International Journal of Research in Engineering and Innovation (IJREI)
journal home page: http://www.ijrei.com
ISSN (Online): 2456-6934

REVIEW ARTICLE

The effect of nutrition by enhancing the absorption of iron in patients with iron deficiency anemia

Sami Khudhur Saeed

Department of Food Science, College of Agriculture, University of Tikrit, Tikrit, Iraq.

Article Information

Received: 27 Jan 2023
Revised: 14 March 2023
Accepted: 26 March 2023
Available online: 03 April 2023

Keywords:

Nutritional anemia
Iron deficiency
Anemia
Iron Absorption.

Abstract

Iron deficiency is a major nutritional problem that affects a large portion of the world's population, particularly in developing countries. Iron is an essential mineral that plays a critical role in the body's production of hemoglobin, a protein in red blood cells that carries oxygen from the lungs to the rest of the body. Without adequate iron, the body cannot produce enough hemoglobin, which can lead to anemia, fatigue, weakness, and a range of other health problems, affecting both males and females of all age groups. However, females and adolescents are particularly vulnerable due to increased iron needs during growth and development, as well as menstruation in females. Iron deficiency can progress through different stages, as you mentioned. Mild or moderate deficiency occurs when iron stores become depleted, while in a mild deficiency, the production of some iron-dependent proteins may be affected but hemoglobin levels remain normal. In contrast, iron deficiency anemia occurs when hemoglobin production is significantly reduced, resulting in a decrease in oxygen delivery to the tissues. While measuring hemoglobin levels is a common method to diagnose iron deficiency anemia, it is not always sensitive or specific enough to detect early stages of iron deficiency. This can be achieved through a combination of dietary changes, iron supplementation, and medical treatment, depending on the severity of the deficiency.

1. Introduction

Iron is an essential mineral that is required by all human cells and is a component of nearly all living cells. Iron plays a vital role in transporting oxygen to tissues, promoting cell growth and regulating immune function and energy metabolism. Iron absorption is also affected by the form of iron consumed. Heme iron, which is found in animal-based foods such as meat, poultry, and fish, is more readily absorbed than non-heme iron, which is found in plant-based foods such as grains, vegetables, and legumes. However, consuming non-heme iron with vitamin C-rich foods can increase its absorption. The body has mechanisms for adjusting iron absorption based on physiological demands, which allows for appropriate increases or decreases in iron absorption as needed. Iron deficiency can occur when the body's iron stores become depleted, which can lead to anemia and other negative health outcomes. Adequate intake of dietary iron, along with proper absorption and utilization of iron, is crucial for maintaining good health. Iron-rich foods include red meat, poultry, fish, beans, lentils, spinach, and fortified cereals. In some cases, iron supplements may be necessary to correct deficiencies [1]. Iron is crucial for meeting the physiological needs of infants, especially during the first six months of life. Adequate intake of iron through breast milk, formula, and iron-rich foods is essential to support the rapid growth and development that occurs during this

Corresponding author: Sami Khudhur Saeed
Email Address: samialobaidi@tu.edu.iq
https://doi.org/10.36037/IJREI.2022.7105

critical period. The average daily dietary requirement for iron in infants between the ages of 7 and 12 months is approximately 0.69 mg. Iron-rich foods, such as meats, fortified cereals, and legumes, can help meet the iron needs of infants. Breastfeeding is also an excellent source of iron and provides other essential nutrients and immune-boosting factors to support infant growth and development. Iron deficiency in infants can lead to anemia, impaired growth, and delayed cognitive development. It is essential to monitor infant iron status and provide appropriate iron supplementation or dietary adjustments if necessary to ensure optimal health and development. Iron requirements decrease after 12 months of age, with an average daily requirement of 0.63 mg/day for an 18-month-old child who is breastfed and has adequate weight. Infants who are exclusively breastfed and have a suitable birth weight rarely experience iron deficiency before the age of 6 months. there is a rapid increase in the risk of iron deficiency for infants who continue to be breastfed beyond six months of age if there is no adequate supply of iron from other dietary sources. Therefore, it is important to introduce iron-rich foods into an infant's diet between the ages of 4 to 6 months and to provide age-appropriate iron supplements if recommended by a healthcare professional. [2]. Iron in food can be classified into two types: heme and non-heme. Heme iron is found only in animal products, such as meat, poultry, and fish, while non-heme iron is present in plant-based foods, including vegetables, fruits, grains, nuts, and meat. Heme iron is absorbed more efficiently from the gut than non-heme iron. Proper regulation of dietary iron absorption is crucial to maintain normal iron levels in the body and minimize the risk of iron deficiency. Factors such as the presence of other nutrients, such as vitamin C, in the diet can enhance the absorption of non-heme iron. Cooking in cast iron pots can also increase the iron content of food. However, excessive iron intake can be harmful, particularly in individuals with certain genetic disorders that increase the risk of iron overload. Therefore, it is essential to maintain a balanced and varied diet to ensure adequate iron intake [3,4].

2. Absorption of iron from foods and supplements

Is facilitated by heme-carrier protein 1 (HCP1) in the small intestine, while absorption of non-heme iron is influenced by a variety of factors, such as the presence of other dietary components, pH, and the form of iron. In addition, the bioavailability of iron from different sources can vary greatly, with heme iron being generally more bioavailable than non-heme iron. iron deficiency can result from inadequate dietary intake, poor absorption of iron, or excessive loss of iron from the body. Certain groups, such as pregnant women, young children, and individuals following vegetarian or vegan diets, are at a higher risk of iron deficiency and need to ensure they are meeting their iron needs through diet or supplementation. [5]. Iron deficiency anemia is a common consequence of severe iron deficiency and can lead to fatigue, weakness, and impaired cognitive function. Iron supplements and iron-fortified foods are commonly used to treat and prevent iron deficiency, but it is important to balance the risks and benefits of these interventions, especially in populations with a high risk of iron overload. Iron deficiency is one of the most common nutrient deficiencies worldwide, and it can have serious consequences for health. Iron is an essential nutrient that plays a key role in many biological processes in the body, including the transport of oxygen in the blood. Iron is found in both heme and non-heme forms in the diet. Heme iron is found in animal-based foods, such as meat, poultry, and seafood, and is generally more easily absorbed by the body than non-heme iron, which is found in plant-based foods, such as beans, lentils, spinach, and fortified cereals [5]. Absorption of iron as heme in the gut takes place via special pathways relying on the kind of iron present. It is worth noting that the absorption of non-heme iron is influenced by various factors, such as dietary factors (e.g., the presence of enhancers or inhibitors of iron absorption in the diet), the individual's iron status, and the presence of other nutrients (e.g., vitamin C) that can enhance or inhibit iron absorption. Non-heme iron in the intestinal lumen is reduced to Fe^{2+} by the ferric reductase CYBRD1 (DCYTB), which is located on the apical membrane of the enterocyte. Once reduced, Fe^{2+} can then be transported into the enterocyte via divalent metal transporter 1 (DMT1). Inside the enterocyte, the Fe^{2+} can either be stored as ferritin or be transported across the basolateral membrane into the bloodstream by ferroportin (FPN1), which is the only known iron exporter in mammals. However, the export of iron by ferroportin is regulated by a hormone called hepcidin. Hepcidin binds to ferroportin and causes its internalization and degradation, which decreases iron export from the enterocyte into the bloodstream. In contrast, low levels of hepcidin increase iron export from the enterocyte into the bloodstream It is worth noting that the regulation of iron absorption and metabolism is complex and involves various factors such as iron status, erythropoiesis, inflammation, and other hormones besides hepcidin. The expression of ferroportin (FPN1) is regulated by hepcidin, a hormone produced by the liver. When iron levels are high, hepcidin binds to FPN1 on the basolateral membrane of the enterocyte, causing internalization and degradation of FPN1. This leads to decreased iron export from the enterocyte into the bloodstream, which helps to prevent iron overload. In contrast, when iron levels are low, hepcidin levels decrease, allowing FPN1 to be expressed on the basolateral membrane of the enterocyte, which leads to increased iron export from the enterocyte into the bloodstream. Hephaestin is an enzyme that is involved in iron metabolism and is primarily found in the small intestine. It plays a role in the conversion of Fe^{2+} to Fe^{3+} and in the binding of apo-transferrin to iron to form transferrin. Transferrin is a plasma protein that binds and transports iron throughout the body.

There are several options available for treating iron deficiency, including oral iron supplements. Iron supplements are often recommended to increase iron intake in individuals with iron deficiency anemia. Oral iron supplements are usually in the form of ferrous iron (Fe^{2+}) salts, such as ferrous sulfate, which can be efficiently absorbed in the gut, especially in the duodenum. The absorption of iron supplements can be enhanced by consuming them with vitamin C, which can improve the solubility and absorption of non-heme iron. It is important to note that excessive iron intake can be toxic and can cause gastrointestinal upset, so it is essential to take iron supplements as directed by a healthcare professional. You are correct! Research has shown that combining juices that are rich in ascorbic acid with legumes and meat can increase the absorption of non-heme iron, which is present in vegetables, legumes, and grains. This is because ascorbic acid (vitamin C) can reduce $Fe3+$ to $Fe2+$ and enhance the solubility and absorption of non-heme iron. However, it is important to note that excessive intake of ascorbic acid may cause gastrointestinal upset, and it is recommended to consume it in moderation. On the other hand, milk has a low iron absorption rate because it contains calcium, which can inhibit iron absorption. The calcium in milk competes with iron for binding to the same transporters in the intestinal cells. Therefore, it is recommended that children and pregnant women avoid consuming milk or dairy products together with iron-rich foods to enhance iron absorption. It is also important to note that iron absorption can be influenced by other dietary factors, such as phytates, tannins, and polyphenols, which can inhibit iron absorption. Phytates, for example, are present in whole grains and legumes and can form complexes with iron, reducing its availability for absorption. However, soaking, fermenting, or sprouting these foods can reduce the phytate content and increase iron availability. Therefore, it is important to consume a balanced diet that includes a variety of iron-rich foods and to consider dietary factors that can affect iron absorption.

[6]. A study conducted on mice found that neither black tea nor green tea had a negative impact on the growth or metabolism of the mice, and they did not pose a risk to iron bioavailability. In fact, the study found that black tea and green tea increased the absorption of iron from iron-fortified diets in mice. However, it is important to note that the results from animal studies cannot always be generalized to humans.

Several studies have examined the effect of tea consumption on iron absorption in humans, but the results have been inconsistent. Some studies have reported a decrease in iron absorption with tea consumption, while others have found no effect or even an increase in iron absorption. The exact mechanisms underlying the interaction between tea compounds and iron absorption in humans are not well understood and require further investigation. It is also important to note that the type and preparation of tea may affect its interaction with iron absorption. For example, black tea, which is fully oxidized, may have a different effect on iron absorption compared to green tea, which is unoxidized. Additionally, the addition of milk to tea may also affect iron absorption, as mentioned earlier. While the results from animal studies suggest that tea consumption may not negatively impact iron absorption, further research is needed to understand the potential effects of tea compounds on iron bioavailability in humans [7]. Iron is an essential nutrient that is required for a variety of important physiological processes, such as oxygen transport, energy production, and immune function. Iron deficiency can lead to a range of negative health outcomes, particularly in infants and young children, including developmental delays, impaired cognitive function, and an increased risk of infections. Breast milk is naturally rich in iron, and the iron in breast milk is highly bioavailable and easily absorbed by the infant's body. However, the iron content of breast milk is relatively low compared to that of iron-fortified formula, which contains added iron in a form that is also easily absorbed. The studies suggest that iron-fortified formula and breast milk may provide similar amounts of iron to infants in the first 3-6 months of life, as measured by hemoglobin-bound iron levels. However, it is important to note that these studies only evaluated iron status and did not assess other aspects of infant health or development. Additionally, as you mentioned, there are several compounds that can enhance iron absorption in the intestine, and these compounds are present in varying amounts in different foods. For example, vitamin C can enhance iron absorption from plant-based foods, while animal-based foods tend to contain heme iron, which is more easily absorbed than non-heme iron from plant-based sources. Therefore, it is important for infants and young children to consume a varied and balanced diet that includes a variety of iron-rich foods, as well as foods that enhance iron absorption [8–11]. Phytates are naturally occurring compounds found in many plant-based foods, such as grains, legumes, nuts, and seeds. Phytates can bind to minerals, including iron, in the intestinal tract, reducing their absorption. However, compounds such as citric acid, ascorbic acid (vitamin C), and polyphenols found in fruits, vegetables, and some beverages can reduce the inhibitory effects of phytates on iron absorption. Polyphenols are a class of compounds that are found in many plant-based foods, including fruits, vegetables, and beverages such as tea and coffee. Some polyphenols have been shown to inhibit the absorption of non-heme iron from food, while others may enhance it. The effects of polyphenols on iron absorption can vary depending on the type and amount of polyphenols consumed, as well as the iron source. Alcohol consumption can also affect iron absorption. Research has shown that alcohol can reduce the absorption of ferrous iron, which is the more easily absorbed form of iron found in some iron supplements and fortified foods. However, alcohol may increase the absorption of ferric iron, which is the form of iron found in many plant-based foods. Prebiotics and probiotics are types of dietary fibers and microorganisms, respectively, that can promote the growth and activity of beneficial gut bacteria. Some studies have suggested that the consumption of prebiotics and probiotics can enhance iron absorption by improving gut health and increasing the production of compounds that promote iron uptake. However, more research is needed to fully understand the effects of prebiotics and probiotics on iron absorption and their potential benefits for iron status [12,13].

3. Management of iron-deficiency anemia

Oral iron supplements can be effective in treating iron deficiency anemia, but they can also have side effects that limit their use and compliance. These side effects can include gastrointestinal symptoms such as constipation, dyspepsia, nausea, stomach discomfort, diarrhea, and vomiting. In some cases, these side effects can be severe enough to cause patients to discontinue treatment. Intravenous (IV) iron therapy is an alternative option for treating iron deficiency anemia, particularly in cases where oral iron supplements are ineffective, not well tolerated, or cannot be used due to underlying medical conditions such as inflammatory bowel disease or celiac disease. IV iron therapy can also be beneficial in cases of severe iron deficiency anemia where a rapid increase in hemoglobin levels is needed. IV iron therapy involves the administration of iron directly into the bloodstream through a vein, typically in a hospital or clinic setting. This allows for the precise calculation and prescription of the appropriate iron dose needed for the regulation of hemoglobin levels and restoration of iron reserves. IV iron therapy has been shown to be effective in treating iron deficiency anemia with fewer gastrointestinal side effects compared to oral iron supplements. However, like any medical treatment, IV iron therapy has potential risks and side effects, such as allergic reactions, hypotension, and infection. Therefore, it is important for patients to discuss the potential benefits and risks of IV iron therapy with their healthcare provider to determine if it is a suitable treatment option for their individual needs [14]. Additionally, intravenous iron therapy may also be preferred in cases where oral iron supplementation is not effective or feasible, such as in patients with malabsorption syndromes or those who cannot tolerate oral iron due to adverse effects. It is important to note that intravenous iron therapy may also have potential side effects, including allergic reactions and hypotension, and should be administered under close medical supervision. The choice of iron therapy for the treatment of iron deficiency anemia should be made on an individual basis, considering the patient's medical history, underlying conditions, and preferences. In some cases, oral iron supplements may be sufficient to correct iron deficiency anemia, while in others, IV iron therapy may be necessary. When considering oral iron therapy, the healthcare provider should consider factors such as the patient's ability to tolerate oral iron supplements, the severity of anemia, and any underlying conditions that may affect the absorption of oral iron. For example, patients with inflammatory bowel disease or celiac disease may have impaired absorption of oral iron and may require higher doses or longer treatment durations. In cases where oral iron therapy is not effective or not well tolerated, IV iron therapy may be a suitable option. However, the healthcare provider should also consider the potential risks and side effects associated with IV iron therapy, such as allergic reactions, hypotension, and infection. Patients should be fully informed of the potential benefits and risks of each treatment option to make an informed decision about their care. Ultimately, the goal of iron therapy is to effectively treat iron deficiency anemia while minimizing potential risks and side effects. The healthcare provider and patient should work together to determine the most appropriate treatment approach based on the individual's unique circumstances. [15]. Figure 1 indicates the essential causes, manifestations, and contemporary remedies for iron-deficiency in humans.

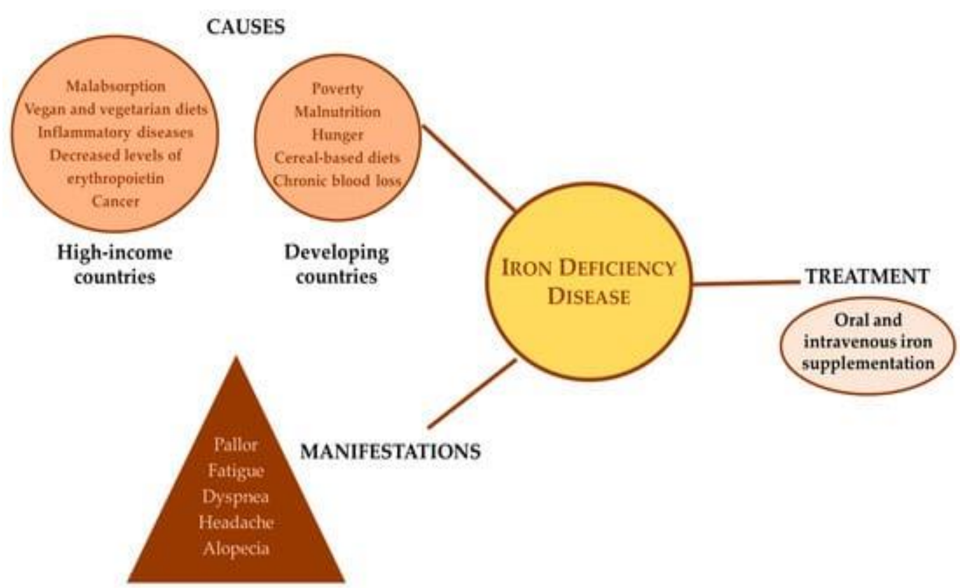

Figure 1: Main causes, manifestations, and modern redress for iron-deficiency in humans [16].

In recent decades, there has been growing interest in hydrolysates derived from the proteolytic digestion of various food sources. Protein hydrolysates are often used as a source of peptides that can bind metal ions, such as iron, and improve their stability, solubility, and bioavailability. Peptides are chains of amino acids that can chelate or bind metal ions through functional groups, such as carboxyl, amino, and imidazole groups. The spatial configuration and various residue chains of peptides allow them to donate electrons and form coordination complexes with metal ions. This can result in the stabilization and solubilization of metal ions, making them more available for absorption and utilization by the body. In addition to their metal-binding properties, protein hydrolysates, and peptides have been found to have other potential health benefits, such as antioxidant, antihypertensive, and antimicrobial properties. They are also generally well-tolerated and have a low risk of adverse effects. Overall, protein hydrolysates and peptides show promise as a means of improving the bioavailability and utilization of metal ions, such as iron, and may have other potential health benefits as well. Further research is needed to fully understand their mechanisms of action and potential applications in various health conditions [17].Evan and Gulec's research sounds interesting and promising. Lentils are a good source of protein and iron, and the hydrolyzed protein-iron complex derived from lentils may be an effective way to improve iron bioavailability in individuals with iron deficiency anemia. The fact that the complex was able to reduce the mRNA levels of DMT1, TFR, and ANKRD37 in the anemic caco-2 cell line suggests that it may help improve iron absorption and utilization in the body. DMT1 and TFR are important proteins involved in the absorption and transport of iron, while ANKRD37 is a gene that is upregulated in response to iron deficiency. However, it is important to note that in vitro studies like this one do not necessarily reflect what happens in the human body. Further research, including in vivo studies and clinical trials, would be needed to determine the safety and effectiveness of the hydrolyzed protein-iron complex derived from lentils in humans with iron deficiency anemia [18]. Gómez et al.'s research on using red tilapia viscera to produce a protein hydrolysate with iron-chelating activity is interesting and promising. The fact that the RTVH-B showed the highest iron-binding capacity and the Fe^{2+}–RTVH-B complex demonstrated significantly higher iron bioavailability than free iron salts suggests that the protein hydrolysate could be an effective way to improve iron absorption and utilization in the body. Furthermore, the fact that iron bioavailability was indirectly measured by ferritin synthesis in a caco-2 cell model is a useful tool for assessing iron bioavailability in vitro. However, it is important to note that in vitro studies like this one do not necessarily reflect what happens in the human body. Further research, including in vivo studies and clinical trials, would be needed to determine the safety and effectiveness of the red tilapia viscera protein hydrolysate as a dietary supplement to improve iron absorption in humans [19]. Iron can form complexes with various compounds, including proteins, that can affect its bioavailability. Studies have shown that whey protein, which is a protein derived from milk, can form complexes with iron and enhance its absorption in the small intestine. Whey protein contains a peptide called lactoferrin, which has a high affinity for iron and can bind to it, forming a complex that is easily absorbed by the body. The complexation of iron with whey protein can increase its solubility and protect it from binding to other compounds that may inhibit its absorption, such as phytates and polyphenols. This can be particularly beneficial for individuals with iron deficiency or those who consume a plant-based diet that is high in phytates, which can bind to iron and reduce its bioavailability. However, it is important to note that excessive intake of iron can be toxic to the body, and individuals should not consume excessive amounts of iron or iron supplements without the guidance of a healthcare professional. Additionally, individuals who are allergic to milk or have lactose intolerance may not be able to tolerate whey protein and should explore other sources of iron or consult with a healthcare professional for alternative options. [20]. Shilpashree et al.'s study on the preparation of whey protein-iron and whey protein-zinc complexes is interesting and suggests that the complexes may have potential benefits over free minerals. The fact that the complexes formed with whey protein had significantly lower pro-oxidant activity suggests that the complexes may be more stable and less likely to undergo oxidation, which could potentially reduce their effectiveness as dietary supplements. This is important because oxidation can reduce the bioavailability of minerals. Additionally, the fact that the complexes had higher bioaccessibility compared to free minerals suggests that the complexes may be better absorbed by the body. Bioaccessibility refers to the amount of a nutrient that is released from food during digestion and is available for absorption by the body. Higher bioaccessibility generally means better absorption and utilization by the body. However, it is important to note that these were in vitro studies, and further research, including in vivo studies and clinical trials, would be needed to determine the safety and effectiveness of whey protein-iron and whey protein-zinc complexes as dietary supplements in humans.

The bioavailability of the minerals in the complexes was also found to be significantly increased compared to free minerals when tested on Caco-2 cells, which are a model for intestinal absorption. The study also suggested that complexing iron with whey protein may inhibit its catalytic activity, which can prevent oxidative damage in the body. These findings suggest that whey protein-bound minerals may have the potential as natural fortificants in various food products. It is important to note that while the study suggests potential benefits of these complexes, further research is needed to determine their safety and efficacy in humans, as well as their potential interactions with other nutrients or medications [21]. Caetano-Silva et al.'s study on whey protein-iron complexes using specific ligands and different iron sources is interesting and suggests that the complexes may have potential benefits for enhancing the bioavailability of iron. The fact that the complexes prepared with small molecular mass peptides and $FeCl_2$ significantly enhanced the bioavailability of iron by approximately 70% compared to $FeSO_4$ is noteworthy. This suggests that the use of specific ligands and iron sources can play an important role in enhancing the bioavailability of iron. However, it is important to note that the bioavailability was assessed indirectly by measuring ferritin synthesis in the caco-2 cell model. While this is a useful tool for assessing iron bioavailability in vitro, it does not necessarily reflect what happens in the human body. Further research, including in vivo studies and clinical trials, would be needed to determine the safety and effectiveness of whey protein-iron complexes as dietary supplements in humans It is important to note that while Caetano-Silva et al. found that the whey protein-iron complexes prepared with small molecular mass peptides and FeCl2 significantly enhanced the bioavailability of iron, the bioaccessibility of the complexes after in vitro gastrointestinal digestion was not significantly different from that of the iron salts alone. This suggests that while the complexes may enhance the bioavailability of iron under certain conditions, their overall impact on iron status and health outcomes may be limited by their bioaccessibility. Furthermore, as you mentioned earlier, the study was carried out under in vitro conditions and further studies, including in vivo studies and clinical trials, would be needed to confirm these findings and to assess the safety and effectiveness of these complexes as dietary supplements in humans. The study by Caetano-Silva et al. on whey protein-iron complexes. The finding that the complexes prepared with small molecular mass peptides and FeCl2 significantly enhanced the bioavailability of iron by about 70% compared to FeSO4 is promising. Additionally, the improvement in the bioaccessibility rate to a level greater than 85% for most of the complexes is noteworthy. However, as you mentioned, it is important to note that the bioavailability was assessed indirectly by measuring ferritin synthesis in a caco-2 cell model, and the impact of these complexes on iron status and overall health outcomes needs to be further investigated. In vivo studies and clinical trials would be needed to determine the safety and effectiveness of these complexes as dietary supplements in humans. Overall, the study by Caetano-Silva et al. provides valuable insights into the potential of whey protein-iron complexes as a strategy for improving the bioavailability of iron. However, further research is needed to confirm these findings and to determine the optimal conditions for preparing and using these complexes [22]. The study by Gandhi et al. assessed the bioavailability of iron from a spray-dried whey protein concentrate-iron (WPC-Fe) complex in weaning and anemic rats. It appears that the study by Alemán et al. showed promising results regarding the potential of whey protein-iron complexes to improve iron bioavailability and combat iron-deficiency-related disorders in rats. The study by Shilpashree et al. on a succinylated sodium caseinate-iron complex also supports these findings. However, as with previous studies, it is important to note that further research is needed to confirm these results under in vivo conditions and to assess the overall impact of these complexes on human health outcomes.

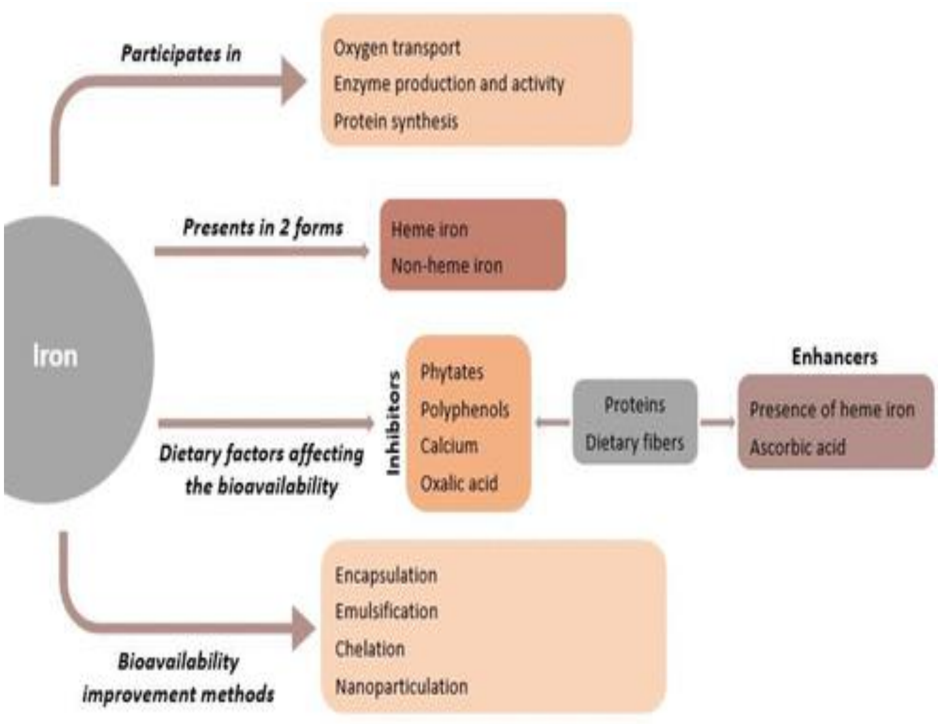

Figure 2: Iron absorption with factors, limitations, and development methods [28].

These studies provide evidence for the potential use of protein-iron complexes as a strategy for improving iron bioavailability and reducing the incidence of anemia and related disorders. However, further research is needed to confirm these findings under in vivo conditions in humans [23] and lactose–iron tricky (Sharma et al.) [24]. range of vitamins and minerals, including iron. For example, iron oxide nanoparticles have been shown to enhance the bioavailability of iron in food matrices by up to 12-fold [26]. Additionally, the encapsulation of iron within nanoparticles can protect it from degradation and improve its solubility, stability, and bioavailability. Several types of nanoparticles have been investigated for their potential use in iron fortification, including liposomes, solid lipid nanoparticles, and polymeric nanoparticles. These nanoparticles can be loaded with iron and incorporated into food matrices, such as beverages, dairy products, and baked goods. The use of nanoparticles in food fortification has the potential to increase the efficiency and effectiveness of iron fortification programs, particularly in populations with high rates of iron deficiency and anemia [25]. Furthermore, nanotechnology has also been explored for the targeted delivery of iron supplements and drugs for the treatment of anemia. For example, iron-loaded nanoparticles can be designed to selectively accumulate in the bone marrow, where they can release iron to support erythropoiesis, the production of red blood cells [26]. The use of nanotechnology for the targeted delivery of iron supplements and drugs has the potential to increase their effectiveness while minimizing side effects and toxicity. In conclusion, the use of nanotechnology in iron fortification and anemia treatment is an emerging area of research that holds great promise for improving the nutritional status and health outcomes of populations affected by iron deficiency and anemia [26,27].

While nanotechnology-based approaches have shown promise in enhancing the bioavailability of iron, their safety, and potential adverse effects are still a concern. The formation and mechanism of action of ferritin-mimetic nanoparticles are not yet fully understood, and further research is needed to determine their safety and efficacy. Additionally, it is crucial to establish regulatory guidelines and standards for the use of nanoparticles in food fortification and drug delivery to ensure their safety for human consumption [29]. It is interesting to note that Li et al. have used negatively charged ferric hydroxide-polyphosphate nanoparticles (PolyP-FeONPs) to enhance iron bioavailability. Their findings suggest that PolyP-FeONPs may be a promising strategy for addressing iron-deficiency anemia. However, it is important to note that the study was carried out in vitro using rat-polarized human intestinal epithelial Caco-2 cells, and further research is needed to confirm these findings under in vivo conditions. However, further studies are needed to evaluate the safety and efficacy of these nanoparticles in vivo [30]. El-Saadony and colleagues used a bacterial supernatant to produce bio iron(II) nanoparticles that were combined with biodegradable amyloid fibrils to create a hybrid material. The resulting iron nanoparticles were stable and did not aggregate in foods or beverages. In vivo testing showed that the hybrid material was easily digested and provided bioavailable iron without negatively impacting the sensory characteristics of the food carriers. The researchers also supplemented yogurt with Bio-Fe(II) nanoparticles and found them to be safe and effective sources of iron with improved sensory properties [31]. Iron absorption can be improved by consuming foods that contain vitamin C, such as citrus fruits, strawberries, and bell peppers. Additionally, avoiding calcium-rich foods and drinks, such as milk and cheese, during meals that are high in iron can also improve absorption. Polyphenols, which are found in tea, coffee, and certain fruits and vegetables, can inhibit iron absorption, so it's best to consume these foods in moderation or separately from iron-rich foods[32]. Additionally, iron supplements or fortified foods can be used to increase iron intake in people who are unable to get enough iron from their diet alone [33]. Heme iron is mainly found in animal products such as red meat, poultry, and seafood, while non-heme iron is found in both animal and plant-based foods such as beans, lentils, spinach, fortified cereals, and tofu. Heme iron is more easily absorbed by the body than non-heme iron, but both types of iron can contribute to meeting daily iron needs when consumed as part of a balanced diet. [34]. Including enhancers of non-heme iron absorption in meals can increase the bioavailability of non-heme iron. For example, vitamin C (ascorbic acid) can enhance non-heme iron absorption by up to six times, while citric acid can increase absorption by up to three times. Malic acid, found in fruits such as apples, can also enhance absorption. Food processing techniques such as fermentation, soaking, and germination can also increase the bioavailability of non-heme iron by reducing the presence of inhibitors and increasing the activity of enzymes that promote iron absorption [35]. Food fortification with iron is a widely implemented strategy to combat iron deficiency anemia. Adding iron to staple food products such as cereals and flour is an effective way to increase iron intake, especially in populations where the consumption of animal-derived foods is low. This approach has been successful in several countries, and it is cost-effective and has a broad reach. However, it is important to ensure that the added iron is bioavailable and does not alter the sensory characteristics of the fortified food product, as this may affect its acceptance and consumption by the target population. [36]. Studies have shown that women tend to consume less meat than men, which can lead to lower iron intake. This is due to various reasons, including cultural and social norms, dietary preferences, and concerns about weight gain. Therefore, it is important to promote a diverse diet that includes both animal and plant-based sources of iron to ensure adequate iron intake for all individuals, regardless of gender. Additionally, education and awareness campaigns can play a significant role in promoting the importance of iron-rich diets and the prevention of iron-deficient anemia. Vegetarian and vegan diets can be lower in heme iron and higher in inhibitors of non-heme iron absorption, such as phytates and polyphenols found in whole grains, legumes, nuts, and vegetables. However, by combining non-heme iron sources with enhancers of iron absorption, such as vitamin C, iron absorption can be improved. Individuals on plant-based diets need to pay attention to their iron intake and ensure they are consuming enough iron-rich foods and enhancers of iron absorption to prevent iron deficiency anemia. Vitamin C, also known as ascorbic acid, is a powerful enhancer of iron absorption. It can help to convert the non-heme iron present in plant-based foods into a more easily absorbed form, and can also increase the absorption of heme iron from meat and fish. As a result, consuming foods rich in vitamin C alongside iron-rich foods can significantly enhance the bioavailability of dietary iron. Phytates, which are found in cereals, legumes, and some nuts, can form insoluble complexes with iron, making it unavailable for absorption. Calcium can also bind with iron to form insoluble complexes, thereby reducing iron bioavailability. Polyphenols, which are found in tea, coffee, red wine, and some fruits and vegetables, can also inhibit iron absorption by forming complexes with iron and reducing the solubility of iron in the small intestine. Therefore, it is important to consider not only the amount of iron in a meal but also the presence of enhancers and inhibitors of iron absorption to ensure optimal iron bioavailability. While reducing phytate levels in foods can potentially increase iron bioavailability, it does not always translate to improved iron status in individuals with suboptimal iron stores. This may be due to the presence of other inhibitors of iron absorption or individual differences in iron metabolism. Therefore, it is important to consider a combination of dietary strategies, such as promoting iron-rich foods and enhancing their bioavailability, to effectively prevent and treat iron-deficiency anemia. [37].

4. Conclusions

It is important to focus on preventative measures, such as promoting a diet rich in iron-containing foods and enhancing the bioavailability of iron through dietary modifications. Education and awareness campaigns targeted toward vulnerable populations, including pregnant women, infants, and young children, can also help prevent and address iron deficiency anemia. Furthermore, efforts should be made to identify and address the underlying causes of anemia, such as chronic diseases and infections, to effectively manage and treat the condition. Overall, a multi-faceted approach is necessary to address the global burden of iron deficiency anemia.

References

[1] Briguglio M, Hrelia S, Malaguti M, Lombardi G, Riso P, Porrini M, et al.The Central Role of Iron in Human Nutrition: From Folk to Contemporary Medicine. Nutrients 2020. 12(6):1761.

[2] Lynch SR, Stoltzfus RJ.Iron and ascorbic acid: proposed fortification levels and recommended iron compounds. J. Nutr. 2003. 133(9):2978S-84S.

[3] Hurrell, R. F. Preventing Iron Deficiency Through Food Fortification. Nutr. Rev. 1997, 55 (6), 210−222.

[4] Roughead, Z. K.; Zito, C. A.; Hunt, J. R. Initial Uptake and Absorption of Nonheme Iron and Absorption of Heme Iron in Humans Are Unaffected by the Addition of Calcium as Cheese to a Meal with High Iron Bioavailability. Am. J. Clin. Nutr. 2002, 76 (2), 419−425.

[5] Martınez-Navarrete, N.; Camacho, M.M.; Martınez-Lahuerta, J.; Martınez-Monzó, J.; Fito, P. Iron deficiency and iron fortified foods—A review. Food Res. Int. 2002, 35, 225–231.

[6] Brazaca, S.G.C.; da Silva, F.C. Enhancers and inhibitors of iron availability in legumes. Plant Foods Hum. Nutr. 2003, 58, 1–8.

[7] Record, I.R.; McInerney, J.K.; Dreosti, I.E. Black tea, green tea, and tea polyphenols. Biol. Trace Elem. Res. 1996, 53, 27–43.

[8] Milne, D.B.; Canfield, W.K.; Mahalko, J.R.; Sandstead, H.H. Effect of oral folic acid supplements on zinc, copper, and iron absorption and excretion. Am. J. Clin. Nutr. 1984, 39, 535–539.

[9] Shu, E.; Ogbodo, S. Role of Ascorbic Acid in the Prevention of Iron-Deficiency Anaemia in Pregnancy. Biomed. Res. 2005, 16, 40–44.

[10] Martínez-Torres, C.; Romano, E.; Layrisse, M. Effect of cysteine on iron absorption in man. Am. J. Clin. Nutr. 1981, 34, 322–327.

[11] García-Casal, M.N.; Layrisse, M.; Solano, L.; Barón, M.A.; Arguello, F.; Llovera, D.; Ramírez, J.; Leets, I.; Tropper, E. Vitamin A and β-Carotene Can Improve Nonheme Iron Absorption from Rice, Wheat and Corn by Humans. J. Nutr. 1998, 128, 646–650.

[12] Amos, A.; Alvan, A.; Florence, A. The Anti-Nutritional Effect of Phytate on Zinc, Iron and Calcium Bioavailabilities of Some Cereals Staple Foods in Zaria, Nigeria. Eur. J. Nutr. Food Saf. 2020, 1–6.

[13] Rosen, G.M.; Morrissette, S.; Larson, A.; Stading, P.; Griffin, K.H.; Barnes, T.L. Use of a Probiotic to Enhance Iron Absorption in a Randomized Trial of Pediatric Patients Presenting with Iron Deficiency. J. Pediatr. 2019, 207, 192–197.e1.

[14] Nickol, A.H.; Frise, M.C.; Cheng, H.Y.; McGahey, A.; McFadyen, B.M.; Harris-Wright, T.; Bart, N.K.; Curtis, M.K.; Khandwala, S.; O'Neill, D.P.; et al. A cross-sectional study of the prevalence and associations of iron deficiency in a cohort of patients with chronic obstructive pulmonary disease. Bmj Open 2015, 5, e007911.

[15] Auerbach, M.; Adamson, J.W. How we diagnose and treat iron deficiency anemia. Am. J. Hematol. 2016, 91, 31–38.

[16] Ângela Liberal, José Pinela, Ana Maria Vívar-Quintana, Isabel C. F. R. Ferreira, Lillian Barros, Fighting Iron-Deficiency Anemia: Innovations in Food Fortificants and Biofortification Strategies, Foods 2020, 9(12), 1871; https://doi.org/10.3390/foods9121871.

[17] Caetano-Silva, M. E.; Netto, F. M.; Bertoldo-Pacheco, M. T.; Alegría, A.; Cilla, A. Peptide-Metal Complexes: Obtention and Role in Increasing Bioavailability and Decreasing the pro-Oxidant Effect of Minerals. Crit. Rev. Food Sci. Nutr. 2021, 61 (9), 1470– 1489,

[18] Evcan, E.; Gulec, S. The Development of Lentil Derived Protein-Iron Complexes and Their Effects on Iron Deficiency Anemia in Vitro. Food Funct. 2020, 11 (5), 4185– 4192,

[19] Gómez, L. J.; Gómez, N. A.; Zapata, J. E.; López-Garciá, G.; Cilla, A.; Alegriá, A. Optimization of the Red Tilapia (Oreochromis Spp.) Viscera Hydrolysis for Obtaining Iron-Binding Peptides and Evaluation of In Vitro Iron Bioavailability. Foods 2020, 9 (7), 883

[20] Caetano-Silva, M. E.; Cilla, A.; Bertoldo-Pacheco, M. T.; Netto, F. M.; Alegría, A. Evaluation of in Vitro Iron Bioavailability in Free Form and as Whey Peptide-Iron Complexes. J. Food Compos. Anal. 2018, 68, 95–100,

[21] Shilpashree, B. G.; Arora, S.; Kapila, S.; Sharma, V. Whey Protein-Iron or Zinc Complexation Decreases pro-Oxidant Activity of Iron and Increases Iron and Zinc Bioavailability. LWT 2020, 126, 109287

[22] Gandhi, K.; Devi, S.; Gautam, P. B.; Sharma, R.; Mann, B.; Ranvir, S.; Sao, K.; Pandey, V. Enhanced Bioavailability of Iron from Spray Dried Whey Protein Concentrate-Iron (WPC-Fe) Complex in Anaemic and Weaning Conditions. J. Funct. Foods 2019, 58, 275– 281,

[23] Shilpashree, B. G.; Arora, S.; Kapila, S.; Sharma, V. Physicochemical Characterization of Mineral (Iron/Zinc) Bound Caseinate and Their Mineral Uptake in Caco-2 Cells. Food Chem. 2018, 257, 101–111

[24] Sharma, A.; Shilpa Shree, B. G.; Arora, S.; Kapila, S. Preparation of Lactose-Iron Complex and Its Cyto-Toxicity, in-Vitro Digestion and Bioaccessibility in Caco-2 Cell Model System. Food Biosci. 2017, 20, 125–130

[25] Kumari, A.; Anil, A.; Chauhan, K.; Chauhan, A. K. Iron Nanoparticles as a Promising Compound for Food Fortification in Iron Deficiency Anemia: A Review. J. Food Sci. Technol. 2021, 1– 17,

[26] Shafie, E. H.; Keshavarz, S. A.; Kefayati, M. E.; Taheri, F.; Sarbakhsh, P.; Vafa, M. R. The Effects of Nanoparticles Containing Iron on Blood and Inflammatory Markers in Comparison to Ferrous Sulfate in Anemic Rats. Int. J. Prev. Med. 2016,

[27] Foujdar, R.; Chopra, H. K.; Bera, M. B.; Chauhan, A. K.; Mahajan, P. Effect of Probe Ultrasonication, Microwave and Sunlight on Biosynthesis, Bioactivity and Structural Morphology of Punica Granatum Peel's Polyphenols-Based Silver Nanoconjugates. Waste Biomass Valorization 2020 125 2021, 12 (5), 2283– 2302,

[28] Elif Piskin, Danila Cianciosi, Sukru Gulec, Merve Tomas Esra Capanoglu, Iron Absorption: Factors, Limitations, and Improvement Methods. ACS Omega 2022, 7, 24, 20441–20456.

[29] Mattar, G.; Haddarah, A.; Haddad, J.; Pujola, M.; Sepulcre, F. New Approaches, Bioavailability and the Use of Chelates as a Promising Method for Food Fortification. Food Chem. 2022, 373, 131394

[30] Li, S.; Guo, T.; Guo, W.; Cui, X.; Zeng, M.; Wu, H. Polyphosphates as an Effective Vehicle for Delivery of Bioavailable Nanoparticulate Iron(III). Food Chem. 2022, 373, 131477,

[31] El-Saadony, M. T.; Sitohy, M. Z.; Ramadan, M. F.; Saad, A. M. Green Nanotechnology for Preserving and Enriching Yogurt with Biologically Available Iron (II). Innov. Food Sci. Emerg. Technol. 2021, 69, 102645

[32] Shen, Y.; Posavec, L.; Bolisetty, S.; Hilty, F. M.; Nyström, G.; Kohlbrecher, J.; Hilbe, M.; Rossi, A.; Baumgartner, J.; Zimmermann, M. B.; Mezzenga, R. Amyloid Fibril Systems Reduce, Stabilize and Deliver Bioavailable Nanosized Iron. Nat. Nanotechnol. 2017, 12 (7), 642– 647,

[33] Skrypnik, K.; Bogdanski, P.; Schmidt, M.; Suliburska, J. The Effect of Multispecies Probiotic Supplementation on Iron Status in Rats. Biol. Trace Elem. Res. 2019, 192, 234–243.

[34] World Health Organization. Nutritional Anaemias: Tools for Effective Prevention and Control; World Health Organization: Geneva, Switzerland, 2017.

[35] Nutritional Institutes of Health. Iron. Available online: https://ods.od.nih.gov/factsheets/Iron-HealthProfessional/ (accessed on 7 April 2022).

[36] Shubham, K.; Anukiruthika, T.; Dutta, S.; Kashyap, A.V.; Moses, J.A.; Anandharamakrishnan, C. Iron deficiency anemia: A comprehensive review on iron absorption, bioavailability and emerging food fortification approaches. Trends Food Sci. Technol. 2020, 99, 58–75.

[37] Dominika Skolmowska, Dominika Głabska, Aleksandra Kołota, Dominika Guzek, Effectiveness of Dietary Interventions to Treat Iron-Deficiency Anemia in Women: A Systematic Review of Randomized Controlled Trials, Nutrients 2022, 14, 2724.

Cite this article as: Sami Khudhur Saeed, the effect of Nutrition by Enhancing the Absorption of Iron in Patients with Iron Deficiency Anemia, International Journal of Research in Engineering and Innovation Vol-7, Issue-1 (2023), 30-38. *https://doi.org/10.36037/IJREI.2022.7105*.