

# Inhibitors

*This is my research notes for this section which I've left in incase they're useful. References are at the end.*

## 1.1. General information

**(Aragón, Ortiz, and Pachón 2012)**

“On the other hand, phytates, calcium, and some polyphenols have been identified as inhibitors of iron absorption. These compounds chelate minerals, forming complexes that inhibit the absorption of these minerals in the duodenum” (Hallberg & Hulthén, 2000).

## 2. Phytate / Phytic acid

### 2.1. Summary

- the main inhibitor of plant based diets.
- found in unprepared legumes, and cereal grains
- dose dependent, but not linear. Even a little can inhibit a lot
- effect can be overcome by enhancers
- phytase can also overcome phytate

### 2.2. Studies

**(Hurrell and Egli 2010)**

“In plant-based diets, phytate (*myo*-inositol hexakisphosphate) is the main inhibitor of iron absorption. The negative effect of phytate on iron absorption has been shown to be dose dependent and starts at very low concentrations of 2–10 mg/meal”

“Food processing and preparation methods, which include milling, heat treatment, soaking, germination, and fermentation, can be used to remove or degrade phytate to a varying extent (8, 10). The addition of exogenous phytase or its activation during food processing, or the addition to a meal just before human consumption, has been shown to improve iron absorption significantly (7, 11–13).”

**(Glahn et al. 2001)**

A caco-2 cell test on tannic and phytic acid. Main thing to note is that even a little of each decreases absorption by a lot.

**(Hallberg, Brune, and Rossander 1989)**

Study showing the inhibitory effect of phytate

## 3. Polyphenols

### 3.1. Summary

- found in black tea, coffee, wine, chilli, cocoa, herbal teas, green tea, rosemary, cereals and legumes

- used to be referred to as vegetable tannin
- dose dependent, and also a difference between the type of polyphenols. eg tea inhibits more than coffee or wine.

### 3.2. Studies

**(Fidler 2003)** “polyphenols inhibit both non-heme natural food and ferrous sulfate (Gillooly et al. 1984a; Bezwoda et al. 1985)”

**(Hurrell and Egli 2010)**

Talks about different types of polyphenols inhibiting more than others. References quite a few other studies

**(Allen 2002)** The polyphenols in espresso coffee and tea reduced iron absorption from the ferrous bisglycinate by 50% but there was no ferrous sulfate control for comparison.

## 4. Calcium

### 4.1. Summary

Conflicting results for calcium. Some studies say it inhibits both heme and non-heme. Other studies which tend to be the newer ones say that it only inhibits at high dose. The reason for the conflict is said to be because the effects of calcium wasn't isolated properly from the effects of other food. Also that calcium can have indirect effects such as inhibiting the release of phytates, so indirectly inhibiting iron. There does seem to be some direct inhibitory going on for both heme and non-heme at high doses though (>280:1). Just low doses it's not definite.

### 4.2. Studies

**(Hurrell and Egli 2010)** – not a study but references other studies

“Calcium has been shown to have negative effects on nonheme and heme iron absorption, which makes it different from other inhibitors that affect nonheme iron absorption only (20–22).”

“Initially, the inhibitory effect was suggested as occurring during the transport of iron across the basolateral membrane from the enterocyte to the plasma because absorption of both forms of iron is equally inhibited, but more recently, it was suggested that the inhibition takes place during the initial uptake into the enterocytes (23, 24). “

**(Hallberg et al. 1991)**

Calcium reduced iron absorption in two ways - during cooking of the bread as it stopped the fermentation and release of phytates, and also directly when added after cooking. Also showed that it affects heme iron too.

“The same amount of calcium also significantly reduced heme-iron absorption, suggesting that the effect of calcium is related to the mucosal transfer of iron.”

**(Cayot, Guzun-Cojocar, and Cayot 2013)**

I think the gist of this study is that it's still unclear the link between calcium and iron absorption.

"Yoghurt, used as substituting material in diet (in order to add 1 % of Ca), did not change iron absorption. Generally, in most of published works, it seems that calcium ions do not change iron absorption. Casein seems to be responsible of the low bioavailability of iron."

**(Cook, Dassenko, and Whittaker 1991)**

Calcium has a negative effect when taken with iron (non-heme) and food. When just taken with iron and no food, calcium carbonate has no effect but calcium citrate and calcium phosphate reduced iron absorption significantly by 49% and 62%, respectively.

This is **(Gaitán et al. 2011)** interpretation of the study

"They did not find any effect of calcium when they administered 300 mg calcium (as carbonate) and 37 mg nonheme iron (as sulfate) doses to healthy volunteers, which corresponds to a Ca:Fe molar ratio of 11:1. They also evaluated a higher Ca:Fe molar ratio (46:1) and did not find any effect. "

**(Gaitán et al. 2011)**

Interesting study, states that a lot of earlier studies that claimed calcium was an inhibitor didn't isolate it enough from other inhibitors. Also states that some of the confusion could come from the indirect effects calcium has like stopping the release of phytates. They state that calcium only has a direct effect on iron absorption at pretty high doses.

"We found that calcium doses <800 mg did not affect the absorption of 5 mg nonheme iron (Ca:Fe molar ratio <223:1); however, calcium doses  $\geq$ 1000 mg diminished nonheme iron absorption by 49.6%. Thus, at a Ca:Fe molar ratio of ;280:1 and above an inhibitory effect was observed."

"Our study showed that 800 mg of calcium diminished the absorption of heme iron by 37.7%, whereas there was no significant effect at lower levels of calcium."

## 5. Proteins

### 5.1. General

- certain proteins like milk, egg white, soybeans (whole milk, casein, whey proteins derived from milk and cheese) inhibit non-heme iron
- soy beans inhibit in part due to the high phytic acid, but also due to the protein.
- milk inhibit mostly due its proteins (casein and whey) but also due to calcium.
- Fermenting the soy bean helps, one study even showed that a particular soy sauce enhanced iron absorption (Fukushima, 1985). Not the normal wheat based sauce though.

### 5.2. Studies

**(Hurrell and Egli 2010)**

"The 2 major bovine milk protein fractions, casein and whey, and egg white were shown to inhibit iron absorption in humans." References **(Hurrell et al. 1988)** and **(Hurrell et al. 1989)**.

"Proteins from soybean also decrease iron absorption. Phytate was shown to be the major inhibitor in soy protein isolates, but even after complete phytate degradation iron absorption from soy protein isolates was only half that of the egg- white control (which allows

interstudy comparison), which suggests that soy protein itself is inhibiting.” References **(Hurrell et al. 1992)**

**(Cook and Monsen 1976)**

A study showing milk, cheese and egg inhibiting iron while various meats enhancing.

“In contrast, iron absorption was sharply reduced in relation to the STD meal with milk (0.29), cheese (0.38), whole egg (0.22), and egg albumin (0.39), all of which were significantly less than unity ( $P < 0.01$ ).”

**(Pérez-Expósito et al. 2005)**

Study comparing absorption of iron when taken with milk in preschoolers, found Ferrous sulfate absorption 7.9%, Ferrous fumarate 2.4%. So the protein and/or the calcium inhibits fumarate more than sulfate. Though other studies show that fumarate doesn't work as well on kids compared to adults.

**(Allen 2002)** this study also talks about FeBC being affected by milk and ascorbic, but not as much as sulfate does).

## 6. Other inhibitors

### 6.1. Infection/inflammation

“The key regulator of iron absorption is the peptide hepcidin. Hepcidin expression is increased in chronic inflammation and obesity (66, 68) and may contribute to the increased prevalence of iron deficiency observed in overweight populations (69, 70).” references and examples of this are in **(Hurrell and Egli 2010)**

## 7. References

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