

# Certain iron supplements may influence the development of colon cancer

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Nathalie Scheers' research focuses on metals in foods and the intestines, and how these metals and their various forms affect the biology of cells. She is particularly interested in molecular changes, caused by the balance of metals, which can lead to issues such as colon cancer, autoimmune diseases and other inflammatory conditions. To study this, she uses human cell lines and molecular biology methods. Metals play a very important role in cellular processes, and deficiencies or excesses can lead to various health issues. Credit: Yen Strandqvist/Chalmers University of Technology

Two common iron compounds increase the formation of a known biomarker for cancer, according to a new study of cancer cells from Chalmers University of Technology, Sweden. The two compounds, ferric citrate and ferric EDTA, are often used in dietary supplements and as a food additive respectively, in worldwide markets including the U.S. and the EU.

The researchers studied ferric [citrate](#) and ferric EDTA, which have both previously been shown to worsen tumour formation in mice with [colon cancer](#). The science behind this has been little understood until now, and possible effects on human cells were not previously investigated.

The new study, which was in collaboration with the UK Medical Research Council and Cambridge University, looked at the effect of normal supplemental doses of these compounds on two types of cultured human colon [cancer cells](#). As a comparison, they also measured the effects of ferrous sulphate, another very commonly available [iron](#) compound.

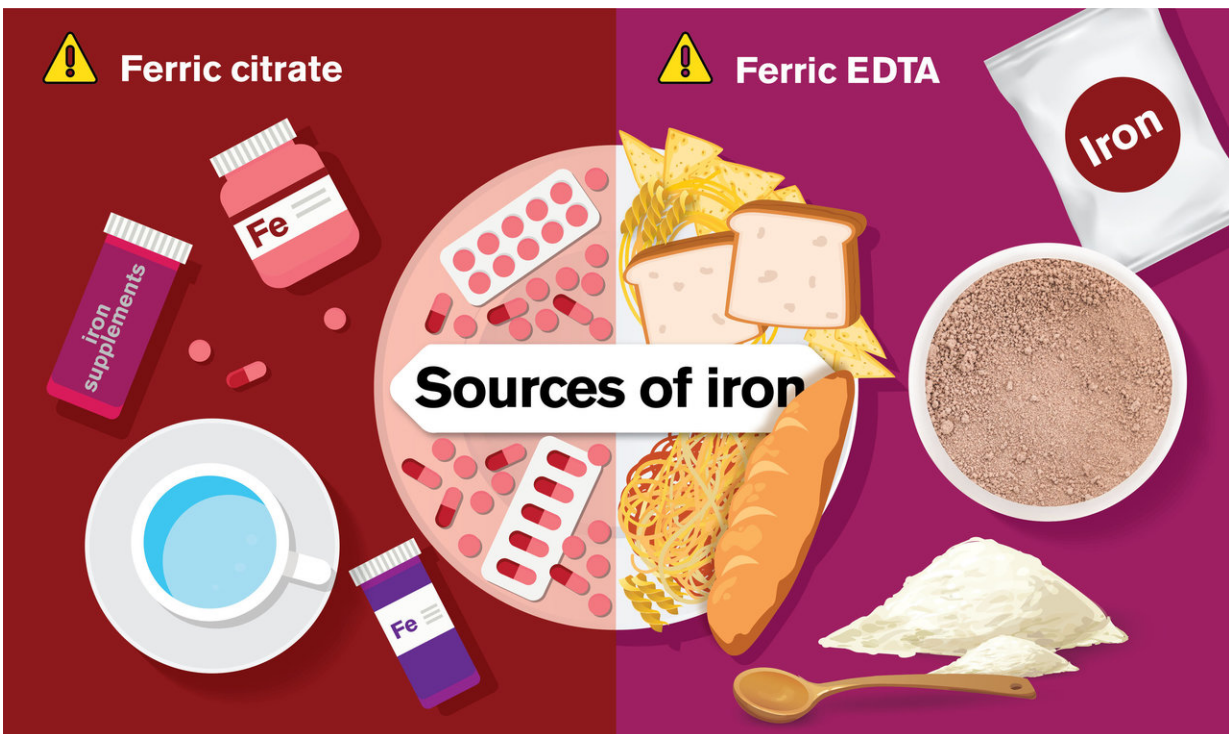
While ferrous sulphate had no effect, both ferric citrate and ferric EDTA caused an increase in cellular levels of amphiregulin, a biomarker for cancer. This was the case even at low doses.

"We can conclude that ferric citrate and ferric EDTA might be carcinogenic, as they both increase the formation of amphiregulin, a known cancer marker most often associated with long-term cancer with poor prognosis," says Nathalie Scheers, assistant professor at Chalmers University of Technology, and lead writer on the study.

Today, there are many types of iron supplements on the market based on at least 20 iron compounds, and sold under a wide range of brands.

Ferric sulphate is one of the most common, but ferric citrate, which is said to be gentler for the stomach, is also widely available. It is also more easily absorbed by the body through foods such as granary bread, beans and nuts.

But for consumers looking to make an informed choice, it can often be difficult to know what exactly they are buying. "Many stores and suppliers don't actually state what kind of iron compound is present—even in pharmacies. Usually, it just says 'iron' or 'iron mineral,' which is problematic for consumers," says Nathalie Scheers.



Ferric citrate and ferric EDTA, are often used in dietary supplements and as a food additive respectively, in worldwide markets including the USA and the EU. Credit: Yen Strandqvist/Chalmers University of Technology

Iron is also added to some foods to combat iron deficiency. Ferric EDTA is approved as a fortifying agent in both the U.S. and the E.U. It is also used in countries such as China, Pakistan, Brazil, Mexico and the Philippines, where it is added to flour and powdered drinks. Additionally, it is present in certain medicines for children with low iron levels in countries such as the UK and France.

With both ferric citrate and ferric EDTA in widespread use, how should consumers or patients relate to these new findings?

"First, we must bear in mind that the study was done on human [cancer](#) cells cultured in the laboratory, since it would be unethical to do it in humans. But the possible mechanisms and effects observed still call for caution. They must be further investigated," says Nathalie Scheers. "At the moment, people should still follow recommended medical advice. As a researcher, I cannot recommend anything—that advice needs to come from the authorities. But speaking personally, if I needed an iron supplement, I would try to avoid ferric citrate," she says.

Beyond this, she is not willing to comment. Research in the field has so far been limited, even concerning the more common ferrous sulphate. The key thing for her is to differentiate between different forms of iron.

"Most importantly, researchers and authorities need to start to distinguish between this form of iron and that form of iron. We need to consider that different forms can have different biological effects," she concludes.

## **Women at greater risk**

Most of the iron that the body needs is obtained through food such as meat, fish, vegetables, fruits and whole grains. But sometimes, this is not enough. Pregnant women may need additional iron, as do people who

have lost blood or have low haemoglobin levels for other reasons. In patients with kidney disease, high doses of iron may be needed to bind phosphates into the bloodstream.

**More information:** Nathalie M. Scheers et al, Ferric citrate and ferric EDTA but not ferrous sulfate drive amphiregulin-mediated activation of the MAP kinase ERK in gut epithelial cancer cells, *Oncotarget* (2018).

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Provided by Chalmers University of Technology

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