FREE

Is Lactoferrin Chelating Your Iron?

There's a more likely explanation for its effects on iron markers.

CHRIS MASTERJOHN, PHD

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Many people believe lactoferrin can chelate iron and bring down excessive iron levels, despite the studies showing it corrects anemia in women. One rationale for this belief is that some people report lactoferrin supplements reduce their transferrin saturation. Others claim it has induced signs of iron deficiency.

As I pointed out in Understanding Iron, transferrin saturation doesn't tell you anything about intracellular iron dynamics.

It's more likely, but not gauranteed, that lactoferrin is helping iron move into cells.

Here we take a look at why.

Lactoferrin is present in milk, saliva, vaginal secretions, semen, mucosal linings, and in polymorphonuclear leukocytes — neutrophils, eosinophils, and basophils — involved in the immune response.

It is 60% similar to transferrin, including it's ability to bind two iron atoms.

It has antimicrobial and immunomodulatory properties, and it may play a role as an iron chaperone, helping the small amounts in milk be absorbed effectively, and shuttling iron away from harmful microbes and toward beneficial microbes.

Natural lactoferrin is 15-20% iron-saturated, while some commercial preparations are 20-30% iron-saturated, those sold in the US are "apo" lactoferrin and less than 6% iron-saturated, and some preparations used for research are "holo" lactoferrin and are 76-100% iron-saturated.

Iron-saturated lactoferrin has greater thermal stability but loses some antimicrobial and anti-biofilm activity. However, it retains certain aspects of antimicrobial activity and it retains its anti-adhesive activity (preventing microbes from adhering to human tissues). Even if digested in the stomach, some of the antimicrobial activity is retained.

Apo-lactoferrin is degraded in the upper small intestine, and in vitro modeling suggests low stomach pH induced by meals makes it more likely to be degraded.

In the successful anemia trial, it was taken before meals to approximate an "empty stomach" effect, and they used 100 milligrams twice a day of 20-30% iron-saturated lactoferrin.

The results of this trial implied that lactoferrin could improve anemia of chronic disease driven by inflammatory sequestration of iron by lowering IL-6, and thereby making iron more available.

Why would lactoferrin lower transferrin saturation in some people?

Lactoferrin brings iron into cells.

Experiments in mouse cells show that lactoferrin is taken up into the cell by the lactoferrin receptor and then its iron is delivered to ferritin.

Experiments in human cells show that a large portion of lactoferrin is released after it is taken up. If its iron had been delivered to ferritin, that means it exited the cell without iron and can now repeat the process of bringing iron into cells all over again.

But if it systemically lowers IL-6, it will reduce ferritin synthesis and the iron it brings into cells will become more bioavailable.

In mice, absorbed lactoferrin from preparations microencapsulated with tannic acid and albumin layers to survive digestion accumulates in the liver.

In pigs, (via gastric intubation or duodenal catheter, in neonatal and weaning pigs, which are more permissive to absorption of proteins) lactoferrin is taken up by intestinal cells, and from the liver goes into the bile, and then from the intestines goes back into the blood; eventually it can reach the milk of a nursing pig through the circulation. This suggests that lactoferrin *can* leave the body through the feces and carry iron with it but that by default it *circulates* rather than leaving the body.

When the immune system secretes iron, it does not go through the digestive tract as a pre-requisite to be in the body because it is already inside the body. Presumably this is fully available for repeated bringing of iron into cells, perhaps to protect the blood from pathogens consuming free iron for their own growth. Lactoferrin can chelate iron at a lower pH than transferrin, and sites of infection are often acidic, so it likely is intended as a way to chelate free iron at acidic sites of infection. Its suppression of IL-6 presumably represents either a negative feedback loop against excessive immune activity, or some kind of cross-talk between the innate and adaptive immune systems.

When humans supplement with lactoferrin, it is likely that apolactoferrin taken with meals is disproportionately degraded in the digestive tract, while naturally iron-saturated lactoferrin taken on an empty stomach is disproportionately absorbed intact.

Now let's do a little math.

Each 100 milligrams of lactoferrin can bind to 3.57 milligrams of iron.

As I pointed out in Understanding Iron, we absorb on average 1 milligram of iron per day but we recycle on average 25 milligrams per day. Most people are eating between 6-14 milligrams of naturally occurring iron per day.

About ten percent of that is heme, which is much more absorbable than non-heme iron, and presumably the heme iron is absorbed intact without being chelated by lactoferrin in the gut.

If lactoferrin did not survive digestion but the fragments retained iron-binding capacity, each 100 milligrams could theoretically bind to 3.57 milligrams of non-heme iron. This would allow a vegan consuming 14 milligrams of iron per day to render that completely unavailable using 400 milligrams of apolactoferrin taken with meals. Someone consuming heme would be less vulnerable to this effect in proportion to their intake of heme. A meat-only carnivore would probably not be affected by it at all.

On the other hand, if the lactoferrin is absorbed intact, it could have some theoretical capacity to move the same amount of non-heme iron from the circulation into the feces. Since most iron in the circulation is non-heme, a vegan, omnivore, and carnivore would all be equally vulnerable to this effect. However, the available data suggest that it would instead simply facilitate the entry of iron into cells in repeat cycling until its eventual degradation rather than removing it from the body.

If inflammation is present, IL-6 could render up to 25 milligrams of recycled iron per day unavailable. 200 milligrams of lactoferrin has been shown to cut IL-6 in half, so theoretically 400 milligrams could normalize it entirely, and that could render up to 25 milligrams of iron per day bioavailable.

So the probability favors lactoferrin making iron more bioavailable by 1) suppressing IL=6 and 2) repeatedly shuttling iron atoms into cells.

This is more likely true to the extent lactoferrin is absorbed in tact, which in turn is more likely when it is taken in naturally iron-saturated form on an empty stomach.

Since there is a possibility that lactoferrin is degraded to fragments that remain unabsorbed but chelate dietary iron, and a possibility that some endogenous iron could be moved out of the body into the bile, there is a gray area for interpretation.

If lactoferrin is improving health issues that are otherwise tied to iron overload by the data, or it is inducing health issues that are otherwise tied to iron deficiency by the data, then this supports it decreasing iron status.

If it is doing the opposite of either of those, then this supports the more probable situation that it is improving iron bioavailability.

This is an example where the soluble transferrin receptor could come into play, where high levels indicate cells that are hungry for iron, and low levels indicate cells that have enough.

The only iron-saturated lactoferrin I know of on the market is Lattoglobina, produced in Italy, although one to two scoops of whey protein will also provide it.

Details for interpreting health issues and soluble transferrin receptor in the context of other iron markers can be found in Understanding Iron, the Cheat Sheet V3, the Iron Deficiency Protocol, and the Iron Overload Protocol.