



Proceeding Paper

Food-Based Intervention Strategies for Iron Deficiency Prevention †

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Abstract: An urgent issue in the development of food technologies is the creation of biologically complete foods. It is well known that deficiency of various elements has noticeable effects on human health. One of these areas is devoted to solving the problem of preventing iron deficiency states. Iron deficiency and iron deficiency anemia are common medical conditions worldwide. The analysis of statistics and the accumulation of new scientific facts about the pathological processes associated with iron deficiency provide grounds for confirming the fact that the fight against this phenomenon is an actual process. Current strategies for the prevention of this condition are one way or another related to food. The analysis of scientific publications made it possible to identify the main food-based intervention strategies: food and nutrition education with food diversification, biofortification, iron supplementation, iron fortification of certain foods, and food-to-food fortification. Finally, we discuss these strategies for the prevention of iron deficiency.

Keywords: iron-enriched foods; iron deficiency anemia; iron-containing supplement; functional foods; fortification



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1. Introduction

Iron deficiency (ID) and iron deficiency anemia (IDA) are among the common diseases that affect the population of many countries of the world [1]. In general, the condition associated with ID is the most widespread nutritional disorder in the world and is a public health problem in low- and middle-income countries [2]. According to studies [3,4], the tendency to ID is most often observed in children, women during menstruation, or pregnant women, as well as in those who follow an iron-deficient diet. If these categories of the population have a long-term negative iron balance, ID is observed, which, like a disease, proceeds in several stages [5]:

- initially, a mild form occurs due to low iron diets or excessive bleeding;
- its further progress is associated with a stage of more severe depletion of iron reserves in the body and a decrease in the number of red blood cells;
- ultimately all this leads to IDA, a condition characterized by depleted iron reserves and a significant loss of total red blood cells.

Iron deprivation from both erythroblasts and other tissues occurs when inflammation causes plasma iron retention or when total body iron stores are low [6]. Anemia is defined as a low blood hemoglobin concentration. As a result, the formation of hemoglobin is disrupted, hypochromic anemia, and trophic disorders in the tissues occur.

Iron deficiency anemia is often associated with other chronic diseases. The latter include chronic kidney disease, chronic heart failure, cancer, and inflammatory bowel disease [7,8]. According to studies [9], ID is associated with lower developmental scores in

infants and lower scores on cognitive function tests in children. Recent studies conducted during the course of the pandemic have shown the impact of anemia on COVID-19 [10,11].

2. Statistical Data of Iron Deficiency

Statistical data, usually based on the results of research by the World Health Organization, indicate that ID and IDA are a significant global health problem and a challenge for developing countries, including Ukraine. However, it should be taken into account that there is a certain difficulty in obtaining quantitative statistical data for an adequate assessment of the epidemiological situation. It is connected with the existence of various methodological approaches to research. Thus, according to WHO estimates in 2011 [12], approximately 43% of children, 38% of pregnant women, 29% of non-pregnant women, and 29% of all women of reproductive age suffer from anemia. Globally, this corresponds to 273 million children, 496 million non-pregnant women, and 32 million pregnant women. According to WHO mortality data, about 0.8 million deaths (1.5% of the total) each year can be attributed to iron deficiency, and in terms of loss of healthy life expressed in disability-adjusted life years (DALYs), iron-deficiency anemia results in the loss of 25 million DALYs (or 2.4% of the global figure) [13]. A later source gives the following data [14]:

- the prevalence of anemia among the world's population of all ages was 22.8%, which is on a downward trend, taking into account the 27.0% in 1990;
- as the prevalence of the disease has declined, the total number of cases of anemia has increased from 1.42 billion in 1990 to 1.74 billion in 2019;
- the population most susceptible to anemia is children under the age of five;
- according to the severity of the course of the disease, the following distribution was obtained: 54.1% of cases of anemia were mild, 42.5%—moderate, and 3.4%—severe;
- in 2019, anemia was responsible for 58.6 million DALYs.

3. Iron Deficiency Medical Condition and Its Prevention Strategies

The above statistics and the accumulation of new scientific facts about the pathological processes associated with iron deficiency provide grounds for confirming the fact that the fight against this phenomenon is an actual process. Current main food-based intervention strategies for the prevention of this condition can be presented in the form of a diagram (Figure 1) (adopted from [15–18]).

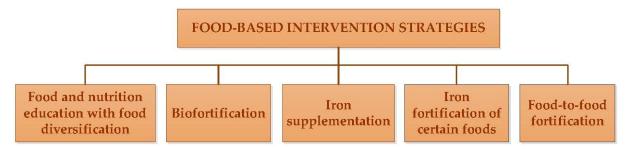


Figure 1. Prevention of iron deficiency: Intervention strategies.

Almost all of the above types of interventions have a single goal associated with improving iron intake and its bioavailability.

3.1. Food and Nutrition Education with Food Diversification

Thus, food diversification in combination with nutritional training achieves this goal of increased intake of iron-rich foods, especially flesh foods [16]. This is especially true for the consumption of fruits and vegetables rich in ascorbic acid content. This component is known to help improve iron absorption. At the same time, there is an emphasis on reducing the consumption of foods that inhibit this process, such as coffee and tea (due to tannins found in black tea and coffee inhibiting iron absorption). Inositol hexaphosphate (phytic

acid) also prevents the absorption of iron. To avoid the influence of this factor, a different approach is used—enzymatic and non-enzymatic methods of processing products, especially of plant origin. Enzymatic methods such as sprouting and fermentation promote the enzymatic hydrolysis of phytic acid in whole-grain cereals and legumes by increasing the activity of endogenous or exogenous phytase enzymes. At the same time, non-enzymatic methods such as heat treatment, soaking, and grinding are used to reduce the phytic acid content of plant foods.

3.2. Biofortification

In addition to consuming foods traditionally high in iron, there are no other opportunities to increase iron content in previously low-iron items. This can be achieved with the help of biofortification, which has a variety of methods aimed at enriching crops with vital macro- and microelements using biotechnological processes. The goal of this approach is to enhance the nutritional value of any food crop [19]. In the implementation of this goal, there are three main approaches to the biofortification of agricultural crops: conventional, agronomic, and transgenic biofortification [20].

3.3. Iron Suplementions

Iron supplementation is a term used to describe the provision of relatively large doses of iron. This is usually a specialty product in the form of pills, capsules, or syrups. According to the authors of the review [13], this type of intervention has two main advantages:

- provides the ability to consume the optimal amount of a specific one or more nutrients in a highly absorbable form,
- the fastest way to control deficiency in individuals or populations [13].

3.4. Iron Fortification of Certain Foods

Food fortification means adding micronutrients to processed foods. Iron fortification of foods is a practice used commercially. Using evidence-based data on the Recommended Dietary Allowance (RDA) allows for an increase in the amount of iron in developed or manufactured foods. This technique is carried out, on the one hand, in order to improve the nutritional value of food products, and, on the other hand, to provide benefits to public health with minimal risk to health. As noted in [21], food fortification has been used for many years in industrialized countries and gives satisfactory results for the successful control of various micronutrient deficiencies, including iron. In almost many situations, this results in a relatively rapid improvement in the micronutrient status of the population at a reasonable cost. In almost many situations, this leads to a relatively rapid improvement in the micronutrient status of the population at a reasonable cost, which is not unimportant. This approach is especially important in countries where there is a lack of adequate levels of appropriate nutrients in the diet due to insufficient existing food supplies or limited access to food [13].

However, a number of requirements must be met: fortified foods must be consumed in sufficient quantities by a significant proportion of target individuals in the population; in the fortification process, fortifiers should be used that are well absorbed and do not affect the sensory properties of products [13]. The first requirement is related to the Recommended Dietary Allowance. So, according to the National Academies of Sciences, Engineering, and Medicine [22], the RDA for all age groups of men and postmenopausal women is 8 mg/day; the RDA for premenopausal women is 18 mg/day. Mean dietary iron intake varies between men and women and is approximately 16–18 mg/day and 12 mg/day, respectively. The tolerable upper intake level (UL) for adults based on gastrointestinal distress as an adverse effect is 45 mg/day of iron [22]. Recommended composition of dietary supplements to complement fortified foods for iron 10 mg [13].

When considering the second requirement, it should be borne in mind that a wide variety of iron compounds, mainly in inorganic form, are currently used as food fortifiers. These can be broadly divided into three categories: water soluble; poorly water soluble but

soluble in dilute acid; water insoluble and poorly soluble in dilute acid [13]. According to the author [23], given the proven effectiveness, such a division is possible into four categories. The first three categories coincide with the previous classification by solubility: (1) iron sulfate and iron gluconate are water-soluble compounds with good bioavailability; (2) iron fumarate has good bioavailability, but poorly soluble in water; (3) iron pyrophosphate is insoluble in water and does not dissolve completely in gastric juice. The fourth category is the compound of ethylenediaminetetraacetic acid with sodium and iron and iron bisglycinate, which are soluble iron chelates. Iron absorption from chelates, when added to foods such as cereals, legumes, or milk, is higher than from soluble compounds [23]. The choice of these iron components pursues the following main objectives of fortification: increasing the nutritional value of food due to the introduction of iron compounds with better bioavailability; limiting the interaction of iron with components of the food matrix; minimization of unwanted organoleptic changes in the product. However, when used in the fortification process, some iron compounds (for example, ferrous sulfate or gluconate) exhibit significant organoleptic deficiencies. The fortified food product has a metallic aftertaste, unacceptable flavor as a result of the oxidation-mediated rancidity of fats and undesirable color changes resulting from interactions with anthocyanins, flavonoids, and tannins [24]. In addition, the degradation of vitamins can occur, which are important for iron absorption and utilization [16].

Another fortifier of iron in food can be heme iron [25]. This study describes the development of a technology for the production of a heme iron-rich dietary supplement from slaughter blood, as well as novel anti-anemic foods. It was noted above that heme iron is an important dietary source of iron because it is absorbed more efficiently than nonheme iron and also enhances the absorption of nonheme iron. Considering that heme iron in animal tissues is formed mainly from hemoglobin and myoglobin, the main fortifying agent is the heme iron polypeptide. It is a concentrate of heme iron obtained as a result of the hydrolysis of hemoglobin with a nonspecific protease and the separation of globin peptones from the heme fraction. The heme iron polypeptide being in the form of a powder can be used directly in the formulations of various food products, such as chocolate filling for confectionery products, jams, baby food in cans, meat products, pies, sweets, dairy products, desserts, bakery products, drinks, etc. [26].

An important step is the selection of products suitable for fortification. It is important to regularly consume them in certain proportions and to be economically available for the broad masses of the population, including target groups [23]. The right combination of iron form and food good vehicles, as well as the dietary context of consumption, are critical [27]. In this matter, the regularity of consumption of fortified food products in certain proportions and their economic accessibility to the broad masses of the population, including target groups, is important [28]. The consumer choice of such products should not be influenced by the fortification process, i.e., it must not lead to undesirable changes in color, taste, and appearance [29]. Bakery products and cereal flours are good vehicles for the delivery of food [30–32]. Another example is foods for specific populations. Such as formula and cereal weaning foods for infants and young children, breakfast cereals, chocolate drink powders, and beverages for older children and older children and adolescents [33].

3.5. Food-to-Food Fortification

Food fortification is a novel food-based strategy that can stand alone and complement the strategies described above [18]. This strategy was defined by the authors as the addition of micronutrient-dense foods to a recipe (household level) or food formulation (food industry level), or the replacement of micronutrient-poor foods for foods with a higher content of them to substantially increase the amount of bioavailable micronutrient/s, with the aim of improving the micronutrient status of populations. Iron-rich plant-based foods are used as fortifiers in this approach. However, the small number of studies does not allow us to make a final conclusion about the effectiveness of this approach.

4. Conclusions

This mini-review presented the applications of main food-based intervention strategies to solve the problem of iron deficiency medical conditions.

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References

- 1. Camaschella, C. New Insights into Iron Deficiency and Iron Deficiency Anemia. Blood Rev. 2017, 31, 225–233. [CrossRef] [PubMed]
- 2. Pasricha, S.-R.; Drakesmith, H.; Black, J.; Hipgrave, D.; Biggs, B.-A. Control of Iron Deficiency Anemia in Low- and Middle-Income Countries. *Blood* **2013**, *121*, 2607–2617. [CrossRef] [PubMed]
- 3. Barragán-Ibañez, G.; Santoyo-Sánchez, A.; Ramos-Peñafiel, C.O. Iron Deficiency Anaemia. *Rev. Médica. Del. Hosp. Gen. México* **2016**, 79, 88–97. [CrossRef]
- 4. Lozoff, B.; Smith, J.B.; Kaciroti, N.; Clark, K.M.; Guevara, S.; Jimenez, E. Functional Significance of Early-Life Iron Deficiency: Outcomes at 25 Years. *J. Pediatr.* **2013**, *163*, 1260–1266. [CrossRef] [PubMed]
- 5. Powers, J.M.; Buchanan, G.R. Disorders of Iron Metabolism. Hematol. Oncol. Clin. N. Am. 2019, 33, 393–408. [CrossRef]
- 6. Pasricha, S.-R.; Tye-Din, J.; Muckenthaler, M.U.; Swinkels, D.W. Iron Deficiency. Lancet 2021, 397, 233–248. [CrossRef]
- 7. Lopez, A.; Cacoub, P.; Macdougall, I.C.; Peyrin-Biroulet, L. Iron Deficiency Anaemia. Lancet 2016, 387, 907–916. [CrossRef]
- 8. Bouri, S.; Martin, J. Investigation of Iron Deficiency Anaemia. Clin. Med. J. R. Coll. Physicians Lond. 2018, 18, 242–244. [CrossRef]
- 9. Osendarp, S.J.M.; Eilander, A. Iron Deficiency and Cognitive Development. In *Lifetime Nutritional Influences on Cognition, Behaviour and Psychiatric Illness*; Benton, D., Ed.; Woodhead Publishing: Sawston, UK, 2011. [CrossRef]
- 10. Tao, Z.; Xu, J.; Chen, W.; Yang, Z.; Xu, X.; Liu, L.; Chen, R.; Xie, J.; Liu, M.; Wu, J.; et al. Anemia Is Associated with Severe Illness in COVID-19: A Retrospective Cohort Study. *J. Med. Virol.* **2021**, *93*, 1478–1488. [CrossRef]
- 11. Hariyanto, T.I.; Kurniawan, A. Anemia Is Associated with Severe Coronavirus Disease 2019 (COVID-19) Infection. *Transfus. Apher. Sci.* 2020, 59, 102926. [CrossRef]
- 12. WHO. The Global Prevalence of Anaemia in 2011; World Health Organization: Geneva, Switzerland, 2011.
- 13. Allen, L.; de Benoist, B.; Dary, O.; Hurrell, R. *Guidelines on Food Fortification with Micronutrients*; Allen, L., de Benoist, B., Dary, O., Hurrell, R., Eds.; World Health Organization and Food and Agriculture Organization of the United Nations: Geneva, Switzerland, 2006.
- 14. Gardner, W.; Kassebaum, N. Global, Regional, and National Prevalence of Anemia and Its Causes in 204 Countries and Territories, 1990–2019. *Curr. Dev. Nutr.* **2020**, *4* (Suppl. S2), 830. [CrossRef]
- 15. FAO/WHO. *Human Vitamin and Mineral Requirements: Report of a Joint FAO/WHO Expert Consultation;* Food and Nutrition Division FAO: Bangkok, Thailand, 2001.
- 16. Abbaspour, N.; Hurrell, R.; Kelishadi, R. Review on Iron and Its Importance for Human Health. *J. Res. Med. Sci.* **2014**, *19*, 164–174. [PubMed]
- 17. Pasricha, S.R.; Drakesmith, H. Iron Deficiency Anemia: Problems in Diagnosis and Prevention at the Population Level. *Hematol. Oncol. Clin. N. Am.* **2016**, *30*, 309–325. [CrossRef] [PubMed]
- 18. Kruger, J.; Taylor, J.R.N.; Ferruzzi, M.G.; Debelo, H. What Is Food-to-food Fortification? A Working Definition and Framework for Evaluation of Efficiency and Implementation of Best Practices. *Compr. Rev. Food Sci. Food Saf.* **2020**, *19*, 3618–3658. [CrossRef]
- 19. Kiran, K. Advanced Approaches for Biofortification. In *Advances in Agri-Food Biotechnology*; Springer: Singapore, 2020; pp. 29–55. [CrossRef]
- 20. Liberal, Â.; Pinela, J.; Vívar-Quintana, A.M.; Ferreira, I.C.F.R.; Barros, L. Fighting Iron-Deficiency Anemia: Innovations in Food Fortificants and Biofortification Strategies. *Foods* **2020**, *9*, 1871. [CrossRef]
- 21. Olson, R.; Gavin-Smith, B.; Ferraboschi, C.; Kraemer, K. Food Fortification: The Advantages, Disadvantages and Lessons from Sight and Life Programs. *Nutrients* **2021**, *13*, 1118. [CrossRef]
- 22. The National Academies of Sciences, Engineering, and Medicine. Iron. In *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*; National Academies Press: Washington, DC, USA, 2001. [CrossRef]

- 23. Hurrell, R.F. Efficacy and Safety of Iron Fortification. In *Food Fortification in a Globalized World*; Elsevier: Amsterdam, The Netherlands, 2018; pp. 195–212. [CrossRef]
- 24. Mehansho, H. Iron Fortification Technology Development: New Approaches. J. Nutr. 2006, 136, 1059–1063. [CrossRef]
- 25. Evlash, V.; Pogozhikh, M.; Aksonova, O.; Gubsky, S. Heme Iron–Containing Dietary Supplements and Their Application in Fortified Foods. In *Bioenhancement and Fortification of Foods for a Healthy Diet*; Paredes-López, O., Shevchenko, O., Stabnikov, V., Ivanov, V., Eds.; CRC Press: Boca Raton, FL, USA, 2022; pp. 237–268. [CrossRef]
- 26. Polo, J.; Rodríguez, C. Heme Iron as Source of Iron in Food Fortification. In *Handbook of Food Fortification and Health*; Preedy, V.R., Srirajaskanthan, R., Patel, V.B., Eds.; Springer: New York, NY, USA, 2013; Volume 1, pp. 133–146. [CrossRef]
- 27. Blanco-Rojo, R.; Vaquero, M.P. Iron Bioavailability from Food Fortification to Precision Nutrition. A Review. *Innov. Food Sci. Emerg. Technol.* **2019**, *51*, 126–138. [CrossRef]
- 28. Mannar, M.G.V.; van Ameringen, M. Role of Public-Private Partnership in Micronutrient Food Fortification. *Food Nutr. Bull.* **2003**, 24 (Suppl. S2), S151–S154. [CrossRef]
- 29. Baltussen, R.; Knai, C.; Sharan, M. Iron Fortification and Iron Supplementation Are Cost-Effective Interventions to Reduce Iron Deficiency in Four Subregions of the World. *J. Nutr.* **2004**, *134*, 2678–2684. [CrossRef]
- 30. Martínez-Navarrete, N.; Camacho, M.M.; Martínez-Lahuerta, J.; Martínez-Monzó, J.; Fito, P. Iron Deficiency and Iron Fortified Foods—A Review. *Food Res. Int.* **2002**, *35*, 225–231. [CrossRef]
- 31. Huma, N.; Salim-Ur-Rehman; Anjum, F.M.; Murtaza, M.A.; Sheikh, M.A. Food Fortification Strategy—Preventing Iron Deficiency Anemia: A Review. *Crit. Rev. Food Sci. Nutr.* **2007**, *47*, 259–265. [CrossRef] [PubMed]
- 32. Derbyshire, E.; Brennan, C.S.; Li, W.; Bokhari, F. Iron Deficiency—Is There a Role for the Food Industry? *Int. J. Food Sci. Technol.* **2010**, 45, 2443–2448. [CrossRef]
- 33. Hurrell, R.F.; Cook, J.D. Strategies for Iron Fortification of Foods. Trends Food Sci. Technol. 1990, 1, 56-61. [CrossRef]