Food Fortification Initiative. Fortification Matters.

Successful atta flour fortification. Using bioavailable iron compounds to increase the absorption of dietary iron

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Potential food fortification vehicles suitable for resource-poor populations

Industrially processed foods regularly consumed by infants, children, adolescents and women of child-bearing age from lower socioeconomic groups

Mass fortification

Cereals

- wheat and maize flours
- artificial rice grains

Condiments

- salt, sugar
- bouillon cubes
- sauces (soy, fish)
- powdered spice mixes

Cooking oils

Targeted fortification

Complementary foods for infants and young children

In-home fortification powders and fat-based spreads for infants and young children, but potential for adolescents, pregnant women

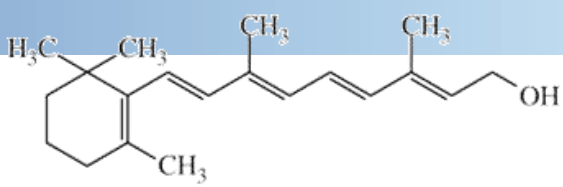
potential for market-driven industrial products, but many families have little or no disposable income and need Food Aid

Common micronutrient deficiencies (due to low intake or bioavailability) that can be prevented by fortified foods

- **Fe, Zn, I and vit. A** deficiencies well-documented in infants, children and young women particularly from the low socioeconomic populations
  - *Fe, Zn deficiency* due to
    - cereal/legume based diets, little animal source foods, fruit, vegetables
    - increased demands for growth
    - increased losses (Fe: menstruation, hookworm; Zn: diarrhea)
  - *Iodine deficiency* due to
    - low soil I
  - *Vit. A deficiency* due to
    - few animal source foods, orange/yellow fruits/vegetables

Opportunities and barriers to efficacious food fortification

☆ **Iodised salt** and **vitamin A** fortified cooking oil

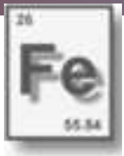


- \+ technically not difficult to manufacture
- \+ efficacy well documented

☆ **Zinc** fortification

- \+ technically not difficult
- \- absorption decreased by phytic acid
- \- no reliable measure of zinc status → no confirmed efficacy

☆ **Iron** fortification



- \+ WHO Guidelines (2006) give recommendation on compounds and levels for efficacious products
- \- technically difficult: highly absorbable compounds lead to sensory changes; no sensory changes with less absorbable compounds
- \- absorption decreased by phytic acid and polyphenol compounds
- \- infection and inflammation (incl. overweight and obesity) block iron absorption

iron fortification of foods

iron is the most difficult mineral to add to foods and to ensure adequate absorption

- highly absorbable ⇨ color and flavor problems

  organoleptically acceptable ⇨ poorly absorbed

- even the highly absorbable compounds may be poorly absorbed

all major vehicles for iron fortification contain potent absorption inhibitors or are consumed with food containing inhibitors ⇨ manufacturers must: protect iron from absorption inhibitors, remove them, or adjust the level of iron fortification accordingly

Stages in the development of an iron-fortified food

I. optimize iron compound: highest potential absorption with no organoleptic problems

select Fe compound with highest relative absorption (WHO Guidelines)

⇒

make organoleptic trials: colour and taste panels, storage, food processing, home cooking

⇓

II. optimize absorbed iron to meet consumers need

- estimate Fe intake ⇒ current need for Fe
- estimate intake of fortification vehicle
- estimate/measure absorption (± enhancer)

⇒ define fortification level

⇐

III. make efficacy study to demonstrate effect on Fe status

monitor prevalence of ID according to WHO/CDC Guidelines

Choice of iron compound

WATER SOLUBLE COMPOUNDS

dissolve instantaneously

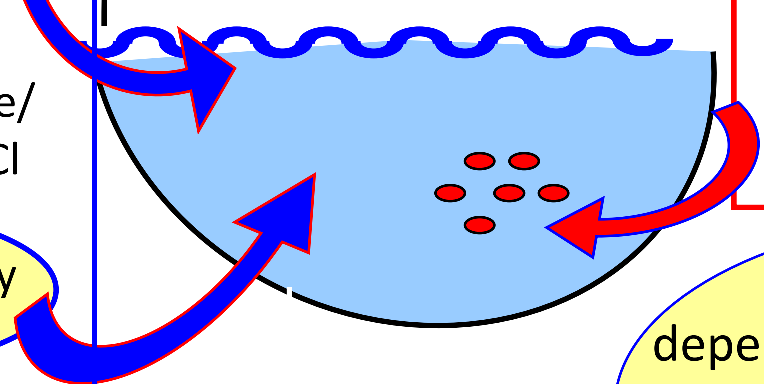
ferrous sulfate
RBV = 100

poorly water soluble/
soluble in dilute HCl

dissolve completely over time

ferrous fumarate
RBV = 100

relative bioavailability depends on solubility in gastric juice



COMPOUNDS WATER INSOLUBLE/POORLY SOLUBLE IN DILUTE ACID

never dissolve completely

electrolytic Fe
RBV = ca. 50
ferric pyrophosphate
RBV = 15 -75

absolute absorption depends on intake of inhibitors (phytate) and enhancers (ascorbic acid) and iron status of consumer

Enhancers and inhibitors of iron absorption: Factors which could influence the efficacy of iron fortified foods

food factors

enhancers ascorbic acid, also muscle proteins and organic acids

inhibitors phytic acid (cereals, legumes)
phenolic compounds (beans, veg.)
milk and legume proteins; calcium

iron fortification compounds

soluble: good bioavailability/often poor sensory
poorly soluble: less bioavailability/better sensory
enhancing: NaFeEDTA, iron bisglycinate

contamination iron soil, cooking pots, milling

subject factors

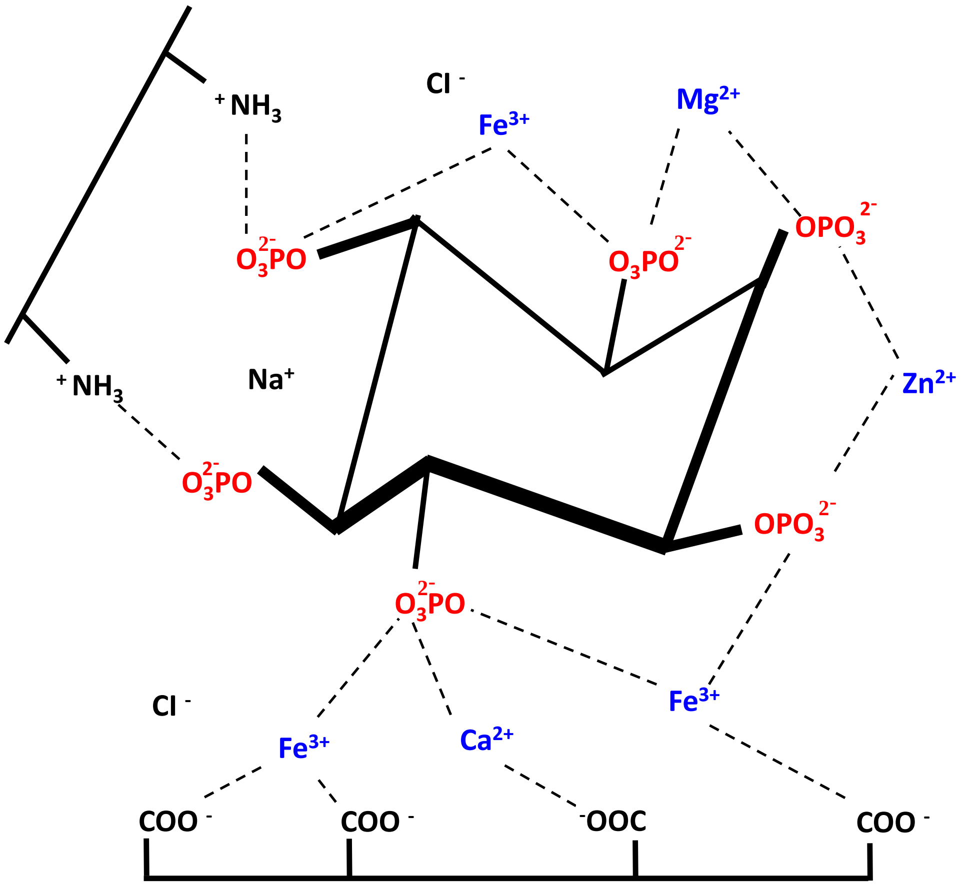
: status of consumer:
low status/high absorption

: other nutrient deficiencies:
vitamins A and B_2 (needed to incorporate Fe into Hb)

: Infection and inflammatory disorders, anemia of other causes

: gut health, gut microflora (?)

Phytic acid inhibits iron absorption



peptide-phytate-mineral-complex

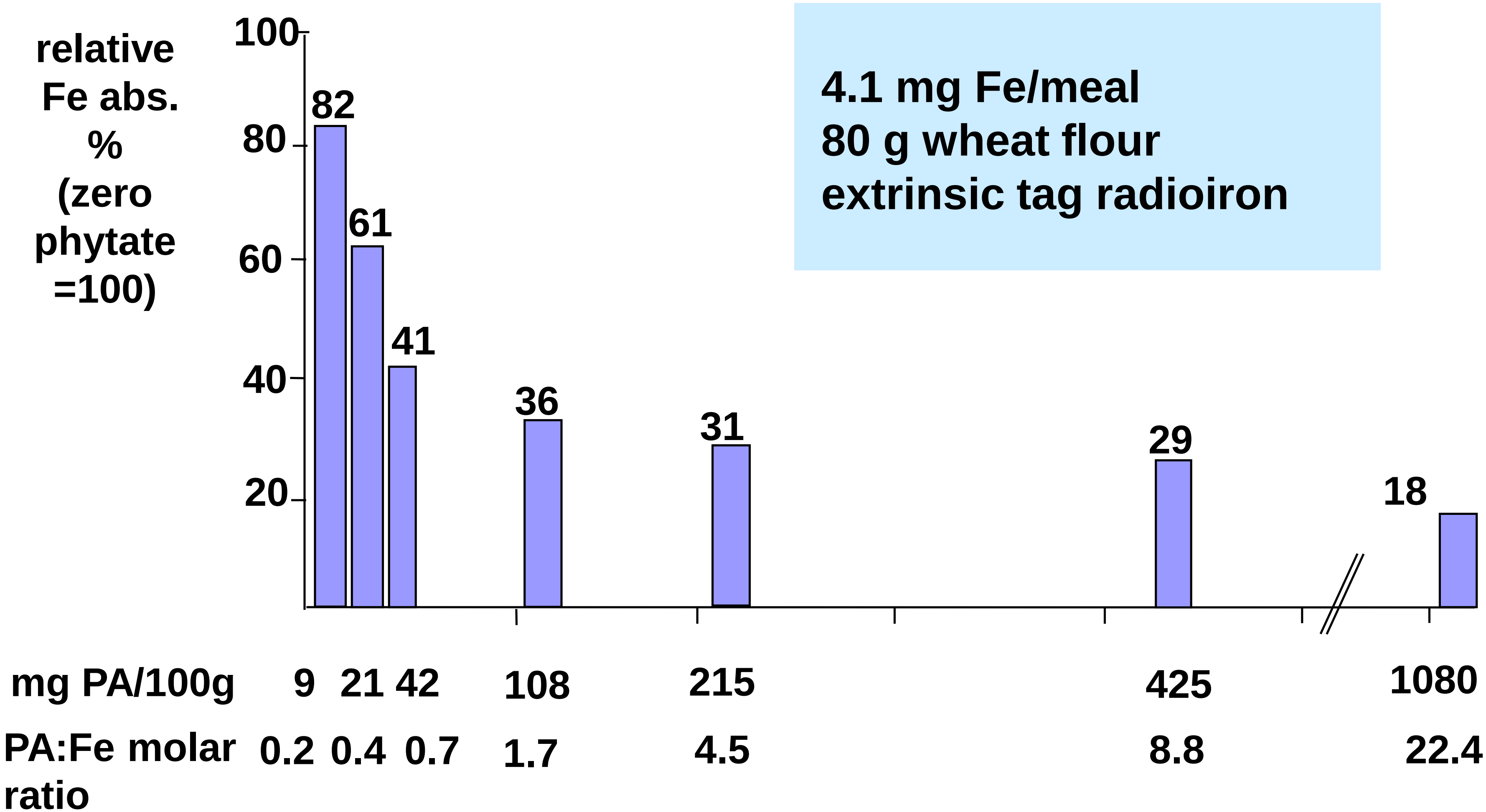
- Atta flour, used to make chapati, roti, naan and puri is whole grain durum wheat flour, high in protein, low in gluten but containing ca. 1% phytic acid

- phytic acid from atta flour forms a complex with minerals and peptides in the GI tract

- prevents absorption of Fe, Zn, Ca, Mg

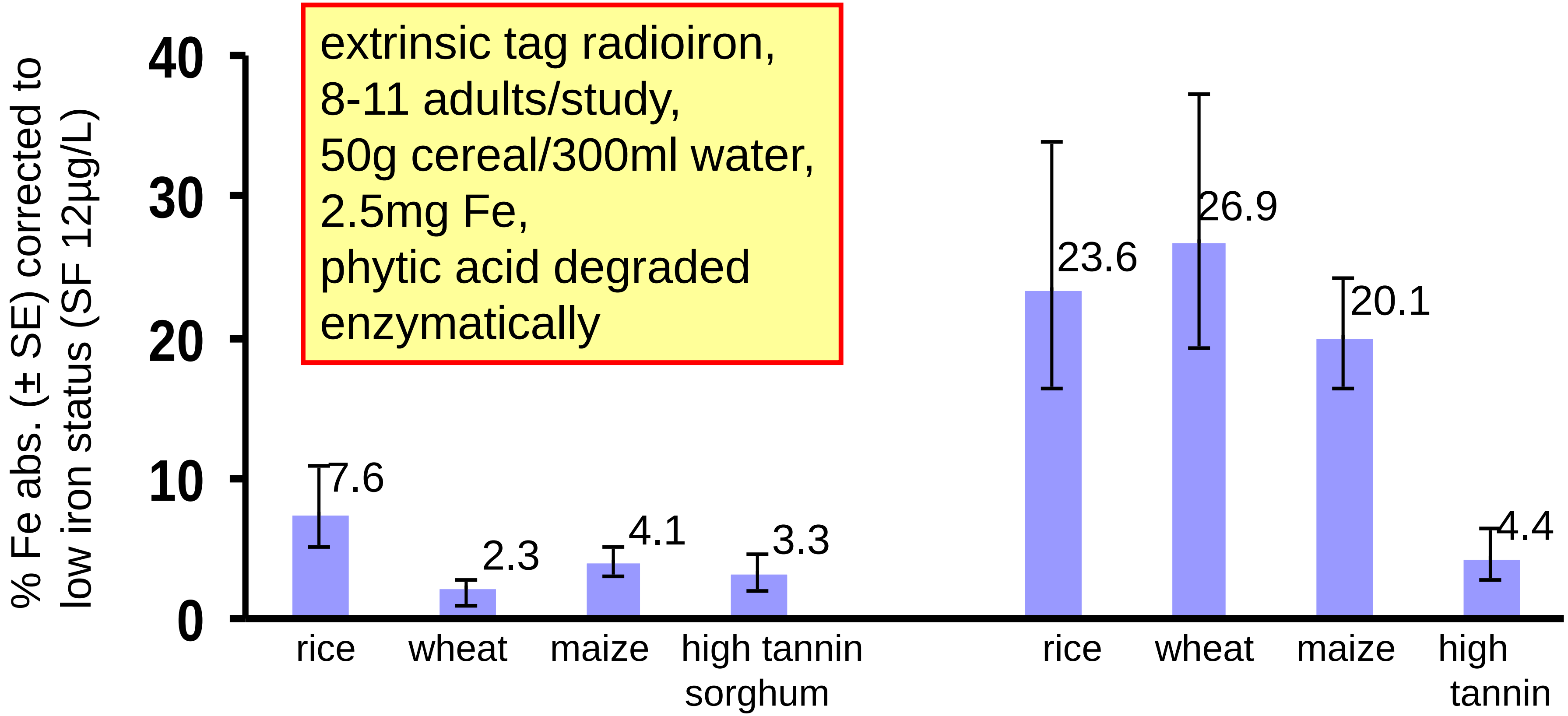
In a bread meal, phytic acid must be drastically decreased before Fe absorption is usefully improved

(Hallberg et al. 1989)



influence of complete dephytinization on iron absorption from cereal porridges

(Hurrell et al. 2003)



PA mg/100g	sorghum						
160	120	260	870	0	0	0	0

Potential ways to increase iron absorption by decreasing the inhibitory effect of phytate in cereals and legumes

Removal

- milling cereals (up to ca. 90% removed)
- dialysis/ultrafiltration of protein isolates after acid/salt or alkali treatment

Enzymatic degradation

- soaking, germination, fermentation activate the native phytases
- fermentation additionally may provide microbial phytases
- steeping at optimum pH and temperature for maximum phytase activity
- add exogenous phytase during food manufacture
- add exogenous phytase at point of consumption

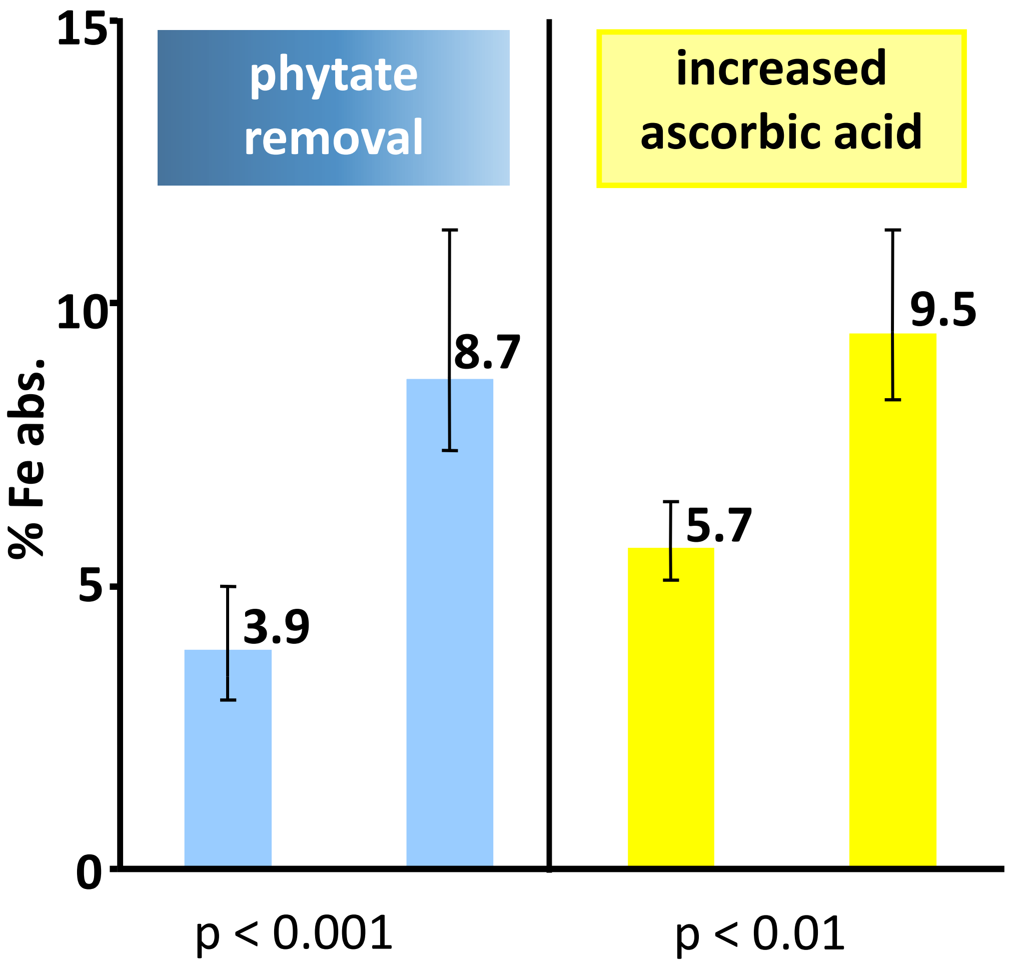
Addition of compounds which prevent phytate-mineral binding

- EDTA and ascorbic acid increase absorption of Fe from high phytate foods. NaFeEDTA and ferrous bisglycinate have 2-3 fold absorption of fe sulphate

Phytic acid degradation or ascorbic acid addition improve iron absorption by 5-8 month old infants from soy formula

(Davidsson et al. 1994)

- soy formula containing
  20 mg Fe/L as ferrous sulfate,
  400 mg phytate/L,
  110 mg ascorbic acid/L
- phytate degraded enzymatically
  < 1.3 mg/L
  normal ascorbic acid
- ascorbic acid increased 220 mg/L
  native phytate 400 mg/L
- iron absorption measured in infants using stable isotopes, paired comparisons



NaFeEDTA effectively counteracts phytate inhibition

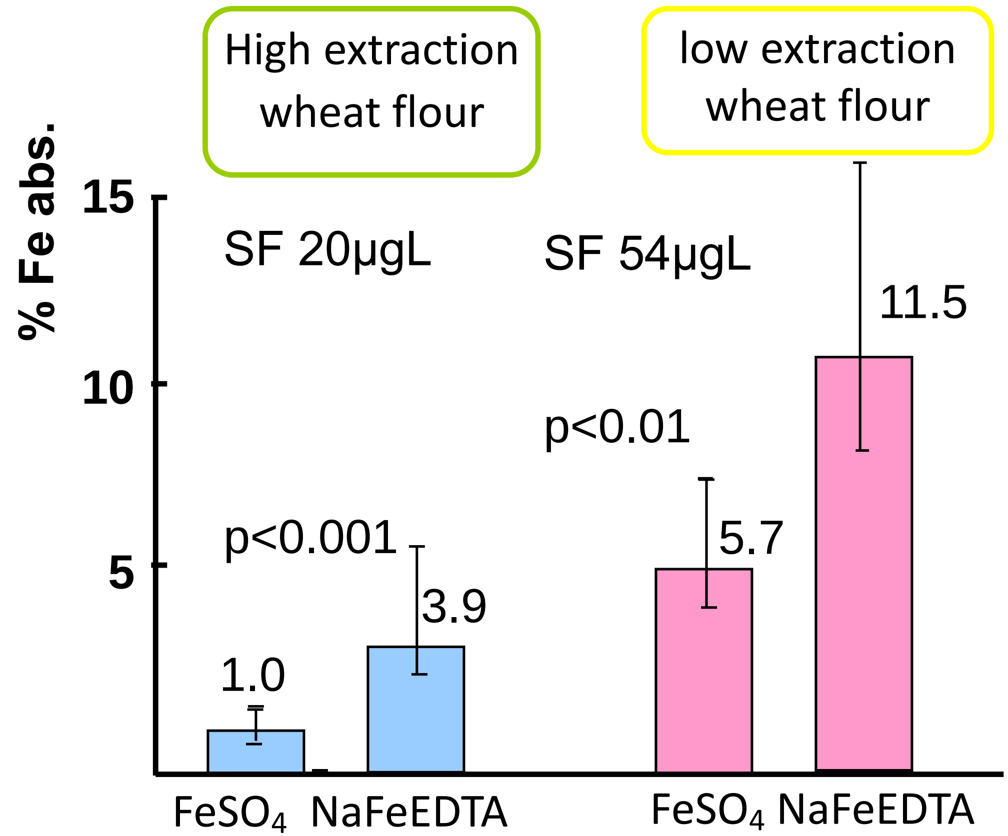
Organoleptic evaluation

- does not provoke fat oxidation in stored cereal flours. May cause colour changes in maize and extruded rice

Relative absorption

- 2-4 times better absorbed than $FeSO_4$ from high phytate meals
- similar or lower absorption than $FeSO_4$ from non-inhibitory meals
- may increase Zn absorption, no effect on Ca or heavy metals
- accepted by JECFA, FDA, EFSA
- ~6 times cost of $FeSO_4$

iron absorption by adults consuming bread rolls with 5 mg Fe *(Hurrell et al. 2000)*



WHO Guidelines (2006) for the choice of iron compound in fortified food

for **most vehicles** the order of preference is:	• ferrous sulphate (FS) • ferrous fumarate • encapsulated sulphate or fumarate • electrolytic iron (2x amount vs. FS) • ferric pyrophosphate (2x amount vs. FS) • NaFeEDTA
for high phytate cereal flours and high peptide sauces (soy, fish)	• NaFeEDTA
for liquid milk products and soft drinks	• ferrous bisglycinate • micronized ferric pyrophosphate • ferric ammonium citrate

for **infant foods** and open-market foods **add ascorbic acid** as an enhancer at 2:1 molar ratio, for high phytate foods at 4:1

Elemental iron for flour fortification

- **Electrolytic iron is the only iron powder recommended**, but only for low extraction flour, not for atta flour.
  Estimated to be about half as well absorbed as ferrous sulfate.
  Add **DOUBLE QUANTITY**.

- H-reduced Fe, atomized reduced Fe, carbonyl iron and CO-reduced Fe powders are not recommended. Inadequate evidence for absorption and efficacy.

- Further studies are needed with H-reduced Fe and carbonyl Fe powders.

Designing efficacious fortified foods

Defining the fortification level of individual micronutrients

- For national programs designed to improve status of critical micronutrients in at risk populations:
  - additional amount of micronutrient consumed should fill the gap between current intake and requirement of targeted population when added to the daily intake of one or more food vehicles
- For Fe specifically: fortification level must be adjusted for relative bioavailability of Fe compound,

  - Compared to ferrous sulphate add: 2x Fe as electrolytic Fe
  2x Fe as FPP
  0.5x Fe as NaFeEDTA,

Confirming the efficacy of iron fortified foods

- Randomised, double blind, controlled design, adequate number of subjects (young women or school aged children with ID)
- 6-9 month feeding needed to change iron status, monitor with WHO recommended iron status biomarkers

Efficacy has been demonstrated for iron fortified wheat flour, atta flour, rice, salt, curry powder, sugar, soy sauce, fish sauce, complementary foods, micronutrient powders and spreads.

WHO, FAO,UNICEF, MI, GAIN and FFI . Evidence-based flour fortification Guidelines (2009)

- Guidelines based on a review of all published iron efficacy studies in adult women, adolescents and children which monitored Hb or iron status parameters. No infant studies.

- Only randomized controlled studies with adequate description of methodology and clearly defined iron compounds were included.

- All iron fortified food vehicles were included

- All studies were >5 months duration

- Studies with added ascorbic acid were excluded, studies with other ---- added micronutrients were included.

Iron efficacy studies with ferrous sulphate

Iron compound	Dose mg/d	Subject / vehicle	Length of study / Country	Impact	Source
Encapsulated Ferrous sulphate[a]	11.8	6-15 year old children salt (bread, fava beans)	9 months Morocco	efficacious	Zimmermann (2003)
Ferrous sulphate	10.3	18-40 year old women wheat flour biscuits	9 months Thailand	efficacious	Zimmermann (2005)
Ferrous sulphate	11	11-18 year old students wheat flour	6 months China	efficacious	Sun (2007)
Encapsulated ferrous sulphate[b]	7.1	18-35 year old women wheat flour biscuits	5.5 months Kuwait	efficacious	Biebinger (2009)

a encapsulated with partially hydrogenated vegetable oil (Balchem)
b encapsulated with hydrogenated palm oil ; mean particle size ca. 40µm

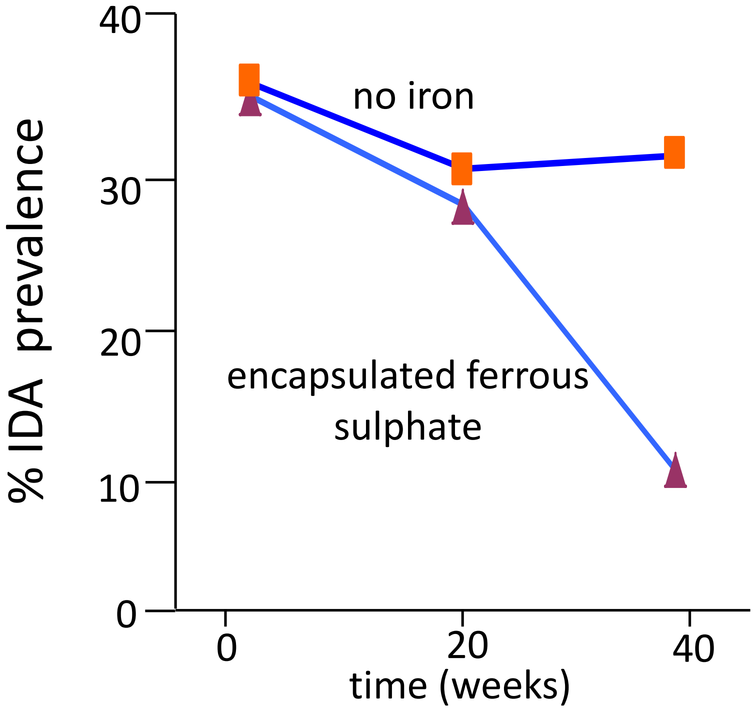
Fortification of salt with encapsulated ferrous sulphate improves iron status in Moroccan school children

(Zimmermann et al. 2003)

- encaps. FS prevents colour changes
- dietary iron intake 9-15 mg/d, low Fe bioav. (5%), salt intake 7-12 g/d,

fortification level defined as 1 mg Fe/g

- salt provided to households, added to bread, fava beans, olives
- 9 months randomized double blind controlled trial in 2x 180 6-15 yr old school children
- monitor Hb, SF and TfR, ZPP



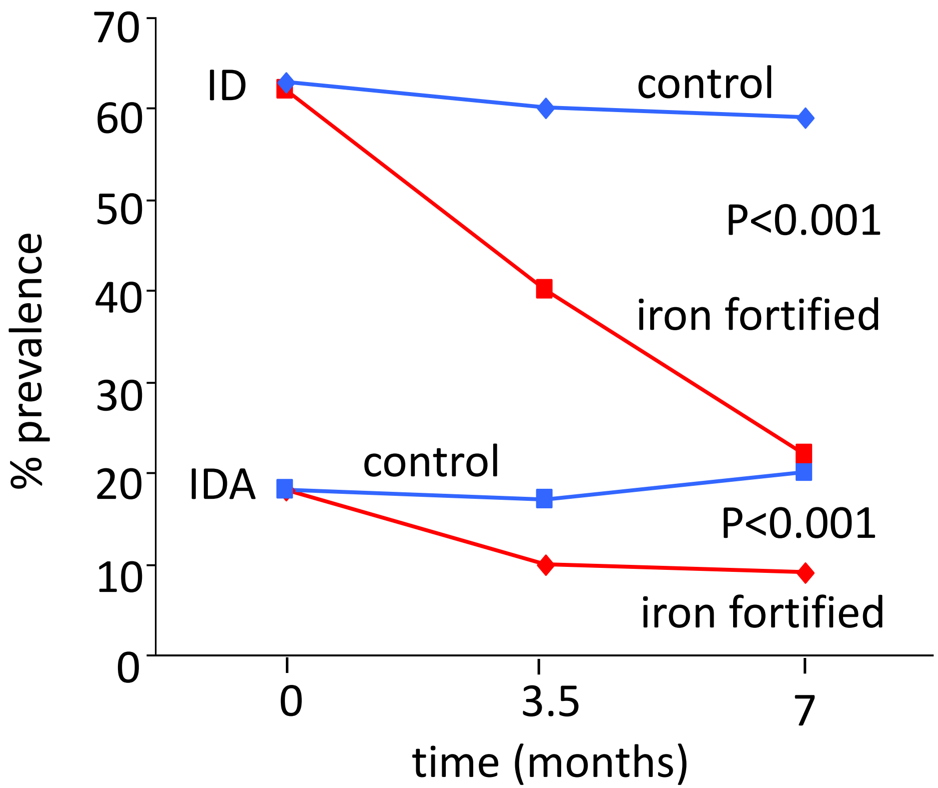
IDA = low Hb +2/3 abnormal iron status parameters

Efficacy and effectiveness studies with NaFeEDTA

Dose mg/d	Subjects/ vehicle	Length of study/ country	Impact	Source
7.1	Both sexes Aged 10+ Curry powder	24 months South Africa	Very efficacious	Ballot (1989)
4.6	Both sexes Aged 1+ sugar	32 months Guatemala	Very efficacious	Viteri (1995)
8.6	Women 17-44 Fish sauce	6 months Vietnam	Moderately efficacious	Thuy (2003)
7.5	Women 16-49 Fish sauce	18 months Vietnam	Very effective	Thuy (2005)
4.9	Both sexes 3+ Soy sauce	18 months China	Very effective	Chen (2005)
7	Both sexes 11-18 Wheat flour	6 months China	Very efficacious	Sun (2007)
7	Children 3-8 Maize porridge	5 months Kenya	Very efficacious	Andang'o (2007)
3.5	Children 3-8 Maize porridge	5 months Kenya	Moderately efficacious	Andang'o (2007)
1.3	Children 6-11 Brown bread	5 months South Africa	No effect on iron status	Van Stuijvenberg (2007abstract)

Fortification of Atta flour with NaFeEDTA improves iron status of Indian School children *(Muthayya et al, 2012)*

- whole grain 'atta' wheat flour fortified with NaFeEDTA at 60 ppm
- 7 month randomized double blind controlled trial in 2 x 200 6-13 yrs old children of low Fe status (SF <20 µg/L)
- 100 g atta flour containing 6 mg Fe as NaFeEDTA fed as chapatis with vegetable dishes 6 d/w
- monitor Hb, SF and TfR



Efficacy and effectiveness studies with electrolytic iron

Dose mg/d	Subject/ vehicle	Length of study/ country	Impact	Source
12.5	Women 16-50 Wheat flour	24 months Sri Lanka	No change in Hb	Nestel (2004)
10	Women 18-50 Wheat flour biscuits	9 months Thailand	Moderately efficacious No change in Hb	Zimmermann (2005)
3.2	Children 6-11 Brown bread	7.5 months South Africa	No change in iron status	Van Stuijvenberg (2006)
21	Children 11-18 Wheat flour	6 months China	Moderately efficacious	Sun (2007)
7	Children 3-8 Maize porridge	5 months Kenya	No change in iron status	Andang'o (2007)
4.5	Children 6-11 Brown bread	8 months South Africa	No change in iron status	Van Stuijvenberg (2007 Abstract)
11	Children 6-14 Wheat flour biscuits	6 months Ivory Coast	No change in iron status	Rohner (2010)

Minimum daily amount of iron from different compounds which have been demonstrated to be efficacious in women

- Ferrous sulfate, 7.1 mg - 4 studies, all efficacious
  NaFeEDTA, 4.6mg - 10 studies, 9 efficacious
  Electrolytic iron 10mg - 7 studies, 2 efficacious

- Evidence-based values from studies with a demonstrated decrease in prevalence of ID/IDA.

Recommendations for iron fortification of wheat flour

Type of extraction	Iron Fortificant	Fortification level (mg/kg) by per capita flour intake (/d)			
		<75g/d	75-149g/d	150-300g/d	>300g/d
Low (low PA)	NaFeEDTA	40	40	20	15
	Sulphate/fumarate	60	60	30	20
	Electrolytic Fe	NR	NR	60	40
High (high PA)	NaFeEDTA	40	40	20	15

- ★ NaFeEDTA is the only iron compound demonstrated to be efficacious in atta flour.
- ☆ Ferrous sulphate/fumarate not tested. Would need to be added at 2-3 times Fe level of NaFeEDTA. Sensory changes are likely.