

Forging Effective Strategies to Combat Iron Deficiency

Fortification: Overcoming Technical and Practical Barriers^{1,2}

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ABSTRACT The main barriers to successful iron fortification are the following: 1) finding an iron compound that is adequately absorbed but causes no sensory changes to the food vehicle; and 2) overcoming the inhibitory effect on iron absorption of dietary components such as phytic acid, phenolic compounds and calcium. These barriers have been successfully overcome with some food vehicles but not with others. Iron-fortified fish sauce, soy sauce, curry powder, sugar, dried milk, infant formula and cereal based complementary foods have been demonstrated to improve iron status in targeted populations. The reasons for this success include the use of soluble iron such as ferrous sulfate, the addition of ascorbic acid as an absorption enhancer or the use of NaFeEDTA to overcome the negative effect of phytic acid. In contrast, at the present time, it is not possible to guarantee a similar successful fortification of cereal flours or salt. There is considerable doubt that the elemental iron powders currently used to fortify cereal flours are adequately absorbed, and there is an urgent need to investigate their potential for improving iron status. Better absorbed alternative compounds for cereal fortification include encapsulated ferrous sulfate and NaFeEDTA, which, unlike ferrous sulfate, do not provoke fat oxidation of cereals during storage. Encapsulated compounds also offer a possibility to fortify low grade salt without causing off-colors or iodine loss. Finally, a new and useful additional approach to ensuring adequate iron absorption from cereal based complementary foods is the complete degradation of phytic acid with added phytases or by activating native cereal phytases. *J. Nutr.* 132: 806S–812S, 2002.

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Iron is the most difficult mineral to add to foods and ensure adequate absorption (1). The main problem is that the water-soluble iron compounds, which are the most bioavailable, often lead to the development of unacceptable color and flavor changes in the food vehicle. When water-soluble compounds are added to cereal flours, for example, they often cause rancidity, and in low-grade salt, they rapidly lead to color formation. Insoluble compounds, such as elemental iron powders, on the other hand, do not cause sensory changes but may be so poorly absorbed as to be of little or no nutritional benefit.

The selection of the iron compound, however, is only part of the problem. The other major difficulty to ensuring adequate absorption is the presence of iron absorption inhibitors in the fortification vehicle itself, or in the accompanying diet. The main inhibitory compound is phytic acid (myo-inositol 6-phosphate) (2), which is widely present in cereal grains and

legume seeds (3). Phytic acid binds iron strongly in the gastrointestinal tract and can decrease the absorption of even the most bioavailable iron compounds to very low levels (4).

Thus, there are two major technical barriers to overcome when developing an iron-fortified food. The first is the selection of an iron compound that causes no sensory changes but is adequately absorbed; the second is to overcome the inhibitory effect of phytic acid and other food components on iron absorption.

These barriers can be overcome, and iron-fortified foods that have demonstrated an improved iron status in the target population include infant formula (5), infant cereal (6,7), sugar (8) and fish sauce (9). It is noteworthy that all of these foods were consumed with an enhancer of iron absorption (ascorbic acid or EDTA) added to overcome absorption inhibitors. Currently, however, there is little direct evidence that iron fortification of major staple foods, such as wheat flour or corn flour, is a useful strategy to combat iron deficiency. This is due mainly to the common use of poorly bioavailable iron compounds and the high level of phytic acid in cereal foods. With salt, despite much progress in fortification (10), there are still major problems of color formation and iodine loss when iron is added to the low-grade iodized salt most frequently consumed by the poorer population groups in developing countries.

Selection of an iron fortification compound

A list of potential iron fortification compounds is given in Table 1 (1). They differ in both their relative bioavailability

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(RBV) and their potential to cause unwanted sensory changes. Their RBV depends largely on their solubility in the gastric juice during digestion. Water-soluble compounds, such as ferrous sulfate, dissolve instantaneously and have the highest RBV. Water-insoluble compounds, such as ferrous fumarate, may be as well absorbed as ferrous sulfate because they dissolve completely, but more slowly, in the dilute acid of gastric juice. The final group of compounds are those poorly soluble in dilute acid; because they never dissolve completely in the gastric juice, they have a lower and variable bioavailability.

The iron compound selected for food fortification should be the one with the highest RBV that causes no sensory changes when added to the food vehicle. The first choice would be a soluble compound, such as ferrous sulfate; a good alternative would be ferrous fumarate, and the last choice would be an elemental iron powder or an iron phosphate compound. Encapsulated ferrous sulfate or ferrous fumarate also have excellent potential for overcoming unwanted sensory changes while maintaining high RBV.

Ferrous sulfate. Like other water-soluble iron compounds, ferrous sulfate has the highest RBV (= 100) (Table 1) (1). It has been successfully used to fortify infant formula, bread and pasta (1) and can be added to white wheat flour stored for short periods (11). It may, however, provoke fat oxidation and rancidity in cereal flours stored for longer periods (1) and has been reported to cause unacceptable color changes in cocoa products (12), infant cereal with fruit (13) and salt (14). It often causes a metallic taste in liquid products and can precipitate peptides from soy sauce and fish sauce. Dried ferrous sulfate is less prooxidant in cereals than the hydrated form (15).

The successful use of ferrous sulfate to fortify wheat flour in

Chile contradicts the general view that this compound is unsuitable for wheat flour fortification. Although shorter storage periods of the fortified flour help prevent oxidative changes, it is possible that the purity of the ferrous sulfate used may also play a role. The influence of sulfate purity on sensory changes warrants careful evaluation.

Ferrous fumarate. This compound is widely used to fortify infant cereals in Europe and may also be used to fortify chocolate drink powders (1). In adults, it has been shown to be as well absorbed as ferrous sulfate from infant cereals (4,15). When added to chocolate drink powders, ferrous fumarate was as well absorbed as ferrous sulfate without processing and twice as well absorbed after the drying process (16). Ferrous fumarate may cause unwanted color and flavor reactions but to a lesser extent than ferrous sulfate.

It is important to note that ferrous fumarate is not soluble in water and that its absorption requires dissolution in the gastric juice during digestion. Although this appears to occur in healthy adults, it has not been demonstrated in children or in populations from developing countries in which gastric acid secretion may be less efficient due to infections or nutrient deficiencies. Recent studies in Bangladesh have indicated that ferrous fumarate may be only 25% as well absorbed by young children as ferrous sulfate (Davidsson, L., Institute of Food Sciences ETHZ, Switzerland, 2001, personal communication).

Encapsulated iron compounds. Ferrous sulfate and ferrous fumarate are commercially available encapsulated with hydrogenated oils, maltodextrin and ethyl cellulose (17). There seems little reason to encapsulate elemental iron powders or ion phosphate compounds. Bioavailability of encapsulated ferrous sulfate was similar to ferrous sulfate in rat assays (15) but must depend on the thickness of the capsule as well as the

TABLE 1

 Characteristics of some common iron fortification compounds¹

Iron compound	~Fe %	Average relative bioavailability		Potential for adverse organoleptic changes	Approximate relative cost ²
		Rats	Humans		
Freely water soluble					
Ferrous sulfate · 7H ₂ O	20	100	100		1.0
Dried ferrous sulfate	33	100	100		0.7
Ferrous gluconate	12	97	89	High	5.1
Ferrous lactate	19	—	106		4.1
Ferric ammonium citrate	18	107	—		2.1
Ferrous ammonium sulfate	14	99	—		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	Low	5.2
Ferric glycerophosphate	15	93	—		10.5
Ferrous citrate	24	76	74		3.9
Ferrous tartrate	22	77	62		3.9
Water insoluble/poorly soluble in dilute acid					
Ferric pyrophosphate	25	45–58	21–74		2.3
Ferric orthophosphate	28	6–46	25–32		4.1
Elemental Fe powders					
Electrolytic	97	16–70	75		— ³
H-reduced	97	13–54	13–148	Negligible	— ³
CO-reduced	97	12–32	ND		— ³
Atomized	97	ND	ND		— ³
Carbonyl	99	35–66	5–20		— ³

¹ Adapted from (1).

² Relative to ferrous sulphate · 7H₂O = 1.0, for the same level of total iron.

³ In general, less expensive than ferrous sulfate. Cost of different powder types varies about sevenfold, with carbonyl iron being the most expensive. ND, not determined.

coating material, and still requires confirmation in human studies. The coating provides a physical barrier between iron and the food matrix and would seem an ideal method to prevent some of the unwanted sensory changes that can occur in iron-fortified foods. Encapsulated iron has proven useful in infant formulas and infant cereals but otherwise has been little exploited. Ferrous sulfate catalyzed fat oxidation reactions in stored wheat infant cereal were prevented by encapsulating the iron compound with hydrogenated soybean oil or mono- and diglycerides (15). A technical problem, which still persists, however, is the heat instability of the capsule. The coatings are removed during the preparation of the infant cereal pap with hot water and during vacuum drying of chocolate drink powders, leading to the same color reactions as with non-encapsulated ferrous sulfate. Thus, for some products, there is still a need for the development of heat-stable capsules that do not negatively influence iron absorption.

As discussed earlier, cereal flours and salt have so far been difficult to fortify with absorbable iron; for these foods, encapsulated ferrous sulfate or encapsulated ferrous fumarate offers new possibilities. Encapsulated iron compounds can prevent color formation in low grade salt and should also prevent fat oxidation reactions in stored wheat flour or corn flour while still maintaining high bioavailability. Although increased cost is a concern, these compounds must be carefully evaluated.

Elemental iron. Elemental iron powders are widely used for food fortification particularly for the fortification of cereal flours and other cereal products, such as breakfast cereals and complementary foods. There is little direct evidence, however, that they have a beneficial effect on iron status. These powders are often referred to collectively as “reduced iron” but they are not a single entity and are manufactured by five different processes. These are the H-reduction, CO-reduction, atomization, electrolytic and carbonyl processes. Thus, elemental iron powders can differ considerably. The main characteristics that govern their solubility in the gastric juice are particle size, shape, surface area, porosity and purity. These characteristics can also differ in different grades of powder made by a single manufacturing process. Although the Food Chemical Codex (18) requires that reduced iron powders used for fortification pass through a 100-mesh sieve ($<149\ \mu\text{m}$) and that electrolytic iron and carbonyl powders pass through a 325-mesh sieve ($<44\ \mu\text{m}$), this is not sufficient to guarantee adequate absorption even though most reduced iron powders used to fortify cereal foods in industrialized countries have a particle size $<44\ \mu\text{m}$.

There are several issues in relation to elemental iron powders that must be considered. First, the Codex recommendations were based in large part on animal and in vitro studies performed during the 1970s and 1980s. Although this helped to standardize the powders at that time, the current recommendation would be to demonstrate adequate bioavailability in human subjects. Another concern is that some of the manufacturing processes have been modified over the last 30 y. The atomization process has been introduced but never tested adequately, even though a large part of the elemental iron used for food fortification is now manufactured by this process. Another difficulty in predicting the bioavailability of elemental iron powders is that their solubility in the gastric juice depends on meal composition and will vary with different meals (19). In addition, gastric acid production, which is essential for the good bioavailability of elemental iron, may be influenced negatively in developing countries by infections such as *Helicobacter pylori* (20) or nutrient deficiencies. All of these concerns make the bioavailability of elemental iron difficult to predict.

The usefulness of elemental iron powders for food fortification was recently addressed by an expert panel (Sustain Elemental Iron Task Force, Washington, DC, 2001, unpublished data). After reviewing the many hemoglobin repletion studies performed in rats, seven human bioavailability studies performed with isotopically labeled powders (19,21–26), and three published efficacy studies (6,27,28), the panel concluded that electrolytic iron was the only iron powder that had been demonstrated to be a useful iron fortificant. This conclusion was based on an improved iron status in infants fed a rice-based complementary food providing 18 mg electrolytic iron/d (6), a human bioavailability study with radiolabeled electrolytic iron having similar (but not identical) physical characteristics as the commercial powder, which reported an absorption of 75% of ferrous sulfate (25), and five independent rat hemoglobin repletion studies with the most common commercial powders (Glidden A131, OMG, Americas, USA) which reported RBV values of 42 to 59 with a mean of 48 (15,29–32). At best, it would seem that electrolytic iron is about half as well absorbed as ferrous sulfate and should thus be added to foods in at least double the amount.

The expert panel was not able to decide whether H-reduced, CO-reduced, atomized or carbonyl iron were useful iron fortificants (Sustain Elemental Iron Task Force, 2001, unpublished data). There are no data in humans demonstrating improved iron status. Animal studies have generally shown that carbonyl iron is as well absorbed as electrolytic iron but that H-reduced iron ($<44\ \mu\text{m}$) is somewhat less well absorbed and more variable (30,31,33). The RBV of CO-reduced iron was reported to vary from only 12 to 32 (31,33,34) and large particle-sized H-reduced ($<149\ \mu\text{m}$) from 18 to 24 (30,35). The panel recommended that the low cost, large particle-sized H-reduced iron powder should not be used for food fortification.

Although, isotopically labeled H-reduced iron has been examined several times in human bioavailability studies, the experimentally labeled compounds were so different from the commercial powders (22,23,26) that the results could not be used to judge the usefulness of commercial powders. Isotopically labeled commercial carbonyl iron has yielded RBV values of only 5 to 20 in human subjects consuming a variety of meals. Although this low bioavailability must be confirmed, its higher cost also makes it less attractive for food fortification.

The way forward is to clarify as soon as possible the characteristics of those elemental iron powders currently used for food fortification. They are manufactured by a small number of large companies. Because it is very difficult, if not impossible, to make isotopically labeled powders with exactly the same physicochemical characteristics as the commercial powders, absorption studies in humans do not appear to be an option. It is necessary therefore to make well-controlled efficacy studies to demonstrate the improvement in iron status of iron-deficient subjects consuming foods fortified with elemental iron powders. At the same time, attempts should be made to manufacture powders with bioavailability equivalent to that of ferrous sulfate, which has occurred to date only on a laboratory scale (22).

Iron phosphate compounds. Ferric orthophosphate and ferric pyrophosphate are often used by European companies to fortify infant cereals and chocolate drink powders. They are poorly soluble in dilute acid, and RBV of isotopically labeled compounds has varied considerably in human studies (Table 1) (1). From the limited information available, ferric pyrophosphate would appear to be the better absorbed but, like electrolytic iron, it is only about half as well absorbed by adults as ferrous sulfate. At least twice as much iron from ferric

pyrophosphate as from ferrous sulfate should thus be used for food fortification.

In a recent stable isotope study in infants (36), ferric pyrophosphate was reported to be only about one third as well absorbed as ferrous fumarate from a wheat-soy infant cereal. Fractional iron absorption from ferric pyrophosphate by infants was 1.3% in that study compared with 0.6–2% from an iron-fortified chocolate drink in iron-replete adults (16). To compensate for this low absorption, fortification levels would have to be relatively high to provide a useful supply of absorbable iron. In the only efficacy study made with ferric pyrophosphate (37), Pakistani infants from a lower socioeconomic class were fed from 4 to 12 mo a wheat-milk complementary food fortified with either ferric pyrophosphate or ferrous fumarate at 7.5 mg Fe/100 g. The infants consumed 3 to 5 mg extra iron per day. Both fortified cereals resulted in small but significant increases in hemoglobin and serum ferritin compared with the nonfortified cereal. However, at 12 mo, ~50% of the infants in both groups were still iron deficient, indicating the need for a much higher level of fortification.

Counteracting inhibitors of iron absorption

Phytic acid, phenolic compounds, calcium and certain milk or soy proteins are common dietary inhibitors of iron absorption. They can considerably reduce the absorption in both native food iron and fortification iron by forming unabsorbable complexes in the gastrointestinal tract. Phytic acid is present in cereal and legume based foods, which are often vehicles for iron fortification; phenolic compounds occur in sorghum but also chocolate-based products, and milk products contain calcium. Phytic acid and phenolics are the most potent inhibitors, and iron absorption from some foods may be unacceptably low unless the inhibitors of absorption are effectively overcome. There are three common strategies to counteract inhibitors of iron absorption. These are the addition of ascorbic acid or sodium EDTA, together with the iron compound; the addition of fortification iron in a form that is protected from combining with dietary inhibitors (NaFeEDTA, ferrous bisglycinate, heme iron); or the degradation or removal of phytic acid.

Ascorbic acid. Ascorbic acid is the most widely used enhancer of fortification iron. It can increase by several fold the absorption of all fortification iron compounds (and native food iron) that dissolve in the gastric juice and enter the common nonheme iron pool. Ascorbic acid appears to act mainly in the stomach and duodenum as both a solubilizing ligand and a reducing agent. It reduces ferric iron to the ferrous state, thus preserving its solubility as the pH rises in the duodenum (38). Ferric iron reacts more readily to form insoluble hydroxides and other nonabsorbable complexes. Ascorbic acid has been demonstrated to be effective in decreasing the negative effects of all major inhibitors of iron absorption including calcium and milk proteins (39,40), phytic acid, polyphenols and soy products (41–43).

Ascorbic acid has been reported to increase in a useful way the absorption of many commonly used iron compounds, including ferrous sulfate, ferric ammonium citrate, ferrous fumarate, ferric orthophosphate and electrolytic iron; however, most of the studies have investigated its influence on ferrous sulfate absorption. In general, increasing amounts of ascorbic acid will progressively increase iron absorption (39,44); however, a plateau is often reached (40,41). An ascorbic acid to iron molar ratio of 2:1 (~6:1 weight ratio) has been reported to increase iron absorption by 2 to 12 fold in adult women fed infant formula, infant cereal and corn porridge fortified with

ferrous sulfate or ferric ammonium citrate (45); by 3-fold in a ferrous sulfate fortified chocolate drink fed to children (44); by 2.5-fold from a ferric chloride fortified liquid formula fed to adults (39); and ~2-fold from a ferrous sulfate fortified infant formula fed to infants (40).

When the phytic acid concentration is high, however, a molar ratio of 2:1 may not be enough to increase iron absorption significantly. A molar ratio of ~3:1 was necessary to approximately double iron absorption in adults from ferrous sulfate fortified corn porridge (46) and high phytate bread (42). Similarly, with a ferrous sulfate fortified soy infant formula, a molar ratio of 2:1 did not increase absorption, whereas a 4:1 ratio increased absorption from 1.8 to 6.9% with no further increase at an 8:1 molar ratio (42). In comparison, with a milk infant formula, absorption increased from 5.3 to 19.5% on increasing the ascorbic acid to iron molar ratio from 2:1 to 4:1 (41). Thus, an ascorbic acid to iron ratio of at least 2:1 will usefully increase the absorption of soluble iron compounds from milk products and low phytate foods, but a ratio of at least 4:1 is required to increase iron absorption in a useful way from fortified foods high in phytic acid or phenolics.

There is some uncertainty, however, concerning the influence of ascorbic acid on the absorption of the insoluble iron compounds. With electrolytic iron powders and the iron phosphate compounds, the concern relates to the amount of ascorbic acid that will increase iron absorption in a useful manner. With ferrous fumarate, the concern is that this compound does not completely enter the common pool and that ascorbic acid may have little or no influence on its absorption. Based on the study of Forbes et al. (25), it is likely that ascorbic acid can be used to increase the absorption of elemental iron powders and iron phosphate compounds in a useful way, although the study was made only with electrolytic iron and ferric orthophosphate. It was reported that adding 100 mg ascorbic acid to a farina meal containing 6 mg Fe (~5:1 molar ratio) as ferric orthophosphate, electrolytic iron or ferrous sulfate increased absorption by 4, 2.4 and 3-fold, respectively. However, Fairweather-Tait et al. (47) reported more recently that using an ascorbic acid to iron molar ratio of ~1.3:1 did not improve the absorption of hydrogen-reduced iron from breakfast cereal.

Two studies have indicated that ascorbic acid may have little or no enhancing effect on the absorption of ferrous fumarate. First, Hurrell et al. (16) added 25 mg of ascorbic acid to chocolate drink powder containing 5 mg iron as ferrous fumarate and reported no significant increase in iron absorption in adults. In contrast, when infants were fed the same chocolate drink fortified with ferrous sulfate, a 2:1 ascorbic acid to iron molar ratio increased iron absorption threefold (44). Hurrell et al. (16) also investigated the influence of adding 100 mg ascorbic acid to a liquid formula meal fortified with 7.2 mg Fe as ferrous fumarate. The relatively small increase in absorption observed (7.1–11.3%) was not significant ($P > 0.05$). In the same study, the absorption of extrinsically labeled native food iron was compared with the absorption of intrinsically labeled ferrous fumarate; with both the chocolate drink and the formula meal, iron absorption from ferrous fumarate was 1.5 to 1.9 times better absorbed than native food iron ($P < 0.05$). This indicates that ferrous fumarate does not completely enter the common iron pool. In support of this conclusion, Davidsson et al. (36) recently reported that there was no significant increase in iron absorption by infants from a ferrous fumarate-fortified wheat soy cereal when the ascorbic acid to iron molar ratio was increased from ~3:1 to 6:1. In contrast, increasing the ascorbic acid to iron molar ratio from ~2:1 to 4:1 in a ferrous sulfate fortified soy formula almost doubled iron absorption by infants (48). Further studies are

required to clarify the effect of ascorbic acid on the absorption of ferrous fumarate and other insoluble iron compounds.

Another major problem with ascorbic acid is its susceptibility to losses during food storage and food preparation (49). Storage losses may be unacceptably high under hot and humid conditions; although sophisticated packages or encapsulation can largely prevent degradation during storage, these solutions may be too expensive for many applications, and extensive losses of ascorbic acid may still occur during food preparation.

Sodium EDTA. Sodium EDTA has been demonstrated to increase iron absorption by adults from ferrous sulfate fortified rice meals (50) and from ferrous sulfate fortified wheat and wheat-soy infant cereals (4). It has also been reported to increase iron absorption by Peruvian children from a ferrous sulfate fortified milk cereal breakfast (51). With the rice meal, a maximum 3-fold increase in absorption was observed, with an EDTA to iron molar ratio between 0.25 and 0.5:1, compared with only a 2-fold increase at a 1:1 molar ratio (50). With the school breakfast and the wheat infant cereal, a maximum increase in absorption occurred at an EDTA to iron molar ratio of 0.7:1, whereas the 1:1 molar ratio was most effective in the high phytate wheat-soy cereal (4,52). It is thought that EDTA binds iron in a soluble complex in the gastrointestinal tract, preventing it from forming insoluble, nonabsorbable complexes with dietary inhibitors or hydroxyl ions. Its main advantage over ascorbic acid is that it is stable to processing and storage. It is a permitted additive to foods in many countries for the prevention of sensory changes.

Unfortunately sodium EDTA does not appear to enhance the absorption of water-insoluble compounds, presumably because it combines with other minerals or food components before these iron compounds dissolve in the gastric juice. Davidsson et al. (52) reported that sodium EDTA, added at an EDTA to iron molar ratio of 1:1, did not enhance iron absorption by adolescent girls fed ferrous fumarate fortified tortillas, a finding that was recently confirmed in our laboratory by feeding adults ferrous fumarate fortified infant cereals with or without sodium EDTA at a 1:1 molar ratio (Fidler, M., Federal Institute of Technology Zürich, personal communication, 2001). Similarly, an EDTA to iron molar ratio of 0.5:1 has been reported not to improve the absorption of H-reduced iron from breakfast cereal (47) and a molar ratio of 1:1 did not improve the absorption of ferric pyrophosphate from infant cereal (4). If the usefulness of sodium EDTA is limited to its enhancing effect on soluble iron compounds, the only advantages to using it in preference to preformed NaFeEDTA would be cost and legislation.

NaFeEDTA. The use of NaFeEDTA for food fortification has several advantages. In the presence of phytic acid, iron is 2 to 3 times better absorbed from NaFeEDTA than from ferrous sulfate (4,53); it does not oxidize lipids during the storage of cereal flours (54,55) and unlike many other soluble iron compounds, it does not cause precipitation of peptides when added to fish sauce or soy sauce. In the absence of phytic acid, NaFeEDTA has an absorption similar to that of ferrous sulfate (53). Its main advantage, however, is that it has been demonstrated several times to be efficacious for food fortification, improving the iron status of target populations consuming NaFeEDTA fortified fish sauce (9,55), curry powder (56) and sugar (8). It is now under consideration at the national level for the fortification of fish sauce in Vietnam and soy sauce in China. Its disadvantages are higher cost (~6 times as expensive as ferrous sulfate) and its tendency to cause unwanted color reactions in a way similar to ferrous sulfate. It has recently been approved by the Joint FAO/WHO Expert Committee on Food Additives (57) for government approved for-

tification strategies but it has not yet been permitted widely at the country level.

Ferrous bisglycinate. The advantage of ferrous bisglycinate over EDTA is that it is more "natural." It is, however, more expensive, it promotes fat oxidation in stored cereals (58) and it promotes off-colors in a similar way to other soluble iron compounds. Another major disadvantage, however, is that it is a patented compound (Albion Laboratories, Clearfield, UT), marketed very aggressively, and it has been extremely difficult to obtain an independent verification of its claimed protective effect against phytic acid because the compound tested is always provided by the company. There are also contradictory reports in the literature with respect to its bioavailability. Fox et al. (59) reported that infants fed vegetable purée or whole grain cereal absorbed iron to a similar extent from ferrous bisglycinate and ferrous sulfate. In contrast, iron absorption was 4-fold better from ferrous bisglycinate fortified whole corn porridge (60) and about 2-fold better from breakfast meals based on corn flour or wheat flour (61) than from the equivalent foods with ferrous sulfate.

Bovell-Benjamin et al. (60) argued that the results of Fox et al. (59) could be explained because ascorbic acid was used to maintain isotopically labeled ferrous sulfate in the ferrous state. The amount added, however, was only 0.83 mg ascorbic acid/mg iron, which is much lower than the 6:1 weight ratio required for a useful increase in absorption as discussed earlier. It is doubtful therefore whether this amount of ascorbate would result in a measurable increase in iron absorption. Ferrous bisglycinate is nevertheless a well absorbed iron compound, which may in the future be confirmed as being protected against phytic acid. Its high cost, however, and tendency to provoke unwanted sensory changes make it an unsuitable choice for many food vehicles. It does appear to be a useful compound in liquid milk (62) and other milk products.

Hemoglobin. Dried RBC have been added to foods as a source of bioavailable iron. Heme iron is absorbed intact and is thus protected from the inhibitors of iron absorption. Absorption is always relatively high and has been reported to vary between 15 and 35% depending on iron status (63). Although hemoglobin fortified foods have been demonstrated to improve the iron status of infants and young children in Chile (64,65), widespread use is unlikely due to its intense color, extremely low iron content (0.34%), potential to carry infections and technical difficulties involved in collection, drying and storage.

Phytic acid degradation. It is technically possible to completely degrade phytic acid enzymatically in cereal and legume based foods. Such an approach could improve the absorption of iron (2), zinc (66) and calcium (67) and would seem ideally suited for manufacturing low cost complementary foods in which added ascorbic acid may not be stable during storage in hot humid climates. It is necessary, however, to decrease phytic acid to very low levels to obtain a meaningful increase in iron absorption; this is possible only enzymatically and not by milling of cereals or by ultrafiltration of protein isolates (68).

Hurrell et al. (68) investigated iron absorption in adults from a liquid soy formula meal fortified with ferrous sulfate containing soy protein isolates of different phytic acid content. There was no improvement in iron absorption when the phytic acid content of the isolate was decreased from 990 to 370 mg/100 g, although absorption increased 2-fold at 100 mg/100 g and 4-fold on complete degradation. Hallberg et al. (2) reported similar results on adding free phytic acid to ferrous sulfate fortified wheat bread rolls. Decreasing the phytic acid

in the flour from 1 g/100 g (equivalent to whole wheat flour) to 100 mg/100 g (equivalent to white wheat flour) increased absorption 2-fold in adults whereas zero phytic acid increased absorption 5-fold. Even small amounts of phytic acid greatly reduced absorption compared with the phytate free roll. At only 10 mg phytic acid/100 g, iron absorption was decreased by 20% and at 20 mg/100 g, iron absorption was decreased by 40%. Based on these two studies with iron fortified foods, complete phytate degradation is recommended; however, if this is not possible, it can be estimated that the phytic acid to iron molar ratio should be reduced to <0.7:1 so as to achieve at least a 2-fold increase in iron absorption.

Commercial phytases can completely degrade phytic acid in ~1 to 2 h when added to an aqueous slurry of cereal held at the optimum pH and temperature for phytase activity (69). Traditional food processes, such as soaking and germination, can also substantially degrade phytic acid (70) although an additional fermentation step is probably necessary for complete degradation (71). Recently Barclay et al. (72) and Egli (73) used whole wheat, whole rye or whole buckwheat as sources of phytase to degrade phytic acid in complementary foods based on wheat/soy, millet/cow pea and rice/chickpea. It was possible to degrade phytic acid completely in 1 to 2 h by holding the mixture in aqueous solution at the optimum pH and temperature of the phytase.

To summarize, the main technical barriers to successful iron fortification are as follows: 1) finding an absorbable iron compound that can be added to the selected food without causing unwanted sensory changes; and 2) overcoming inhibitors of iron absorption in the food vehicle itself or in the diet with which the fortified food is consumed. The main inhibitor of iron absorption is phytic acid.

These two barriers have largely been overcome in relation to some food vehicles but not with others. Soy sauce, fish sauce, infant formulas, dried milk and cereal-based complementary foods can be successfully fortified with iron and have been shown to improve iron status in targeted populations. Major problems remain, however, in relation to the fortification of cereal flours and salt, foods that perhaps have the greatest potential for iron fortification in developing countries.

In relation to cereal flours, it is urgently necessary to evaluate the utility of the currently used elemental iron powders, which has not been questioned for >30 y. Current evidence would support only the use of electrolytic iron for food fortification, provided that increased quantities of iron are added. Other widely used powders may or may not be useful, and one powder (atomized) has been introduced into the food supply without careful nutritional evaluation, although it does conform to current regulations. A close collaboration with the few companies manufacturing food grade elemental iron powders is necessary to evaluate whether powders can be manufactured with an absorption equivalent to that of ferrous sulfate, or at least with an absorption adequate to guarantee a beneficial effect on iron status.

An alternative iron compound for cereal flour fortification is encapsulated ferrous sulfate. This compound has been overlooked even though lipid coatings have been demonstrated to prevent ferrous sulfate catalyzed fat oxidation in stored infant cereals. Encapsulation technology would also seem to be a solution for the iron fortification of salt, which is often one of the only foods purchased in rural communities in developing countries. Much of the salt in these countries, however, is low grade, high in impurities and moisture, and fortified with iodine. Adding encapsulated iron to such salt should prevent adverse color reactions and iodine losses. There is a need to develop capsules that prevent sensory change in salt and

bread. The capsules should be removed during digestion so that the iron is released for absorption.

Phytate degradation with phytases is technologically possible and should be considered especially for low cost complementary foods. However, virtually all phytate must be degraded so as to achieve a meaningful increase in iron absorption. This involves holding the food for at least 1 h at optimum pH and temperature (~pH 5, 50°C) for phytase activity, making it more suitable for industrial application. At the household level, traditional processes such as germination and fermentation, which activate native phytases, may be more suitable. The challenge is to introduce phytate degradation technology into food manufacture or food preparation without significantly increasing the cost.

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