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The Potential of Encapsulated Iron Compounds in Food Fortification: A Review

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Abstract: Iron (Fe) encapsulation has the potential to help overcome several major challenges in Fe fortification of foods. It may decrease unwanted sensory changes in fortified products and reduce interactions of Fe with food components that lower Fe bioavailability. However, the effect of encapsulation *per se* on Fe bioavailability is a concern. Rat studies comparing encapsulated ferrous sulfate, ferric ammonium citrate, and ferrous fumarate to non-encapsulated compounds indicate that a ratio of capsule:substrate of ≥ 60:40 may decrease the relative bioavailability (RBV) of the Fe by approximately 20%. At a ratio of capsule:substrate of ≤ 50: 50, the RBV of encapsulated ferrous sulfate appears to be similar to ferrous sulfate. Even minor changes in capsule composition may influence Fe bioavailability. Encapsulated ferrous fumarate given with ascorbic acid as a complementary food supplement and encapsulated ferrous sulfate fortified into salt have been shown to be efficacious in anemic children. For salt fortification, further refinements in Fe capsule design are needed to increase resistance to moisture and abrasion, while maintaining bioavailability. Studies evaluating the potential efficacy of encapsulated Fe in staple cereals (wheat and maize flours) are needed. A potential barrier to use of encapsulated forms of Fe in staple food fortification is the relatively low melting point of the capsules, which may cause unwanted sensory changes during food preparation. Research and development efforts to improve the quality of coatings and their resistance to high temperatures are ongoing. Process costs for encapsulation can be high, and unless they can be reduced, may limit applications. Further research is needed to determine which encapsulation technologies are most effective in ensuring iron bioavailability from encapsulated compounds.

Key words: iron, encapsulation, bioavailability, deficiency, salt

Introduction

A number of encapsulated iron (Fe) compounds are in development or commercially available. These include forms of ferrous sulfate, ferrous fumarate, ferric pyrophosphate, and elemental Fe. Water-soluble coating materials, such as maltodextrin and cellulose, do not provide adequate protection against iron oxidation in moist environments. Therefore, most encapsulated Fe compounds are coated with hydrogenated oils that provide a good water barrier at a relatively low cost. Encapsulated Fe compounds are mainly used to fortify infant formulas and cereals, but are added to other foodstuffs as well. Fe encapsulation has the potential to help overcome several major challenges in Fe fortification of foods. It may decrease the Fe-catalyzed oxidative processes in fatty acids, amino acids, and other micronutrients that can produce unwanted sensory changes and decrease the nutritional value of foods. Also, it may reduce interactions of Fe with food components that lower Fe bioavailability, such as phytates,

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tannins, and polyphenols. However, the effect of encapsulation *per se* on Fe bioavailability is a concern. Several factors may influence bioavailability from encapsulated products, including capsule material, ratio of capsule material to Fe, and the technology and process used for encapsulation. It is likely that a combination of lipase activity, emulsifiers as well as time, moisture, and temperature contribute to Fe release and subsequent bioavailability in the gastrointestinal (GI) tract.

Animal studies on the bioavailability of encapsulated Fe

The relative bioavailability (RBV) of a series of encapsulated Fe compounds has been tested in rat hemoglobin (Hb) repletion tests [1, 2]. The compounds were obtained from Durkee (Cleveland, Ohio, USA) and had a 40:60 ratio of capsule material: $FeSO_4 \cdot H_2O$. As shown in Table I, the RBV of ferrous sulfate encapsulated with hydrogenated soybean oil, hydrogenated palm oil, or mono- and diglycerides was comparable to that of ferrous sulfate. Ferrous sulfate encapsulated with maltodextrin showed a non-significant reduction in RBV compared to ferrous sulfate. Ethyl cellulose encapsulated ferrous sulfate (Eurand International, Milan, Italy) was also tested (20:80 capsule:substrate ratio), and had 33% higher RBV (Table I).

Unpublished data (D. Barclay, Nestec Ltd., personal communication, 2003) indicate that the RBV of ferrous sulfate encapsulated in hydrogenated soybean oil (Balchem, Slate Hill, NY, USA) varies between 78–99%, depending on the capsule material and the capsule:substrate ratio (Table I). Ferrous sulfate encapsulated in hydrogenated soybean oil at a 50:50 capsule:substrate ratio showed an RBV equivalent to non-encapsulated ferrous sulfate. However, there was a 20% reduction in RBV when the capsule:substrate ratio was increased to 67:33. Also, there was a 20% reduction in RBV when the capsule was modified to include glycerol monostearate and tricalcium phosphate (Table I).

The relative bioavailability (RBV) of encapsulated forms of ferrous fumarate was also tested in rat Hb repletion tests (D. Barclay, Nestec Ltd., personal communication, 2003) (Table II). Ferrous fumarate encapsulated in hydrogenated castor oil (Biodar, Yavne, Israel) at 70:30 and 60:40 ratios of capsule:substrate, and encapsulated in hydrogenated soybean oil (Balchem) at a 40:60 ratio, had RBVs equal to ferrous sulfate. However, ferrous fumarate encapsulated in carnauba wax (Westreco, Marysville, Ohio, USA) had a RBV of only 66% compared to ferrous sulfate. In a separate study, the RBV of ferric ammonium citrate was equivalent to ferrous sulfate, but when encapsulated with hydrogenated palm oil in a 60:40 ratio, its RBV was decreased by 25% (Table II).

Table II: Relative bioavailability (RBV) of non-encapsulated and encapsulated ferrous fumarate and ferric ammonium citrate as measured by the rat Hb repletion test

Compound	RBV[1]
Ferrous fumarate	101 ± 7
Encapsulated ferrous fumarate	
In hydrogenated castor oil	
(30% ferrous fumarate)	103 ± 9
(40% ferrous fumarate)	111 ± 10
In hydrogenated soybean oil	
(60% ferrous fumarate)	98 ± 10
In carnauba wax	66 ± 6
Fe ammonium citrate	107
Encapsulated ferric ammonium citrate in hydrogenated palm oil	
(60% capsule: 40% ferric ammonium citrate)	82

[1]As mean or as mean ± SEM

Table I: Relative bioavailability (RBV) of encapsulated ferrous sulfate as measured by the rat Hb repletion test

Form	Fe content[1]	RBV[2]
Ferrous sulfate·H_20 (non-encapsulated)	33	102 ± 5
Ferrous sulfate encapsulated		
In ethyl cellulose (20:80 ratio of capsule:Fe $SO_4 \cdot H_20$)	27	133 ± 103
In 40:60 ratio with:		
Part. hydrogenated soybean oil	20	114 ± 7
Part. hydrogenated palm oil	20	95
Mono- and diglycerides	20	116 ± 7
Part. hydrogenated soybean and cottonseed oil	20	79
Maltodextrin	20	87
In 50:50 ratio with part. hydrogenated soybean oil	16.7	99
In 50:50 ratio with part. hydrogenated soybean oil (44% hydro. soy oil, 5% glyceromonostearate, 1% tricalcium phosphate)	16.7	78
In 67:33 ratio with part. hydrogenated soybean oil	10.9	81

[1] As percent. [2] As mean or mean±SEM. [3] Increased compared to ferrous sulfate ($p < 0.05$).

Sensory testing of encapsulated Fe in cereals

Encapsulated Fe was dry mixed into precooked wheat flour (10 mg/100g) and the samples were stored at 37 °C for 3 months [1]. The compounds tested were ferrous sulfate encapsulated with hydrogenated soybean oil, hydrogenated palm oil, mono- and diglycerides, maltodextrin, or ethyl cellulose. All of the compounds performed as well as electrolytic Fe and an unfortified control. They did not cause fat oxidation as measured by pentane generation, nor did they generate off-flavors as measured by a taste panel. However, when prepared at temperatures above the melting points of the capsules (52–66 °C), the encapsulated Fe compounds produced green-gray color changes in paps made with hot water and wheat flour. Ferrous sulfate encapsulated in either hydrogenated soybean oil or mono- and diglycerides was dry mixed into a wheat cereal at 10 mg and 50 mg/100 g, and the samples were stored at 37 °C for 3 months [2]. Both compounds performed as well as electrolytic Fe and an unfortified control. Ferrous sulfate encapsulated with ethyl cellulose, dry mixed into a rice cereal at 18.5 mg Fe/100 g and stored at 37 °C for 3 months, also performed as well as carbonyl Fe and the control [2].

Ferrous sulfate + ascorbic acid encapsulated in soy lecithin liposomes (SFE-171)

Boccio *et al* reported in a series of studies from Argentina on the bioavailability of ferrous sulfate (6.6% Fe) with ascorbic acid (2%) encapsulated in soy lecithin liposomes in a fluid suspension (SFE-171, Biofer™) [3]. They reported that the bioavailability of SFE-171 was comparable to that of non-encapsulated ferrous sulfate in animals and humans. Table 3 shows the absorption of SFE-171 in milk compared to that of ferrous sulfate and ferrous ascorbate in both milk and water in rats. Absorption of SFE-171 given with milk was not significantly different from ferrous sulfate or ascorbate given with water, but was greater than ferrous sulfate given with milk ($p < 0.01$). The authors suggested that encapsulation of the Fe improved its bioavailability by reducing its interaction with protein, calcium, and other milk components [3].

In a series of further absorption studies in rats, the absorption of SFE-171 was comparable to or greater than ferrous sulfate when given with different meals [3] (Table IV). In humans (n = 29) without iron deficiency anemia (IDA) (mean Hb 16.8 ± 1.4; serum ferritin 113 ± 74 µg/L), mean absorption ± SD of SFE-171 given with 250 mL of milk (6.6% Fe) was 10.4 ± 4.9%. In an uncontrolled study, preschool children with IDA (n = 10, mean age 23.1 ± 8.9 months) received a daily milk portion (250 mL) fortified with SFE-171. All of the subjects receiving the fortified milk attained normal Hb concentrations; the mean number of days required was 50.7 ± 19.2 [3] (Table V).

Table III: Absorption of encapsulated ferrous sulfate (SFE-171, Biofer™) in milk compared to non-encapsulated ferrous sulfate and ferrous ascorbate in rats

	n	Absorption (% ± SD)
Ferrous sulfate in water	30	13.2 ± 4.3
Ferrous ascorbate in water	30	13.1 ± 4.9
Ferrous sulfate in milk	30	7.9 ± 3.2*
SFE-171 in milk	30	11.6 ± 4.5

* $p < 0.01$ compared to other groups

Table IV: Absorption of encapsulated ferrous sulfate (SFE-171, Biofer™) compared to non-encapsulated ferrous sulfate when added to different meals in rats

Product	Absorption (% ± SD)	
Milk + ferrous sulfate	7.7 ± 2.7	
Milk + SFE-171	12.3 ± 2.9	$p < 0.01$
Yogurt + ferrous sulfate	6.9 ± 2.9	
Yogurt + SFE-171	8.1 ± 3.0	NS
Maté 5% + milk + ferrous sulfate	9.5 ± 3.0	
Maté 5% + milk + SFE-171	11.0 ± 2.0	NS
Cereals 5% + milk + ferrous sulfate	6.7 ± 3.0	
Cereals 5% + milk + SFE-171	8.3 ± 2.2	NS

Table V: Time to normalization of Hb in children with IDA receiving milk fortified with encapsulated ferrous sulfate (SFE-171, Biofer™)

n = 10	mean ± SD
Hb (g/L)	
Initial	10.1 ± 0.9
Final	12.6 ± 0.7
SF (µg/L)	
Initial	12.7 ± 1.3
Final	28.5 ± 26.4
Plasma Fe (µg/dL)	
Initial	37.2 ± 16.1
Final	132.6 ± 47.3
Days treated to reach normal Hb	50.7 ± 19.2

Encapsulated ferrous fumarate plus ascorbic acid as "sprinkles" in Ghana

Using a prospective, randomized design, Zlotkin *et al* studied 557 anemic children aged 6–18 months (Hb: 70–99 g/L) in Ghana [4]. One group received a daily sachet of "sprinkles" containing ferrous fumarate encapsulated in hydrogenated soybean oil (80 mg elemental Fe) (Descote ferrous fumarate 60 Ultra, Particle Dynamics, St. Louis, USA). The sachets also contained ascorbic acid (50 mg), and were to be mixed into complementary foods at the home (sprinkles group). A second group received ferrous sulfate drops 3 times/day for 2 months (total daily dose: 40 mg elemental Fe). There was no placebo control group. The total dosage of Fe in the sprinkles sachet was double that in the ferrous sulfate drops. On the basis of algorithms, estimated absorption of microencapsulated Fe added to cereal was 2–8%. Thus, the total amount of available Fe in an 80-mg sachet was estimated to be 1.6–6.4 mg. The Fe absorption from the drops was estimated to be 4–18%, making the total amount of available Fe 1.6–7.2 mg/day. Thus, the range of potentially absorbed Fe was thought to be similar for the two forms of Fe.

Hb and serum ferritin (SF) concentrations were measured at baseline and at the end of treatment. In both groups, there was a significant increase in Hb concentrations from baseline to the end of treatment study ($p < 0.001$; Table VI). The change in Hb concentrations was not significantly different between groups. Fifty-eight percent of infants in the sprinkles group improved from an anemic to a non-anemic state (hemoglobin 100 g/L), while 56% of the drops group improved to a non-anemic state. Mean SF concentrations increased significantly in both groups from baseline to the end of treatment ($p < 0.001$). The final mean SF value was significantly higher in the drops group than in the intervention sprinkles group. The change in the prevalence of Fe-deficiency anemia (IDA) was not reported.

Table VI: Hemoglobin and ferritin concentrations and the percentage of anemic infants in Ghana, by treatment group, at baseline, and after 2 months of treatment

	Sprinkles group (n = 245)	Drops group (n = 247)
Baseline		
Hemoglobin (g/L)	87 ± 8	87 ± 9
Anemic subjects (%)	100	100
Ferritin (µg/L)	38.8	40.0
End of treatment		
Hemoglobin	102 ± 16	100 ± 17
Anemic subjects (%)	42.3	43.7
Ferritin (µg/L)	71.2	106.8

Anemia was defined as Hb < 100 g/L.

Despite the presence of ascorbic acid in the sprinkles, the bioavailability of Fe appeared to be lower from the sprinkles than from the drops. This may have been due to the fact that the sprinkles were mixed with food, which may have inhibited Fe absorption relative to drops that were taken without food. There were minimal side effects in both groups. Compliance was less with the sprinkles (67% never missed a dose) compared to the drops (81% never missed a dose), at least partly because the sprinkles turned gummy in the initial packaging sachet (this was later resolved by using a packaging material with a sufficient moisture barrier). Although this study had several limitations-the high "therapeutic" dose (80 mg/day) of Fe in the sprinkles; the difference in Fe dose in the drop and sprinkles groups; lower compliance with sprinkles – the authors suggested that improved safety and ease of use may favor the use of sprinkles to deliver Fe [4].

Dual fortified salt with encapsulated ferrous sulfate and iodine in Morocco

Although dual fortification of salt with iodine (I) and Fe could be an effective fortification strategy, ensuring iodine stability and Fe bioavailability in dual fortified salt (DFS) is difficult. Water-soluble Fe compounds, which are the most bioavailable, react with moisture and impurities in salt and produce unacceptable color changes. Moreover, in the presence of ferrous ions and oxygen, the I in DFS is unstable due to catalytic oxidation of iodate or iodide to I_2. Insoluble Fe compounds, such as elemental Fe powders or Fe phosphate compounds, cause fewer sensory changes but may be so poorly absorbed as to be of little nutritional value. The ideal Fe compound for DFS would be one with high bioavailability that causes no sensory changes or I losses when added to salt. Encapsulated Fe has excellent potential for overcoming unwanted sensory changes and I losses in salt, while maintaining high bioavailability [5].

Zimmermann *et al* reported a study of DFS in rural villages in the Rif Mountains of northern Morocco [5]. To establish the DFS fortification level, salt intake was measured by three-day weighed food records and Fe bioavailability estimated from the local diet using published algorithms. In school-age children, salt intake was 7–12 g/day and Fe intake was 9.2 to 14.5 mg/day, 97% of which was non-heme Fe. Because the diet was high in phytic acid

and low in ascorbic acid, estimated non-heme Fe bioavailability from the local diet was 0.4–4.3%.

Local salt was dual fortified with 25 µg iodine/g salt as (potassium iodide) KI and 1 mg Fe/g salt as ferrous sulfate hydrate encapsulated with partially hydrogenated vegetable oil (Cap-Shure FS-165E-50, Balchem, Slate Hill, NY, USA). The encapsulated Fe compound contained 50% $FeSO_4 \cdot H_2O$. As a control, iodized salt (IS) was prepared with 25 µg iodine/g salt as KI. After storage for 20 weeks, there were no significant differences in I content between the DFS and IS. During the dry season, when the moisture content of the local salt was low (< 1%), there was no significant color difference between IS and DFS. However, during the damp winter season, when the moisture content of the local salt is high (~3%), the DFS developed a mild yellow color during storage. The DFS was added to local Moroccan meals and their flavor, odor, and color were compared by triangle testing. There was no significant detectable difference in color, odor, and/or taste in the foods containing the DFS.

In a 9-month, randomized, double-blind trial in iodine-deficient 6- to 15-year-old children (n = 377), the efficacy of the DFS was evaluated. Hb, SF, whole-blood zinc protoporphyrin (ZnPP), and serum transferrin receptor (TfR) were determined at baseline. Because each participating family shared a 2 kg monthly salt portion for 9 months, children were randomized at the household level into two groups. One group (n = 188) was given IS while the second group (n = 189) was given DFS. Both investigators and households were blind to group assignment. The salt was dispensed directly to the head of the household. At 20 and 40 weeks, Hb, SF, ZnPP, and TfR were remeasured. Of the 377 children who began the study, 367 completed it. As shown in Table VII, mean Hb significantly increased in the DFS group compared to the IS group at 40 weeks ($p < 0.02$). All indices of Fe status (SF, TfR, ZnPP) were significantly improved in the DFS group compared to the IS group at 40 weeks ($p < 0.05$). The prevalence of IDA and Fe-deficiency without anemia was sharply lower in the DFS group at 40 weeks ($p < 0.01$) (Figure 1).

Although the DFS was well accepted (Table VIII), Fe encapsulation did not entirely prevent color changes. As previously stated, the color of the DFS was indistinguishable from IS during the dry season, but less satisfactory

Table VIII: Results of acceptability interviews in participating households after 8 months of salt use, comparing iodized salt (IS) and salt dual fortified with iodine and Fe (DFS)

	Efficacy trial salt group	
	IS (n = 52)	DFS (n = 52)
1. Salt quantity used monthly in the household?		
< 1 kg	17	14
Between 1 and 2 kg	31	30
= 2 kg (amount distributed monthly to each household)	44	45
> 2 kg	8	11
2. Salt consumed every day by children?	100	98
3. Salt color acceptable in damp season?	100	861
4. Salt color acceptable in dry season?	100	100
5. Salt used for all foods during cooking and at table?	98	98
6. Salt changed the color of foods?	4	17[2] (milk, onion)
7. Salt taste acceptable in all foods?	98	96
8. Salt overall acceptable?	98	94

Numbers are positive answers as percentages.
[1,2] Significantly different from IS: [1]$p < 0.02$; [2]$p < 0.001$.

Table VII: Concentrations of hemoglobin (Hb)[1,3], serum ferritin (SF)[1,3], transferrin receptor (TfR)[2,3], zinc protoporphyrin (ZnPP)[1,3] in the iodized salt (IS) (n = 184) and dual fortified salt (DFS) (n = 183) groups over 40 weeks

	Hb (g/L)		SF (µg/L)		TfR (mg/L)		ZnPP (µmol/mol heme)	
Time	IS	DFS	IS	DFS	IS	DFS	IS	DFS
0	111 ± 14	113 ± 13	23 ± 18	20 ± 16	8.2 (4.4–82.6)	8.7 (4.3–77.1)	63 ± 47	63 ± 47
20 wks	115 ± 14	116 ± 13	29 ± 20	36 ± 26[6]	8.5 (4.4–78.5)	7.8 ± 4.5–23.9)	58 ± 43	44 ± 24[4, 8]
40 wks	116 ± 12	127 ± 12[4, 5]	17 ± 12	40 ± 25[6, 7]	8.9 (3.8–118.0)	6.5 (3.0-15.3)[6, 7]	57 ± 43	35 ± 24[4, 9]

[1] Means (SD. [2] Medians (range).
[3] Significant treatment × time interaction, $p < 0.01$ (ANOVA).
[4, 6] Significantly different from baseline of DFS: [4]$p < 0.01$; [6]$p < 0.05$.
[5, 7, 9] Significantly different from IS at 40 weeks: [5]$p < 0.02$; [7]$p < 0.05$; [9]$p < 0.01$.
[8] Significantly different from IS at 20 weeks: $p < 0.02$.

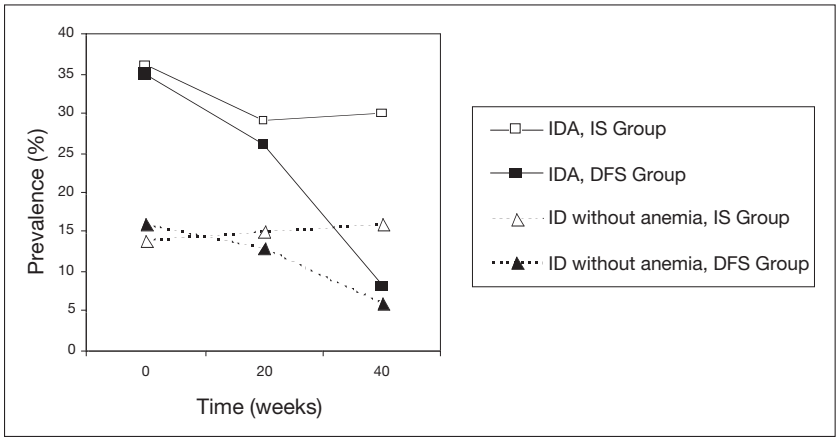


Figure 1: The prevalence of iron deficiency anemia (IDA) and iron deficiency (ID) in 6- to 15-year-old Moroccan children receiving dual fortified salt (DFS) containing encapsulated iron and iodine (n = 183) was significantly reduced compared to a group receiving iodized dalt (IS) (n = 184) ($p < 0.01$ at 40 wks.

during the damp season. Although the partially hydrogenated vegetable oil capsule is water resistant, some loss of capsule likely occurs from abrasion during mixing. When the salt moisture content is high, in the presence of water and oxygen the ferrous Fe is oxidized and precipitation of yellow-brown ferric hydroxide occurs.

The fortification goal was to provide ~0.5 mg/day of absorbed Fe to the children in the study. Based on local salt intakes of 7–12 g/day in children and an estimated Fe bioavailability of 1–4%, the DFS was fortified at 1 mg Fe/g salt. This provided an additional 7–12 mg dietary Fe/day, doubling the children's baseline Fe intakes. The DFS demonstrated good bioavailability without an enhancer, despite the high phytic acid content of the diet. To fully liberate Fe encapsulated in partially hydrogenated vegetable oil requires lipase digestion in the proximal duodenum. This brief delay in Fe appearance may reduce Fe binding to inhibitory substances (such as phytic acid) in the stomach and upper duodenum, and thereby potentially increase Fe absorption.

Although a stable and efficacious DFS could provide new opportunities for control of IDA, the cost-effectiveness of the approach remains to be determined. Current cost estimates for encapsulated ferrous sulfate are four to seven times that of non-encapsulated ferrous sulfate, but the price could fall if production was large-scale. These findings suggest a DFS containing encapsulated ferrous sulfate is an effective fortification strategy in the conditions of northern Morocco. But because performance of encapsulated Fe may vary depending on climate, salt quality, and diet, more studies are needed in other countries under local conditions [5].

Fortification of salt with encapsulated Fe: stability and acceptability testing in Morocco and Côte d'Ivoire

In the Morocco intervention trial just described [5], salt containing ferrous sulfate encapsulated with hydrogenated soybean oil was effective in reducing the prevalence of IDA, but it underwent undesirable color changes in the salt during the damp winter season. Wegmüller *et al* [6] recently tested the potential of various encapsulated Fe compounds as salt fortificants. In temperate Morocco and tropical Côte d'Ivoire, native salt was dual fortified with iodine and 15 different encapsulated Fe compounds commercially available or in development. In Morocco, the fortified salts were prepared using unground, unwashed salt from a local cooperative. In Côte d'Ivoire, the fortified salts were prepared using unwashed imported Senegalese salt.

The Fe content, manufacturer, and capsule material of the compounds tested are shown in Table IX. Tests were done comparing:

1. Ferrous sulfate to encapsulated ferrous sulfate (7 different capsule materials)
2. Ferrous fumarate to encapsulated ferrous fumarate (6 different capsules)
3. Ferric pyrophosphate to encapsulated micronized ferric pyrophosphate
4. Electrolytic Fe to encapsulated electrolytic Fe

The salt fortification level chosen for the different Fe compounds was equivalent to 1 mg of Fe as ferrous sulfate/g salt, considering the estimated relative bioavailability of the Fe compounds compared to ferrous sulfate [7]. The

Table IX: Encapsulated Fe compounds tested in salt in Morocco and Côte d'Ivoire

	Fe compound	Capsule material/Additives	Fe [%]	Producer
	Electrolytic			
1	Electrolytic Fe	**None**	10	OMG Americas
2	Electrolytic Fe	Partially hydrogenated soybean oil	70	Balchem
	Pyrophosphate			
3	Fe pyrophosphate	**None**	21	Lohmann
4	Fe pyrophosphate	Dextrin, glycerol esters of fatty acids, hydrolyzed lecithin	8	Taiyo Kagaku
	Fumarate			
5	Fe fumarate	**None**	33	Lohmann
6	Fe fumarate	Partially hydrogenated palm oil	16	Lohmann
7	Fe fumarate	Hydrogenated soybean oil	20	Watson Foods
8	Fe fumarate	Cellulose derivative	28	Bio Dar
9	Fe fumarate	Granulated with dextrin, cellulose, SHMP, coated with soy stearine	12	MI
10	Fe fumarate	Wax matrix	18	Particle Dynamics
11	Fe fumarate	Mono- and diglycerides	21	Particle Dynamics
	Sulfate			
12	Fe sulfate	**None**	29	Lohmann
14	Fe sulfate	Partially hydrogenated soybean oil	17	Balchem
15	Fe sulfate	Mono and diglycerides	15	Bio Dar
16	Fe sulfate	Cellulose derivative	27	Bio Dar
17	Fe sulfate	Partially hydrogenated palm oil	23	Lohmann
18	Fe sulfate	Partially hydrogenated oil	20	Watson Foods
19	Fe sulfate	Soy stearine	20	MI
20	Fe sulfate	Stearic acid	20	Particle Dynamics

electrolytic Fe and ferric pyrophosphate compounds were added to the salt at a level of 2 mg of Fe/g salt, and the ferrous sulfate and ferrous fumarate compounds were added at a level of 1 mg of Fe/g salt. Iodine was added at 40 (g/g salt. All DFS and an iodized salt (IS) control were stored in loosely woven high-density polyethylene bags, and in transparent low-density polyethylene bags. The mean temperature and relative humidity ± SD during 6 months of storage were 19 ± 2 °C and 67 ± 5% in Morocco, and 28 ± 1 °C and 81 ± 4% in Côte d'Ivoire.

The color and iodine content were measured at baseline and after storage for 1, 2, 4, and 6 months. Color changes were evaluated using reflectance colorimetry. Acceptability of the salt color was judged at 4 months by standardized interviews (n = 132) comparing 100 g DFS and IS samples side-by-side on white backgrounds. Changes in color and iodine content comparing DFS to IS are shown in Tables X and XI for the Moroccan and Côte d'Ivoire salts, respectively. The calculated color difference was a good predictor of local acceptability of the salt color as judged by the interviews. In both countries, interviewees rated as acceptable those salts with a color difference (ΔE^*_{ab} value) less than 10.

For almost all compounds, encapsulation did not prevent adverse sensory changes. There was a rapid and marked color change in many formulations of the DFS, particularly the ones fortified with forms of elemental Fe and ferrous sulfate. In general, the color change in Morocco was greater than in Côte d'Ivoire. Color instability was likely the result of the formation of ferric oxides of Fe with a rusty orange color, and the formation of I_2 which has an dark brown color.

Two of the salts fortified with encapsulated ferrous fumarate were judged acceptable at 4 months. One was encapsulated in soy stearine and granulated with dextrin, cellulose, and sodium hexametaphosphate (SHMP). Its color stability was likely to be at least partly due to the presence of SHMP. The reduction in color changes when SHMP is added as a stabilizing agent to dual-fortified salt has been noted previously [8]. The other ferrous fumarate that performed well and showed only a slight color change was encapsulated in an edible wax matrix. The bioavailability of the Fe in this edible wax capsule has not been tested (L. Weir, personal communication, 2003).

Two forms of ferric pyrophosphate, one non-encapsulated and small in particle size (≈ 2.5 μm) and one encapsulated and micronized (≈ 0.5 μm) performed best and may show promise as salt fortificants. The color of the DFS fortified with ferric pyrophosphate was acceptable. At 4 months, they retained 92% and 56% of their original I content in Morocco and Côte d'Ivoire, respectively, similar to iodized salt (Tables X and XI). Their color and iodine stability may be due to the fact that Fe phosphate compounds are insoluble in water and only poorly solu-

Table X: Morocco. Mean color difference (SE) of DFS compared to iodized salt determined by colorimetry[1], iodine retention (IR) (%), and acceptability of dual fortified salts

Sample[b]	Months of storage			
	2[1]	Color at 2 months	4[1]	6[1]
Nos. 1, 2 (electrolytic Fe)	21.6 (0.2) –31.6 (0.2)	Unacceptable dark brown		
3. non-encapsulated Fe PP	8.9 (0.1)	***Acceptable*** pale beige	8.1 (0.4) [92% IR]	8.3 (0.3) [71% IR]
Nos. 5–8, 11 (Fe fumarate)	9.5 (0.1) –27.7 (0.1)	Unacceptable orange pink brown		
9. Fe fumarate granulated with dextrin, cellulose, SHMP and coated with soy stearine	2.0 (0.1)	***Acceptable*** pale grey+dark flecks	3.3 (0.4) [92% IR]	2.9 (0.3) [98% IR]
10. Fe fumarate in edible wax matrix	6.5 (0.3)	***Acceptable*** pale grey+dark flecks	5.8 (0.5) [92% IR]	5.5 (0.3) [99% IR]
Nos. 12–20 (Fe sulfate)	20.8 (0.5) –27.5 (0.1)	Unacceptable yellow orange brown		

[1] Closest to zero = color closest to iodized salt

Table XI: Morocco. Mean color difference (SE) of DFS compared to iodized salt determined by colorimetry[1], iodine retention (IR) (%), and acceptability of dual fortified salts

Sample[3]	Months of storage			
	2[1]	Color at 2 months	4[1]	6[1]
Nos. 1, 2 (electrolytic Fe)	24.5 (1.0) –29.8 (0.5)	Unacceptable dark brown		
3. non-encapsulated Fe pyrophosphate	3.8 (0.2)	***Acceptable*** pale beige	4.9 (0.3) [56% IR]	5.6 (0.4) [35% IR]
4. Fe pyrophosphate with dextrin, glycerol esters of fatty acids, hydrolyzed lecithin	4.4 (0.4)	***Acceptable*** pale beige	4.6 (1.1) [54% IR]	4.8 (1.6) [34% IR]
Nos. 5–8, 11 (Fe fumarate)	10.6 (0.1) –18.3 (1.1)	Unacceptable orange pink brown		
9. Fe fumarate granulated with dextrin, cellulose, SHMP and coated with soy stearine	2.1 (0.5)	***Acceptable*** withe+brown flecks	3.4 (0.3) [23% IR]	4.9 (0.4) [11% IR]
10. Fe fumarate in edible wax matrix	6.2 (0.4)	***Acceptable*** pale grey	9.0 (1.0) [48% IR]	9.2 (0.5) [29% IR]
Nos. 12–20 (Fe sulfate)	9.6 (0.4) 13.5 (1.5)	Unacceptable yellow		

[1] Closest to zero = color closest to iodized salt

ble in dilute acid, which reduces their reactivity, even in salt with a high moisture content. Although ferric pyrophosphate with a particle size ≥ 10 μm has a relative bioavailability of 20–70% compared to ferrous sulfate, reducing its particle size to ≈ 0.5 μm increases its bioavailability in humans [9].

The findings suggest currently available encapsulation techniques for Fe do not sufficiently reduce moisture penetration and/or Fe solubility when the encapsulated Fe is mixed into salt. Mechanical abrasion of the capsules during mixing may also contribute by damaging capsules and exposing and/or freeing Fe [6].

Conclusions

- Data on the bioavailability of encapsulated Fe are scarce. For this review, three published rat studies (two of which partially report the same data) and a small series of unpublished rat studies from Nestlé were available. Most of these used the rat Hb repletion method to assign an RBV to Fe compounds. There are three published reports of the efficacy of encapsulated Fe in humans; two were randomized, controlled studies.
- Data from rat Hb repletion studies directly comparing encapsulated ferrous sulfate, ferric ammonium citrate, and ferrous fumarate to non-encapsulated compounds indicate that a ratio of capsule:substrate of ≥ 60:40 may decrease the RBV of the Fe by approximately 20%. At a ratio of capsule:substrate of ≤ 50: 50, the RBV of encapsulated ferrous sulfate appears to be similar to ferrous sulfate (D. Barclay, Nestec Ltd., personal communication, 2003).
- Data from one rat Hb repletion study (D. Barclay, Nestec Ltd., personal communication, 2003) suggests that even minor changes in capsule composition may influence Fe bioavailability.
- In the "sprinkles" study (Zlotkin *et al*, 2001), a high dose of ferrous fumarate encapsulated in hydrogenated soybean oil (Descote 60 Ultra, Particle Dynamics) given with ascorbic acid as a complementary food supplement was efficacious in anemic infants.
- The salt efficacy study (Zimmermann *et al*, 2003) and the series of rat Hb repletion studies (Hurrell *et al*, 1989; D. Barclay, Nestec Ltd., personal communication, 2003) indicate that the bioavailability of ferrous sulfate encapsulated in hydrogenated soybean oil in a 50:50 ratio (Balchem FS-165-50) is high.
- For salt fortification, further refinements in Fe capsule design are needed to increase resistance to moisture and abrasion, while maintaining bioavailability.
- Studies evaluating the potential efficacy of encapsulated Fe in staple cereals (wheat and maize flours) are needed
- Process costs for encapsulation can be high, and unless they can be reduced, may limit applications. Technology transfer to low-income countries could reduce costs and encourage sustainability of fortification programs using encapsulated iron.
- A potential barrier to use of encapsulated forms of Fe in staple food fortification is the relatively low melting point of the capsules (45–65 °C), which may cause unwanted sensory changes during food preparation (Hurrell, 1985; Hurrell *et al*, 1989).
- Further research is needed to determine which encapsulation technologies (i.e. coacervation, spray cooling, fluidized bed, spinning disk) are effective in ensuring iron bioavailability from encapsulated compounds.
- Due to large variations in the technical properties of commercially available encapsulated iron compounds, industry standards would be valuable to define specifications for these products.

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