

Folate: Essential and Beneficial, but is it Safe?

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Editorial

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Editorial

Folate or vitamin B9 covers a large group of water-soluble compounds with similar vitamin activity. They play a key role in one carbon metabolic reactions that are involved in DNA synthesis and repair, methylation of DNA, cell proliferation, and amino acid synthesis [1]. Folate deficiency is associated with impairments in reproductive health and fetal development, most notably by an increased prevalence in neural tube defects [2]. As a preventative strategy, folic acid (pteroyl glutamic acid), the oxidized form of the naturally occurring folate (reduced polyglutamate compounds), is fortified in foods in over 50 countries to prevent such birth defects [3,4].

The association between excess folic acid and folate-sensitive cancers, such as colorectal cancer [5], has raised concerns regarding its safety with the need to find ways to minimize these risks to the public. Fortunately, a systematic review and meta-analysis of folate status and colorectal cancer risk just published by Moazzen et al. [6], found no significant effect of folic acid on colorectal cancer risk. The role of folic acid intake and folate status in the risk of colorectal cancer risk or adenoma was assessed in a meta-analysis of randomized control trials, cohort and control studies. They claimed that this was the first systematic review and meta-analysis that included all types of controlled studies that pointed to the root of discrepancies.

In conclusion, they suggested that differences between the bioavailability and metabolism of synthetic folic acid and dietary folate plus variation in baseline characteristics between subjects and the different methods of assessing folate status may be responsible for the controversies.

Besides its nutritional role, there is a growing body of evidence associating folate deficiency with depression [7,8]. Folate is metabolized into S-adenosylmethionine (SAMe) and both are involved in the production of dopamine, norepinephrine and serotonin, all neurotransmitters implicated in depression. These neurotransmitters affect the production of tertrahydrobiopterin, an antioxidant and cofactor in the synthesis of these neurotransmitters [9,10].

A deficiency in folate produces low levels of these neurotransmitters resulting in a neurochemical predisposition for depression. A metaanalysis by Bender et al. [11] found that individuals suffering from depression had low serum folate levels as well as a low dietary intake. Previous literature suggested folate supplementation enhanced the efficacy of traditional antidepressant medications suggesting it as a possible treatment for individuals suffering from depression.

Nutritional deficiencies are a common occurrence in people suffering alcohol use disorder (AUD) [12]. Folate deficiency, in AUD for example is not only the result of an inadequate diet, but has also been associated with diseases that increase the requirements for folate such as malabsortive conditions, impaired hepatic uptake, increased renal excretion as well as some drugs [13,14].

Sanvisens and co-workers [15] characterized serum and erythrocyte folate deficiency in patients admitted for detoxification between 2007 and 2015 in an Addiction Hospital Unit in Barcelona, Spain. One in four patients had low serum levels of folate while one in ten lacked appropriate tissue deposits, with the potential for megaloblastic anemia. The relative frequency of folate deficiency in patients suffering alcohol use disorder points to the potential role of folate in treating these patients.

The importance of folate in human nutrition is well documented with folic acid now shown to be safe. Its use in treating other disorders, including depression and alcohol use disorder (AUD), points to the potential of folate as a therapeutic agent.

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