron depends to a large extent on the concentration of iron present in the body and enhancers such as ascorbic acid and some muscle tissue proteins. One of the strategies for the replenishment of iron deficiency is the use of food supplements. However, the World Health Organization recommends fortification of foods as an approach to increase iron intake [5].

2. Iron biological functions

Iron is an essential metal for human life, and its main biological function is as a part of the heme group proteins such as hemoglobin and myoglobin, which is responsible for oxygen transport [6]; also, iron is an essential component of many enzymes that catalyze redox reactions, due to its ability to rapidly accept electrons, under physiological conditions [7].

More than 2 billion people worldwide suffer from anemia. Iron deficiency anemia is the most common nutritional disease in the world; around 800 million children and women are the most vulnerable and suffer from this type of anemia, which can affect the physical and immune development [3, 8]. This disease is usually asymptomatic and is often not diagnosed; however, some of its symptoms are weakness, fatigue, exhaustion, and decreased cognitive efficiency [9]. The iron status in the body is maintained by a complex process that regulates the balance between iron absorption in the duodenum, the recycling of iron by macrophages and iron storage in the liver because there is no physiological way for its excretion [10]. Hemic

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iron is present in foods of animal origin and in some plants proteins, such as leghemoglobin present in legume nodules; however, non-hemic iron is mainly present in foods such as vegetables [6].

3. Iron absorption

The absorption of iron is defined as the passage from the intestinal lumen to the circulation through the enterocytes and is mainly carried out in the duodenum and the proximal jejunum [11]. Non-hemic iron must be in a soluble form to be absorbed, since the insoluble forms cannot be absorbed and are eliminated with the feces. The ferrous forms of iron are much more soluble than ferric forms, since the latter rapidly precipitate in the intestine alkaline medium. That is why iron that has been released by the action of gastric and pancreatic proteases binds to intraluminal ligands whose function is to stabilize the ferrous form, keeping the iron soluble and consequently biologically available to be captured and transferred to the interior of the enterocyte [12].

The non-hemic iron complexes present in foods are degraded during digestion in the gastrointestinal tract due to the action of pepsin and hydrochloric acid. Once released from the food components, most non-hemic iron is present in the ferric form (Fe^{+3}) which is more common in vegetables, it is considered to be of low solubility and bioavailability, but this depends on the physiological status and the presence of other minerals such as zinc, magnesium, copper, and calcium [13], as well as phytates, polyphenols, and metal chelators. In addition, there are numerous compounds present in foods capable of reducing Fe^{+3} and Fe^{+2} (bioavailable non-hemic iron form), including ascorbic acid and amino acids such as cysteine and histidine, and

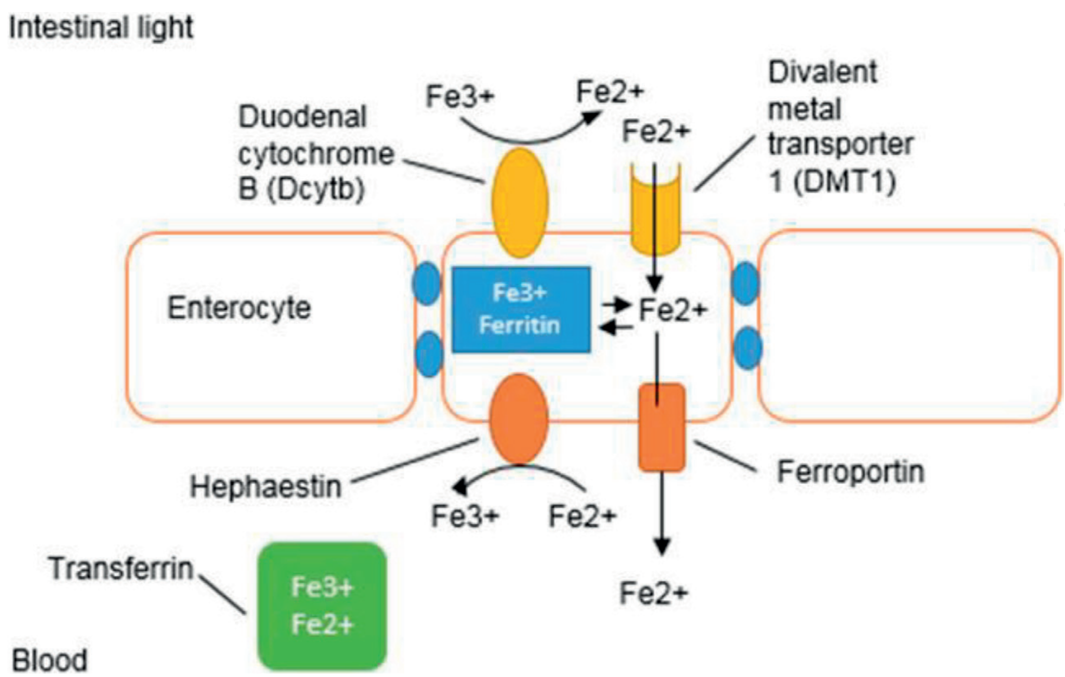

Figure 1. Iron uptake in the apical enterocyte membrane [8].

also, the main reduction activity is carried out by duodenal cytochrome b reductase activity (DCYTB), a hemoprotein located in the enterocyte apical membrane using ascorbate to facilitate iron reduction [14]. The soluble form of Fe^{+2} is transported to the enterocyte through the divalent metal transporter-1 (DMT-1), which is a proton simulator that requires a low pH for metal transport (**Figure 1**) [15].

4. Vegetable sources of iron and its bioavailability

Non-hemic iron includes different organic forms, such as ferric citrate, ferric gluconate, ferrous fumarate, and ferritin and inorganic forms such as ferrous sulfate, carbonate, and chloride as well as ferric, and each form of iron has different forms of absorption and efficiencies [16] and is mainly found in legumes, cereals, and other vegetables (**Table 1**).

Legumes throughout the history have been a very important food resource, accounting for approximately 20% of the daily protein intake in humans. They are also an economical source of dietary fiber and minerals such as iron [17, 18].

The iron in food is found as hemic iron, forming part of the structure of proteins and as non-hemic iron. The most common forms of non-hemic iron present in foods are low-molecular-weight compounds such as ferric citrate, phosphate, phytate, oxalate, and hydroxide [19].

Hemic iron is also present in vegetables forming part of some proteins such as ferritin and leghemoglobin. The distribution of ferritin in the edible parts of plants is variable. Its concentration in seeds can range from 50 to 70 mg/kg, which corresponds to the iron content of 10 mg/kg [20].

Both ferritin and leghemoglobin accumulate in the nodules of the root of legumes such as soybean and lupine. The concentration of iron in the nodules of soy is high compared to the leaves [21].

Valdés-Miramontes et al. [22] reported a concentration of iron in the seed of *L. rotundiflorus* of 6.12 mg/100 g and a concentration of 70 mg/100 g in the whole root; this concentration in nodules is probably due to the fact that the root has nodules rich in leghemoglobin, an iron-rich protein, due to its high activity in nitrogen fixation. Leghemoglobin hemoprotein is found in root nodules of legumes, containing high concentrations of iron [23].

Values obtained from the "Table of practical use of foods with the highest consumption" by Chávez et al. [24] and "Effect of thermal treatment on the chemical composition and minerals of wild lupine seeds" by Valdés-Miramontes et al. [20].

In a study conducted by Martínez-Zavala et al. [25] about the iron content in the bean plant leaves (*Phaseolus vulgaris*), a recovery of hematic biomarkers was observed, such as hemoglobin, erythrocyte count, and hematocrit in rats with induced anemia, when diets with iron source from this legume were administered.

It is known as bioavailability of iron to the proportion of this dietary mineral that is absorbed and used by the body. **Figures 2** and **3** show some of the dietary and physiological factors that influence the bioavailability of iron in foods [6, 8].

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Food	Iron (mg / 100 g)	Humidity (g / 100 g)
Pumpkin seed (*Cucurbita pepo*)	14	4.07
Soy (*Glycine max*)	13.70	
Sunflower seed (Helianthus annus L).	5.25	4.80
Cocoa (*Theobroma cacao L.*)	3. 4	3.60
Lentils (*Lens succulent*)	5.80	7.86
Bean (*Phaseolus) vulgaris L.*)	5.70	10.10
Bean flour	13.50	
Chickpea (*Cicer arietinum L.)*	8.90	8.10
Bean flour (*Vicia faba*)	18.20	4.70
Soybeans, cooked seed	15.70	
Green Creole pumpkin (*Cucurbita pepo*)	22	91
Cilantro (*Coriandrum) sativum L.*)	6.10	90.1
Endive leaf (*Cichorium endivia*)	12.5	94.5
Parsley (*Petroselinum sativum*)	6.20	80
Leeks (*Allium porum L.)*	28	82.7
Quelite or Chinese spinach (*Amaranthuschlorostachys*)	6.20	
Pepermint (*Mentha sativa L.*)	7.5	85
Chives (*Allimun porum*)	8.40	94
L. albus	8.06	7.5
L. angustifolius	7.6	7.9
L. mutabilis	1.08	8.0
L. exaltatus	6.18	7.4
L. elegans	7.09	7.1
L. mexicanus	6.31	7.5
L. montanus	7.77	7.2
L. rotundiflorus	8.28	7.8
Root of *L. rotundiflorus*	70.0	0.0

Table 1. Iron content (mg) and moisture in different foods.

Recent research on iron bioavailability from legume ferritin, especially soy ferritin, suggests a high bioavailability of soy ferritin, comparable to the bioavailability of $FeSO_4$, on in vitro experiments, rat assays, and clinical studies. This is probably due to the fact that the root presents nodules that contain leghemoglobin, a protein rich in hemic iron [3, 8].

Figure 2. Dietary factors that influence the bioavailability of iron in foods.

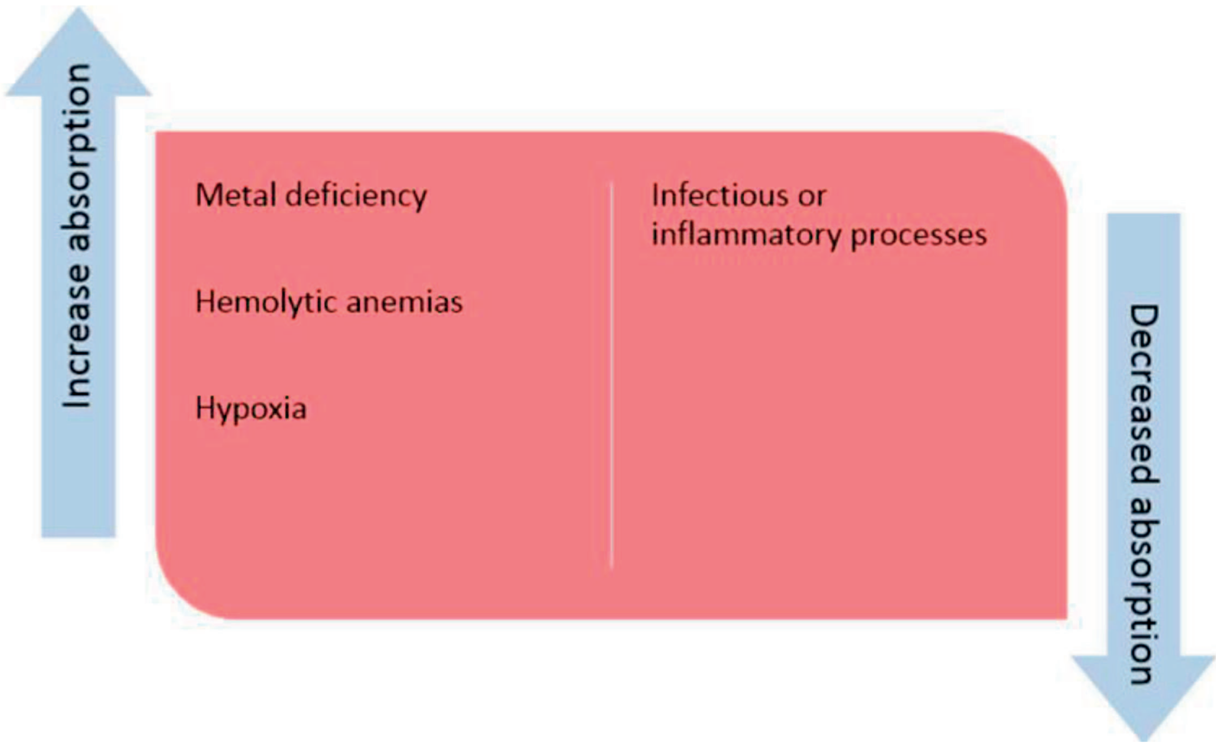

Figure 3. Physiological factors that influence the bioavailability of iron in foods [3, 8].

In this way, Proulx and Reddy [26] report an iron bioavailability from soybean nodules of 28 ± 10% and a partially purified soybean leghemoglobin bioavailability of 19 ± 17%, with a relative biological value (RBV) of 125 and 113, respectively, with a reference to ferrous sulfate (considered as 100%).When 50 ppm of partially purified leghemoglobin soybean extracts and bovine hemoglobin were added to corn tortillas, bioavailability was 27 and 33%, respectively [26].

It has been reported that iron bioavailability in bean leaves is 8.5%, while fava beans reported an absorption rate of 37.10 for a basal diet supplemented with 21 g of dry thyme leaves/kg of diet that contributed a concentration of iron 70.67 ppm [27, 28].

Valdés-Miramontes et al. [22] reported that the bioavailability of iron in the root nodules and cooked seeds of *L. rotundiflorus* of 13.80 and 13.70%, respectively, evaluated through the depletion hemoglobin repletion method in Wistar strain rats.

5. Fortification of foods with vegetable iron

Because of the importance of Fe deficiencies in health, the study of plants with higher content of bioavailable Fe is crucial, as biofortification which is considered as an innovative strategy for the micronutrient malnutrition in a sustainable way, since the micronutrients' deficiency is responsible for what is known as silent malnutrition, in particular iron deficiency, which has adverse effects on growth, immune function and causes anemia [29].

Figure 4 represents the three strategies to diminish iron deficiency in the population.

Biofortification is the process of improving micronutrient content of crops base to our feeding, through fertilization, breeding, and use of genetically modified varieties, comparing the cost-benefit and long-term sustainability, which can help increase the daily intake of micronutrients to low-income populations. Biofortification is a feasible means for malnourished populations in rural areas, offering naturally fortified foods to people with limited access to commercialized fortified foods, which are more available in urban areas. The biofortification and commercial fortification are highly complementary [30].

Biofortification is a novel strategy for producing crops with high micronutrient contents, and it reduces the levels of antinutritional factors that promote the increase of substances that promote nutrient absorption [31].

There is still ignorance regarding important parts of the biofortification process, also effectiveness more trials are needed to identify and refine the nutrients synergies. Additionally, more marketing strategies must be done to ensure maximum consumption of biofortified crops. Improvement can be made more cost-effective by selecting high levels of vitamins and minerals from a single variety, and transgenic methods can be more effective with conventional breeding crops [32].

In this way, Miller et al. [33] suggest to follow the next recommendations:

1. Commercially expand fortified food programs as a strategy to prevent micronutrient malnutrition (iron).
2. Develop and implement technologies to fortify foods, with the purpose of increasing the micronutrients consumption, especially in rural populations of developing countries.
3. Reduce the loss of food and food waste, especially in fruits and vegetables that should be used in a sustainable manner.
4. Training in agriculture, food processing, and nutrition education, especially in developing countries and their rural areas.

Velu et al. [34] report that a strategy of fertilization combined with genetic improvement in wheat enriches this crop with high iron content of high availability.

The improvement in popular consumption plants would be through increasing the concentration of absorption promoters such as nicotianamine, ascorbic acid, inulin, and carotenes.

Much research has been done recently regarding nicotianamine specifically, suggesting that genetic engineering is likely to have an even greater potential for biofortification, since nicotianamine concentrations in transgenic plants exceed the range found naturally, which would be complemented by studies concerning nicotianamine efficiency in human consumption.

Since it has been observed an enhancing effect of nicotianamine on the absorption of Fe by intestinal epithelial cells during passage through the human or digestive system, the continuation of research along these and other pathways will soon lead to even more effective and sustainable biofortification solutions [35].

Recently, new technologies have emerged with significant advances in iron biofortification programs. These include mutagenesis oligo-directed, reverse reproduction, DNA methylation directed by RNA, and specific sequence technology nuclease or genome edition. These

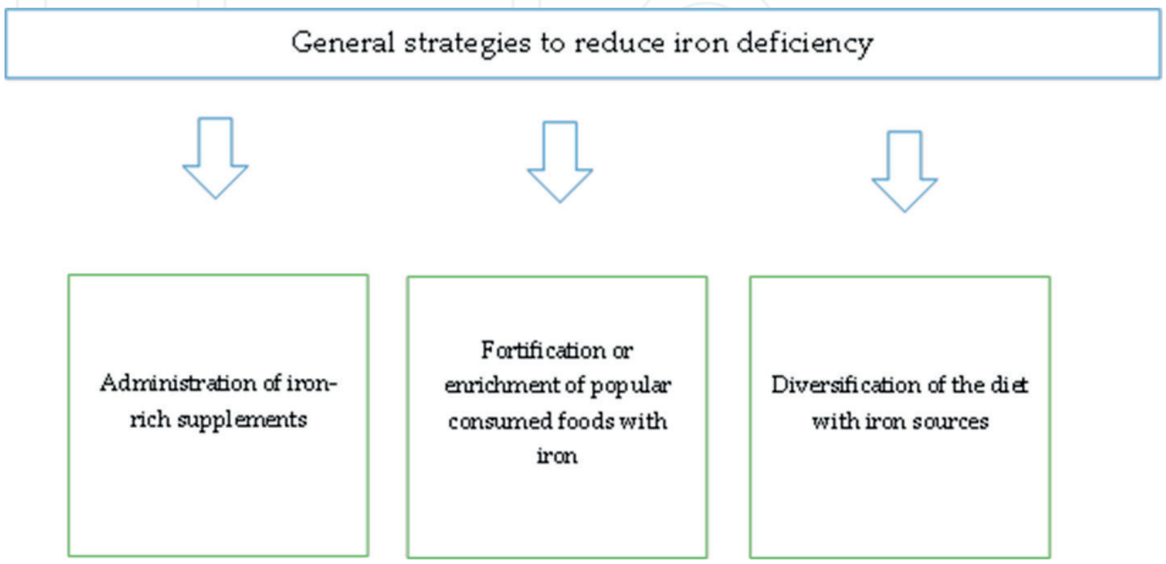

Figure 4. General strategies to reduce iron deficiency [3].

technologies have obtained very fast benefits and at low cost. At this time, it is a common practice to combine different molecular crops and genomic methods such as marker-assisted selection [36].

Recent success stories can be found in www.HarvestPlus.org.

Additionally, the use of ferritin is currently being explored as a strategy in iron supplementation or biofortification, which showed by Lv et al. [37] in a study of in vitro and in vivo digestibility (with Caco-2 cells).

6. Conclusions

Iron deficiency is a big health problem that affects a large proportion of the world's population, especially in developing countries, causing what is known as "hidden malnutrition." In this chapter, the importance of iron is mentioned, as well as its functions within the organism as an oxygen transporter and forming part of some enzymes. The absorption of this mineral depends on several factors such as the ferrous forms, hemic and non-hemic, presence of other minerals, phytates, and some polyphenols. Plant-based foods commonly contain non-hemic Fe, which is considered to be of low solubility and bioavailability; however, some plants contain hemic Fe, forming part of proteins such as ferritin and leghemoglobin, also some plant foods contain high amounts of Fe as pumpkins, cocoa, and various legumes such as beans, soybeans, fava beans, especially their roots that form nodules with bacteria, which will convert atmospheric nitrogen to form soluble by the plant; consequently, they have a large amount of leghemoglobin, which is an oxygen carrier protein and rich in hemic Fe.

Likewise, strategies to reduce iron deficiency are mentioned, as well as the diversification of foods rich in this mineral, supplementation, and fortification of popular consumed foods enriched in Fe. One of the strategies that has worked so far is the biofortification of staple crops in rural areas in developing countries, with high iron contents and low levels of absorption inhibitor compounds. The biofortification is done through the combination of fertilization with conventional genetic or transgenic improvement that enriches crops with high iron content of high bioavailability, which is estimated that more than 20 million people in developing countries consume biofortified crops.

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Conflict of interest

The authors declare no conflict of interest.

Author contributions

All authors participated in the analysis of information and write and corrections of this chapter.

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