

Possible risk of folic acid overexposure

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A new study has shown that synthetic folic acid, the form taken in folic acid supplements we can buy over the counter, is not processed by the body in the same way as natural folates, the form found in green vegetables.

This can lead to unprocessed [folic acid](#) circulating in the blood stream, with unknown potential health effects.

Folic acid in bread

With the Government considering adding folic acid to all bread flour, this new finding from the Institute of Food Research and Newcastle University suggests we need to think about using a different [folate](#) form for the fortification, or better understand the implications of excess folic acid.

Professor David Jones and his team in Newcastle were able to directly sample blood from the hepatic portal vein of patients who had previously been fitted with a stent, or shunt. Volunteers were fed either labelled folic acid or labelled natural folate. The dose of folic acid and natural folate was below that which is currently recommended for supplement use for women who are planning a pregnancy. The hepatic portal vein carries blood from the gut directly to the liver. This blood, and blood from the main circulatory system, was then analysed by the team at the Institute of Food Research, which is strategically funded by the Biotechnology and Biological Sciences Research Council.

"Folic acid fortification has been advised and adopted on the basis that the body treats it in the same way as natural folates we get from vegetables, but now we know that's just not the case," said Paul Finglas from the IFR.

The new study clearly showed that 86% of folic acid in the hepatic portal vein is unmetabolised, whilst almost all of the natural folate was converted correctly.

This contradicts previous findings, which were based on metabolism in rats, but agrees with work done in the late 1960s using much higher doses of labelled folic acid in humans.

Natural folate, which we get from eating green leafy vegetables, is absorbed and metabolised by cells lining the gut. Folic acid is a synthetic version of folate, created in the 1940s to be more stable and cheaper to manufacture, for use in supplements. Women thinking of becoming pregnant are advised to take these supplements, as low folate levels in pregnancy are associated with neural tube defects (NTDs) such as Spina Bifida and Anencephaly. But in the UK, many pregnancies are unplanned. This has led to recommendations that UK flour should be fortified with folic acid, to reduce the 900 neural tube defect births in the UK every year, and the Department of Health are now considering this.

Professor David Jones, Dean of Research & Innovation in the faculty of Medical Sciences at Newcastle University, said: "This work doesn't mean that folic acid is not safe. It suggests, however, that the assumption that it will be automatically safe because the body can handle it is not correct."

Folic fortification

Several countries, including the USA, Canada and Australia have introduced mandatory [folic acid fortification](#). This has led to a reduction in neural tube defects of up to 46%, but has also seen intakes three times higher than the recommended amount, with one study finding three quarters of post-menopausal women had folic acid circulating in their blood stream. A number of studies have flagged potential problems with excess folic acid, including compromising the immune system, masking vitamin B deficiency, and possibly increasing the risk of some forms of cancer. The Scientific Advisory Committee on Nutrition considered these in making its recommendation that UK's flour should be fortified with folic acid, but alongside measures to restrict the maximum exposure. The new findings, published in the *American Journal of Clinical Nutrition*, throw up new questions of how much we would be exposed to unmetabolised folic acid following mandatory fortification.

Because of this, the scientists suggest that fortification can also be done with the natural forms of folate. These are already licensed for use, under the names Metafolin and Quatrefolic. These have been approved for use as a food supplement and are metabolised in the same way as natural folates, and so avoid the problem identified in the present study. If these can be adapted for use in food fortification, they present a way of improving the folate status of the population, reducing the risk from unmetabolised folic acid in the blood and any possible risks to health.

More information: Imran Patanwala, Maria J King, David A Barrett, John Rose, Ralph Jackson, Mark Hudson, Mark Philo, Jack R Dainty, Anthony JA Wright, Paul M Finglas, and David E Jones. "Folic acid handling by the human gut: implications for food fortification and supplementation." *Am J Clin Nutr* 2014 100: 2 593-599; First published online June 18, 2014. [DOI: 10.3945/ajcn.113.080507](https://doi.org/10.3945/ajcn.113.080507)

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