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Food Fortification to Combat Iron Deficiency Anaemia

Shruti Pandey and Vasudeva Singh

Grain Science and Technology Department, Central Food Technological Research Institute, Mysore, Karnataka, India

Correspondence should be addressed to Shruti Pandey, shruti@cftri.org, shruti@cftri.res.in

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Abstract Among the various blood disorder anemia is a widespread health problem associated with an increased risk of morbidity and mortality, especially in pregnant women and young children. The major causes for anemia are both nutritional (vitamin and mineral deficiencies) and non-nutritional (infection and hemoglobinopathies). In particular, the major factors that contribute to the onset of anemia are iron deficiency and malaria. The present review focuses on the various intervention programmers for eradicating iron deficiency anaemia.
Keywords *Iron Deficiency Anemia, Iron Fortification, Elemental Iron, Hemoglobin*

1. Introduction

The reduced capacity of blood to deliver oxygen to body cells and tissue is called anemia (Provan, 1999). One of the major causes of anemia is Iron deficiency. This anemia can be defined as a defect in hemoglobin synthesis, resulting in red blood cells that are abnormally small (microcytic) and decreased amount of hemoglobin (hypochromic). Iron deficiency is the most common and widespread nutritional disorder in the world which is affecting a large number of children and women in developing countries (Figure 1). Malaria, HIV/AIDS, hookworm infestation, schistosomiasis, and other infections such as tuberculosis are particularly important factors contributing to the high prevalence of anemia in some areas (WHO Report, 2002). According to the third National Health and Nutrition Examination Survey (NHANES III) data, iron deficiency is defined by two or more abnormal measurements (serum ferritin, transferrin saturation and/or erythrocyte protoporphyrin). Iron deficiency anemia, a more severe stage of iron deficiency (defined as low hemoglobin in combination with iron deficiency), was found in 3.3 million females (Looker et al., 1997). Adolescence in India goes hand in hand with iron-deficiency anemia, medically known as IDA; according to the latest NFHS report, 56% of adolescent girls and 30% of adolescent boys are suffering from anemia. The National Family Health Survey (NFHS-3) conducted in 2005-06, presents the statistics that mark a growth in cases pertaining to anemia. Most of the anemic patients, especially women, suffer from mild to severe deficiency of iron. The hemoglobin count in most of the adolescent girls in India is less than the standard 12 g/deciliter, accepted worldwide (National Family Health Survey Report, 2008). The present review explain the depth study on, need for iron fortification, common fortificants, foods available for fortification and success stories pertaining to it.

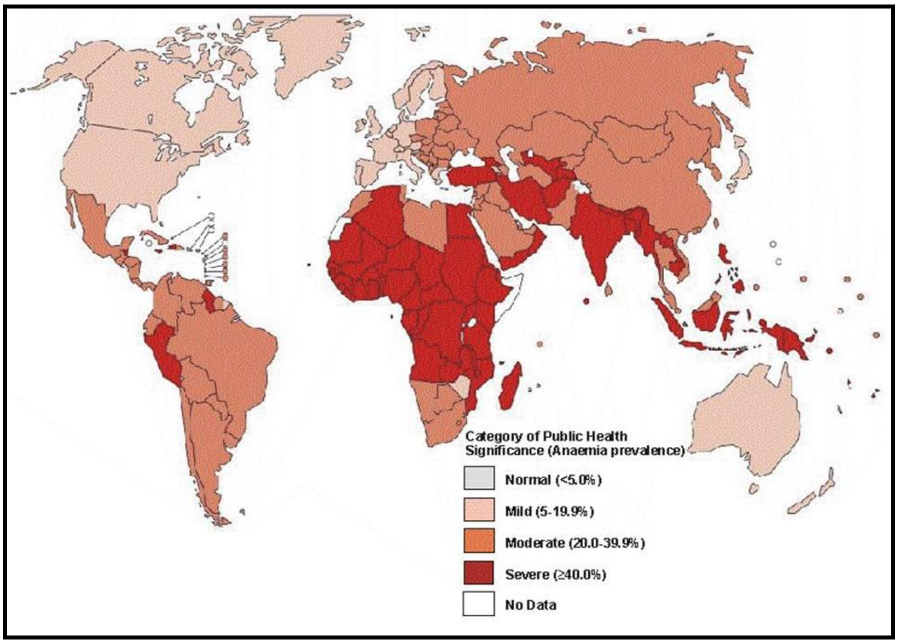

Figure 1: *Prevalence of Anemia on a Global Level*

Source: WHO, CDC. Worldwide prevalence of anaemia 1993-2005. WHO global database on anaemia. Geneva, World Health Organization, 2008.

2. Significance

Iron is essential to all cellular function in the body. It involves in varied cellular functions namely, energy metabolism, gene regulation, cell growth and differentiation, oxygen binding and transport, muscle oxygen use and storage, enzyme reactions, neurotransmitter synthesis, and protein synthesis (Beard et al., 2001). Potential consequences of iron deficiency, which occur in relation to its severity, are summarized in Table 1, while symptoms associated with anemia are listed in Table 2.

Table 1: *Potential Consequences of Iron Deficiency*

S. N.	Potential Consequences	S. N.	Potential Consequences
1.	Decreased maximum aerobic capacity	7.	Increased rates of infection
2.	Decreased athletic performance	8.	Impaired cognitive functioning and memory
3.	Lowered endurance	9.	Decreased school performance
4.	Decreased work capacity	10.	Compromised growth and development
5.	Impaired temperature regulation	11.	Increased lead and cadmium absorption
6.	Depressed immune function	12.	Increased risk of pregnancy complications, including prematurity and fetal growth retardation

Source: Provan, 1999

Table 2: *Symptoms Associated with Iron Deficiency Anemia*

S. N.	Symptoms	S. N.	Symptoms
1.	Fatigue	9.	Pallor
2.	Lethargy	10.	Flattened, brittle nails (spoon nail)
3.	Dizziness	11.	Angular stomatitis (cracks at mouth corners)
4.	Headaches	12.	Glossitis
5.	Shortness of breath	13.	Blue sclera (whites of eyes)
6.	Ringing in ears	14.	Pale conjunctivae
7.	Taste disturbances	15.	Pica (ice chewing)
8.	Restless leg syndrome		

Source: Provan, 1999

3. Etiology

Adolescents are vulnerable to iron deficiency because of increased iron requirements related to rapid growth (Wharton, 1999). About three fourths of adolescent females do not meet dietary iron requirements, compared to 17% of males (Centre for Disease Control and Prevention Report, 1998). Conditions which increase the risk for iron deficiency in adolescents are summarized in Table 3.

Table 3: *Risk Factors for Iron Deficiency*

S. N.	Inadequate Iron Intake / Absorption / Stores	S. N.	Inadequate Iron Intake / Absorption / Stores
1.	Vegetarian eating styles, especially vegan diets	7.	Meal skipping
2.	Macrobiotic diet	8.	Substance abuse
3.	Low intakes of meat, fish, poultry or iron fortified foods	9.	History of iron deficiency anemia
4.	Low intake of foods rich in ascorbic acid	10.	Recent immigrant from developing country
5.	Frequent dieting or restricted eating	11.	Special health care needs
6.	Chronic or significant weight loss		

Source: Provan, 1999

S. N.	Increased Iron Requirements/losses
1.	Heavy/lengthy menstrual periods
2.	Rapid growth
3.	Pregnancy (recent or current)

4. Intervention and Strategies

To maximize absorption, iron supplements should be taken with liquids such as fruit juices etc. Iron supplements should not be taken with milk, coffee, tea or phosphate-containing carbonated beverages such as soft drinks (Cook[a], 1999).

Dietary iron sources include meat, fish and poultry, lentils, dried beans, grain products, vegetables, dried fruit, and molasses (Table 4). The only approach would provide long term improvement of iron and cost effective is through food fortification using iron.

Table 4: Dietary Factors that Enhance and Inhibit Iron Absorption

Enhance	Inhibit
Meat	Phosphate
Fish	Calcium
Poultry	Tea (tannic acid)
Seafood	Coffee
Gastric Acid	Colas/Soft Drinks
Ascorbic Acid	Soy Protein
Malic Acid	High doses of Minerals
Citric Acid	Bran/Fiber

Source: Provan, 1999

5. Iron Fortificants

Some characteristics of commonly used iron compounds are shown in Table 5. They can be conveniently divided into four groups: (i) those that are freely water soluble; (ii) those that are poorly water soluble but soluble in dilute acids such as gastric juice; (iii) those that are water insoluble but poorly soluble in dilute acid; and (iv) protected iron compounds. The table gives guideline values for relative bioavailability in rat and man and a relative cost factor (Bothwell et al., 1992; Hurrell, 1985; Taylor et al., 1986).

Table 5: Characteristics of Iron Sources Commonly Used to Fortify Food (Adapted from Hurrell 1985, 1992; Bothwell & Mcphail 1992)

	Approximate Fe Content (%)	Average Relative Bioavailability		Approximate Relative Costa
		Rat	Man	
Freely Water Soluble				
Ferrous Sulfate 7H2O	20	100	100	1.0
Dried Ferrous Sulfate	33	100	100	0.7
Ferrous Gluconate	12	97	89	5.1
Ferrous Lactate	19	—	106	4.1
Ferric Ammonium Citrate	18	107	—	2.1
Poorly Water Soluble				
/Soluble In Dilute Acid				
Ferrous Fumarate	33	95	100	1.3
Ferrous Succinate	35	119	92	4.1
Ferric Saccharate	10	92	74	5.2
Water-Insoluble				
/Poorly Soluble In Dilute Acid				
Ferric Orthophosphate	28	6–46	25–32	4.1
Ferric Ammonium Orthophosphate (EKA Nobel, Sweden)				
Ferric Pyrophosphate	25	45–58	21–74	2.3
Elemental Fe Powders:				
Electrolytic	98	4–48	5–100	0.5
Carbonyl	98	39–66	5–20	1.0
Reduced	97	24–54	13–148	0.2
Protected Compounds				
Nafe EDTA	14	—	28–416	6.0
Hemoglobin	0.34	—	100–700	—

A relative to ferrous sulfate $7H_2O$ = 1.0, for the same level of total iron

The bioavailability of iron for intake is depending upon the solubility in water. The water soluble iron compound is highly bioavailable compared to soluble in gastric juice as well as non soluble. The cost of the more recent or experimental compounds such as NaFeEDTA, ferric ammonium orthophosphate, and haemoglobin depend to some extent on the amounts ordered (Hallberg et al., 1989). In general, the freely water-soluble compounds are highly bioavailable in rodents and humans, as are compounds that are water insoluble but soluble in dilute acids.

5.1. Freely Water-Soluble Compounds

Ferrous sulphate is the least expensive compound and is widely used to fortify infant formulas and pasta and cereal flour that are stored for only short periods. Other possibilities are ferrous gluconate, ferrous lactate, and ferric ammonium citrate. (Forth et al., 1987) reported that there is no evidence that soluble ferric salts are absorbed to a lesser extent than soluble ferrous salts when iron is in an ionized form it is possible that ferric iron binds more strongly with inhibitors of absorption such as phytic acid and polyphenols.

5.2. Compounds Poorly Soluble in Dilute Acids

Compounds poorly soluble in dilute acids include ferric pyrophosphate, ferric orthophosphate, and ferric ammonium orthophosphate (Taylor et al., 1986; Patrick, 1985). They are the most often-used compounds in food fortification and their main advantage is that they cause no organoleptic problems. Their disadvantage is that they have a variable absorption because they do not readily dissolve in gastric juice.

5.3. Encapsulated Iron Compounds

Both ferrous sulphate and ferrous fumarate are available commercially in encapsulated form. Commonly, the coatings are partially hydrogenated oils, such as soybean and cottonseed, or ethyl cellulose. The coating has little influence on the Relative Bioavailability (RBV) as measured in rodent assays (Hurell, 1985) and can prevent fat oxidation changes during storage of cereals or in infant formulas fortified with the easily oxidizable longchain polyunsaturated fatty acids.

5.4. Characteristic of Good Vehicle for Fortification

The choice of food matrix and iron source should have optimal combination for effective biological impact. The best iron compounds (ferrous fumarate/sulphate, bisglycinate or NaEDTA) with carrier that have high levels of inhibitors will not be effective. For effective food fortification, that the fortified food is consumed by the target population is low in cost and has good organoleptic properties. Failure of fortification efforts to prevent iron deficiency can be explained in most cases by lack of compliance with these criteria. The process of selecting the best food vehicle and iron source may appear simple but is actually a complex process that requires evaluation at every step. The physical properties of iron compound reacting with food carrier is a concern for fortification particularly color and flavor.

6. Major Vehicles for Iron Fortification

6.1. Cereals

Cereals are the most widely used vehicles for iron fortification. (Baurenfiend et al., 1990). The contribution of fortified iron to iron intake is highest in the United States, where it accounts for 20–25% of total iron intake (Subar, 1988; Lachance, 1989). The contribution of fortified iron to iron intake in the United Kingdom is much lower; around 6% (Hurrell et al., 1996). Whole grain rice is fortified by coating, infusing, or by using extruded grain analogues. Other commonly fortified foods are breakfast cereals and infant cereals. While fortification of wheat flour, sugar and salt with iron is a common strategy in industrialized countries, fortification of millet flours with the same element has gained little attention (Subbulakshmi et al., 1999).

6.2. Salt

Iodine-fortified salt has successfully used to eradicate iodine deficiency in many countries (Dunn et al., 1986). However, iron fortification of salt poses many technical problems. Moreover, an efficient production and distribution system is important. Salt that contains fewer impurities would undoubtedly be easier to fortify, but the extra cost for purification passed to the consumer is always a major consideration in developing countries. Technical constraints do exist with salt fortification, but it is possible to overcome these limitations. In addition, there is always the possibility that the iron-fortified salt will cause unacceptable color reactions if added to vegetables in a meal.

6.3. Sugar

Sugar is an alternative vehicle for iron fortification particularly in regions of the world where it has been produced enormously is produced, such as the Caribbean and Central America. However, in other developing countries, the consumption of refined sugar is more common in major socioeconomic segments of the population (Cook et al., 1983).

6.4. Milk

Infant formulas are usually milk based with added vegetable oils, minerals, and vitamins. Iron is almost always added as ferrous sulphate from 5 to 12 mg per liter (Lynch, 1990). Its absorption can be improved considerably by the addition vitamin C (Stekel, 1986). The inhibitors which limit the availability of iron in the milk are calcium (Hallberg et al., 1991) and the milk protein casein (Hurrell et al., 1989). Though vitamin C increases the availability of ferrous sulphate it is difficult to add vitamin C to fluid milk since it degrade milk rapidly to diketogluconic acid leading to changes in flavor (Hegenauer et al., 1979).

6.5. Condiments

Condiments that are traditionally used in developing countries, such as monosodium glutamate, fish sauce, curry powder, and bouillon cubes, could be useful fortification vehicles.

6.6. Coffee

In some countries coffee is consumed by most adults as well as some children, and it is technically and economically feasible to fortify coffee with iron. Johnson and Evans 1977 reported the use of ferrous fumarate in roasted and ground coffee, in which one cup (200 mL) provided 1 mg added iron. The addition of iron to soluble coffee is also relatively easy. (Klug et al., 1973) reported that the addition of a range of soluble ferrous and ferric compounds was possible. Flavor and color changes, however, are a potential problem, and coffee, like tea and cocoa, contains phenolic compounds that strongly inhibit iron absorption.

7. Success Stories of Iron Fortification

Experiences from the above trials conducted, should help to accelerate the implementation of effective large-scale iron fortification programs. They underscore the fact that when a carefully selected food vehicle and a relatively bioavailable iron compound are combined and consumed by at-risk groups under supervised or normal market conditions, there can be a measurable and important improvement in iron status associated with the introduction of the fortified foods.

These included the need for appropriate quality control at mills; nutrient losses due to cooking in excess water; and lack of information on nutrient loss during storage. Decades of research on rice enrichment and fortification practices have provided a better understanding of the technology needed; however, some technical problems remain. With the exception of vitamin A, the cost of the added nutrients to cereal grains is negligible. Ranges from 1.5 cents per person per year for added iron to 29 cents per person per year for added vitamin A have been reported (Lotfi et al., 1996). Commercial vitamin mineral premixes can reduce the quality control costs by providing uniform nutrient levels. The capital costs of launching a food enrichment/fortification program, however, must be balanced against the cost of not implementing a program which may result in public health problems, increased medical costs, and decreased productivity due to resulting deficiencies. United States Agency for International Development and Opportunities for Micronutrient Interventions (USAID/OMNI) has investigated the cost-effectiveness of various strategies to improve micronutrient status, including food fortification programs. Program planners can learn from the decades of experience in rice fortification technology. Applying known rice fortification technology in rice consuming countries where deficiencies are common provides an opportunity to reduce the economic and social burdens that are placed on the population due to micronutrient deficiencies. The benefits to the producer and the miller of adding value to 1 rice by improving its nutritional quality needs to be determined to promote food fortification programs.

8. Conclusion

Fortification requires careful selection of vehicle and then adopting a proper technique to fortify the raw material, and then proper amount of consumption of the fortified material.

Considerations

- Fortification of staple/complementary foods and condiments can be successfully implemented with proper attention to the selection of fortificants.
- Product research and development, operational research, program planning, communication strategy, advocacy, private/public partnerships and legislation are vital for effectiveness.
- Operational research on how to overcome practical barriers for successful implementation of fortification, from which practical lessons can be learned, should be undertaken.
- Fortification is one of several approaches to achieve this goal and, specifically, to combat iron deficiency. However, fortification should always be considered as one component of an integrated strategy.

References

Bauernfiend J.C., et al., 1991*: Foods Considered for Nutrient Addition: Cereal Grain Products*. In: Bauernfiend PA, Lachance PA, Eds. Nutrient Additions to Foods. Food and Nutrition Press, Trumbull, CT, 143-209.

Baurenfiend J.C., et al. 1991: *Foods Considered for Nutrient Addition: Cereal Grain Products*. In: JC Baurenfiend and PA Lachance, Eds. Nutrient Additions to Food. Food and Nutrition Press, Connecticut.

Beard J.L. *Iron Biology in Immune Function, Muscle Metabolism and Neuronal Functioning*. J. Nutr. 2001. 131 (2S-2) 568S-579S.

Bothwell T.H., et al., 1992: *Prevention of iron deficiency by food fortification.* In: Fomon S, Zlotkin S, Eds. Nutritional Anemias. Nestlé Nutrition Workshop Series 30. Raven Press, New York, 183-192.

Chen J. *Regulatory Control of Functional Food in China.* Scandinavian J of Nutrition. 2000. 44; 130-131.

Cook J.D. *Iron Fortification: An Update*. Am J Clin Nutr. 1983. 38; 648–659.

Cook J.D.[a]. *The Measurement of Serum Transferrin Receptor*. Am J Med Sci. 1999. 318; 269-276.

Dunn J.T., et al. 1986: *Towards the Eradication of Endemic Goitre, Cretinism and Iodine Deficiency*. Scientific Publication No., 502. Pan American Health Organization, Washington, DC.

Forth W., et al. *Absorption of di- and Trivalent Iron: Experimental Evidence*. In Arzneimittelforschung/ Drug Res. 1987. 37; 96–100.

Hallberg L., et al. *Calcium: Effect of Different Amounts on Non-Heme and Heme-Iron Absorption in Humans.* Am J Clin Nutr. 1991. 53; 112-119.

Hallberg L., et al. *Low Availability of Carbonyl Iron in Man: Studies on Iron Fortification of Wheat Flour.* Am J Clin Nutr. 1986. 43; 59-67.

Hallberg L., et al. *Iron Fortification of Flour with a Complex Ferric Orthophosphate*. Am J Clin Nutr. 1989. 50; 129-135.

Hegenauer J., et al. *Degradation of Ascorbic Acid (Vitamin C) in Iron-Supplemented Cow's Milk*. J. Dairy Sci. 1979. 62; 1037-1040.

Hurrell R., 1999: *Iron.* In: Hurrell R., Eds. The Mineral Fortification of Foods. Leatherhead International Ltd, Leatherhead, England.

Hurrell R.F., et al. *Iron Fortification of Infant Cereals: A Proposal for the Use of Ferrous Fumarate or Ferrous Succinate.* Am J Clin Nutr. 1989. 49; 1274-1282.

Hurrell R.F., et al., 1996: The *Role of the Food Industry in Iron Nutrition: Iron Intake from Industrial Food Products*. In: Hallberg L., Asp N., Eds. Iron Nutrition in Health and Disease. Swedish Nutrition Foundation, Lund, Sweden, 339-347.

Hurrell R.F., et al. Iron Absorption in Humans as Influenced by Bovine Milk Proteins. Am J. Clin Nutr. 1989. 49; 546-52.

Hurrell R.F., et al. *Ferrous Fumarate Fortification of a Chocolate Drink Powder*. Br J. Nutr. 1991. 65; 271-283.

Hurrell R.F., 1984: *Bioavailability of Different Iron Compounds Used to Fortify Formula and Cereals: Technological Problems*. In: Stekel A., Ed. Iron Nutrition in Infancy and Childhood. Raven Press, New York, 147-178.

Hurrell R.F., 1985: *Types of Iron Fortificants: Nonelemental Sources.* In: Clydesdale FM, Wiemer KL, Eds. Iron Fortification of Foods. Academic Press, Orlando, FL, 39-53.

Johnson P.E., et al. *Coffee as a Low Calorie Vehicle for Iron Fortification*. Nutr Rep Int. 1977. 16; 89-92.

Klug S.L., et al. 1973*: Iron Fortified Soluble Coffee Method for Preparing the Same*. US Patent 4006, 263.

Lachance P.A. *Nutritional Responsibilities of the Food Companies in the Next Century*. Food Technol. 1989. 43; 144-150.

Looker A.C., et al*. Prevalence of Iron Deficiency in the United States*. JAMA. 1997. 277 (12) 973-976.

Lynch S.R., et al. 1990: *Iron in Formulas and Baby Foods*. In: Lönnerdal B., Ed. Iron Metabolism in Infants. CRC Press, Boca Raton, FL, 109-126.

National Family Health Survey Report, July 17, 2008.

Patrick J., 1985: *Types of Iron Fortificants: Elemental Sources.* In: Clydesdale F.M., Wiemer K.L., Eds*.* Iron fortification of Foods. Academic Press, Orlando, FL, 31-38.

Provan D. *Mechanisms and Management of Iron Deficiency Anaemia.* Br J. Haematol. 1999. 105 (11) 19-26.

Stekel A., et al. *Absorption of Fortification Iron in Milk Formulas by Infants*. J. Am Clin Nutr. 1986. 43; 917-922.

Subar A.F., et al. *The Contribution of Enrichment and Fortification to the Nutrient Intake of Women.* J. Am Diet Assn. 1988. 88; 1237-1245.

Subbulakshmi G., et al. *Food Fortification in Developing Countries–Current Status and Strategies.* Journal of Food Science and Technology. 1999. 36 (5) 371-395.

Taylor P.G., et al. *The Effect of Cysteine-Containing Peptides Released during Meat Digestion on Iron Absorption in Humans*. Am J Clin Nutr*.* 1986. 43; 68-71.

Wharton B.A. *Iron Deficiency in Children: Detection and Prevention*. Br J. Haematol. 36; 1140-1151.

Working Group on Fortification of Salt with Iron*. Use of common salt fortified with iron in the control and prevention of anemia: a collaborative study*. Am. J. Clin. Nutr. 1982. 35; 1142-1151.