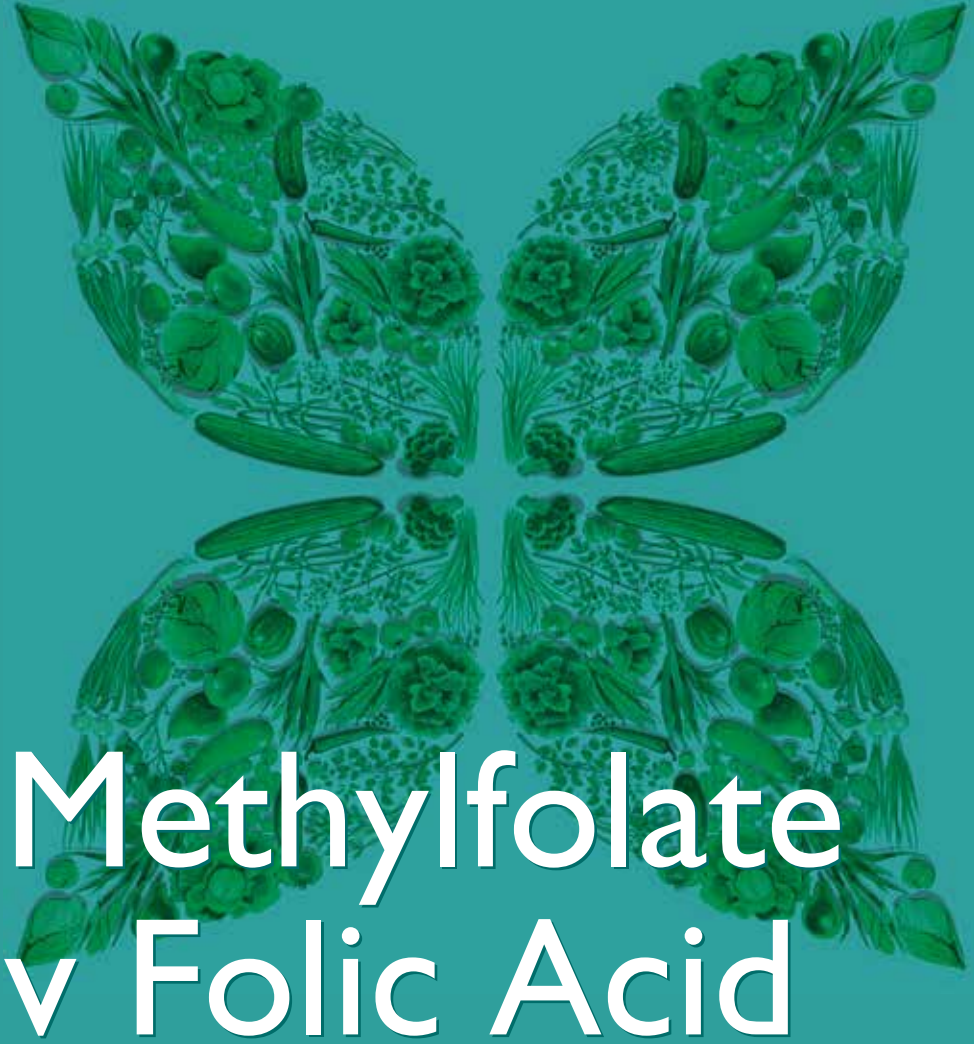




CYTOPLAN

# THE TECHNICAL INFORMATION SERIES



# Methylfolate v Folic Acid

The superior benefits of Methylfolate

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## Folic Acid as Methylfolate (5-MTHF)

Methylfolate is emerging as a new and exciting food supplement for anyone who needs to supplement with folate (folic acid). Methylfolate (also known as 5-MTHF and L-methylfolate) is the most stable, safe and bioeffective form of folate.<sup>1,2</sup> An adequate intake of folate is essential for the prevention of many disorders. Adequate folate levels are of particular importance for pregnant women and women planning pregnancy. The following are permitted health claims for folate/folic acid as approved by EFSA (The European Food Safety Authority). Folic acid contributes to:

- normal amino acid synthesis
- normal blood formation
- normal homocysteine metabolism
- normal psychological function
- normal function of the immune system
- the reduction of tiredness and fatigue
- the process of cell division
- maternal tissue growth during pregnancy;
- and increases maternal folate status. Low maternal folate status is a risk factor in the development of neural tube defects in the developing foetus\*

\*This claim may be used only for food supplements which provide at least 400 µg of folic acid per daily dose. The beneficial effect is obtained with a supplemental folic acid daily intake of 400 µg for at least one month before and up to three months after conception.

## Folate and Deficiencies

Folate is derived from the term 'foliage' which indicates where this vitamin is found. Some of the best natural sources of folates are green leafy vegetables such as broccoli, spinach and sprouts. It is also found in oranges, rice, brewer's yeast and liver.

Food is the major source of folates. However, in a large percentage of the population, folate intake from food is insufficient for good health both due to the fact that insufficient quantities of folate rich foods are eaten and food preparation and cooking result in folate being lost. Other factors which can increase folate needs are excessive alcohol and some medications eg aspirin, antacids and others. Certain diseases can affect folate absorption and these include Coeliac disease and Crohn's disease.

## Methylfolate (5-MTHF)

Folate from food and folic acid from supplements is inactive and has to be converted to the active form 5-MTHF (5-methyltetrahydrofolate or L-methylfolate). This pathway involves a number of steps and genetic polymorphisms (mutations) can reduce the efficiency of this pathway. The final step uses the enzyme methylenetetrahydrofolate reductase (MTHFR). Genetic single nucleotide polymorphisms (SNPs) mean the MTHFR enzyme has reduced function in around 48% of the population! Thus, carriers of an MTHFR SNP may not effectively convert folic acid to the active 5-methyltetrahydrofolate form.

As well as meaning there is insufficient active folate for methylation reactions, inefficiencies in conversion of folic acid can also lead to high levels of un-metabolised folic acid which has been linked with certain cancers (no causal effect has been established, but an association has been seen).

## Folate and Pregnancy

Folate (folic acid) is of particular importance for pregnant women and women planning pregnancy. Folate contributes to 'normal maternal tissue growth during pregnancy' and 'increases maternal folate status. Low maternal folate status is a risk factor in the development of neural tube defects in the developing foetus'. The UK Department of Health has stated:

"Women who are planning a pregnancy or might become pregnant, or who are already pregnant, should also take folic acid and vitamin D supplements."

As methylfolate is the most natural, stable, safe and bioeffective form of folate (folic acid) it is ideal as a supplement for pregnant women and women planning pregnancy; particularly in accordance with the recommendations of the UK Department of Health.<sup>3,4,5</sup>

Many experts would recommend that breastfeeding mothers continue with good levels of folate for some time after birth as nutritional needs of both mother and baby are high.

## Methylfolate and Homocysteine

Low levels of active methylfolate can lead to raised homocysteine levels. Folic acid has the permitted EFSA health claim “folic acid contributes to normal homocysteine metabolism”.

Methylfolate provides the methyl group for the re-methylation of homocysteine to methionine in the methylation (or methionine) cycle. The purpose of this cycle is to generate S-adenosyl methionine (SAM) the universal methyl donor and homocysteine is regenerated to methionine in the process. As homocysteine is such an inflammatory radical, if elevated levels are unresolved this will start a cascade of inflammatory responses in an individual. Homocysteine is now known to be an independent risk factor for heart disease and Alzheimer’s disease. Homocysteine levels can be increased when insufficient levels of ‘methyl group’ foods are consumed.<sup>9,10</sup> Or where genetic mutations (eg MTHFR) mean that insufficient folate (from food or folic acid supplements) is converted to the active form.



## Methylfolate and Psychological Function

Folate has the permitted health claim of 'contributing to normal psychological function' and another important aspect of methylfolate is that it is able to cross the blood-brain barrier, unlike folic acid.<sup>11,12</sup>

This is especially important for people with cognitive difficulties as methylfolate can enhance the synthesis of acetylcholine in the brain. Acetylcholine is found in the central and peripheral nervous systems and is the neurotransmitter associated with memory.



Order code 3319

## Bibliography

A David Smith Folic acid fortification: the good, the bad, and the puzzle of vitamin B-12. 2007 Am J Clin Nutr January vol. 85 no. 1 3-5

<http://www.nutraingredients.com/Industry/Merck-s-Metafolin-receives-EU-approval>

Amy Scheuerman, 2012. Too Much of a Good Thing? Folic acid in supplements and fortified foods might exacerbate vitamin B12 deficiency, which has been linked to cognitive decline in older adults. February 3rd 2012

<http://now.tufts.edu/articles/folic-acid-too-much-good-thing>

Mason JB, Dickstein A, Jacques PF, Haggarty P, Selhub J, Dallal G, Rosenberg IH. 2007 A temporal association between folic acid fortification and an increase in colorectal cancer rates may be illuminating important biological principles: a hypothesis. Cancer Epidemiol Biomarkers Prev. Jul;16(7):1325-9.

Todd M Gibson, Stephanie J Weinstein, Ruth M Pfeiffer, Albert R Hollenbeck, Amy F Subar, Arthur Schatzkin, Susan T Mayne, and Rachael Stolzenberg-Solomon. 2011 Pre- and post-fortification intake of folate and risk of colorectal cancer in a large prospective cohort study in the United States. Am J Clin Nutr October vol. 94 no. 4 1053-1062

Luai Z. Hasoun, Steven W. Bailey, Kitti K. Outlaw, June E. Ayling. 2013. Folate in human skin: its correlation with serum levels, and the unusual abundance in the epidermis of 5-methyltetrahydrofolate. The FASEB Journal. 2013;27:1077.2



## References

- 1** Pietrzik K, Bailey L, Shane B. 2010 Folic acid and L-5-methyltetrahydrofolate: comparison of clinical pharmacokinetics and pharmacodynamics. *Clinical Pharmacokinet.* Aug;49(8):535-48  
doi: 10.2165/11532990-000000000-00000
- 2** Francesco Scaglione and Giscardo Panzavolta. 2013 Folate, folic acid and 5-methyltetrahydrofolate are not the same thing.  
<http://informahealthcare.com/doi/abs/10.3109/00498254.2013.845705>
- 3** James A Greenberg, MD and Stacey J Bell, DSc, RD 2011 Multivitamin Supplementation During Pregnancy: Emphasis on Folic Acid and L-Methylfolate . *Reviews Obstetrics Gynecology* 4 (3-4):126-127
- 4** James A Greenberg, MD, Stacey J Bell, DSc, RD, Yan-hong Yu, MD, PhD. 2011 Folic Acid Supplementation and Pregnancy: More Than Just Neural Tube Defect Prevention *Reviews Obstetrics Gynecology* 4 (2):52-59
- 5** Seremak-Mrozikiewicz A Klinika Perinatologii i Chorób Kobietych, Uniwersytet Medyczny w Poznaniu, Polska. 2013. Metafolin--alternative for folate deficiency supplementation in pregnant women. *Ginekologia Polska* [2013, 84(7):641-646]  
<http://europepmc.org/abstract/MED/24032278>
- 6** Obeid R, Holzgreve W, Pietrzik K. 2013 Is 5-methyltetrahydrofolate an alternative to folic acid for the prevention of neural tube defects? *J Perinat Med.* Sep 1;41(5):469-83. doi: 10.1515/jpm-2012-0256
- 7** Czeizel A.E. Dudás I. Paput L. Bánhidly F. 2011 Prevention of Neural-Tube Defects with Periconceptional Folic Acid, Methylfolate, or Multivitamins? *Ann Nutr Metab* ;58:263–271 (DOI:10.1159/000330776)
- 8** Scientific Opinion on the substantiation of a health claim related to increasing maternal folate status by supplemental folate intake and reduced risk of neural tube defects pursuant to Article 14 of Regulation (EC) No 1924/2006 *EFSA Journal* 2013;11(7):3328 [9 pp.].  
doi:10.2903/j.efsa.2013.3328 Adopted: 10 July 2013 Published: 26 July 2013
- 9** Stam F, Smulders YM, van Guldener C, Jakobs C, Stehouwer CD, de Meer K. 2005 Folic acid treatment increases homocysteine remethylation and methionine transmethylation in healthy subjects. *Clin Sci (Lond).* May;108(5):449-56
- 10** Henk J. Blom & Yvo Smulders. 2011 Overview of homocysteine and folate metabolism. With special references to cardiovascular disease and neural tube defects. *J Inherit Metab Dis* 34:75–81 DOI 10.1007/s10545-010-9177-4

## References

continued

- 11** George I. Papakostas, M.D.; Richard C. Shelton, M.D.; John M. Zajecka, M.D.; Bijan Etemad, M.D.; Karl Rickels, M.D.; Alisabet Clain, M.S.; Lee Baer, Ph.D.; Elizabeth D. Dalton, B.A.; Garret R. Sacco, B.A.; David Schoenfeld, Ph.D.; Michael Pencina, Ph.D.; Allison Meisner, M.A.; Teodoro Bottiglieri, Ph.D.; Erik Nelson, M.D.; David Mischoulon, M.D., Ph.D.; Jonathan E. Alpert, M.D., Ph.D.; James G. Barbee, M.D.; Sidney Zisook, M.D.; Maurizio Fava, M.D. 2012 L-Methylfolate as Adjunctive Therapy for SSRI-Resistant Major Depression: Results of Two Randomized, Double-Blind, Parallel-Sequential Trials. *Am J Psychiatry* 169:1267- 1274. doi:10.1176/appi.ajp.2012.11071114
- 12** Rolin L. Wade, RPh, MS; Sylvia L. Kindermann, MPH; Qingjiang Hou, MS; and Michael E. Thase, MD 2014 Comparative Assessment of Adherence Measures and Resource Use in SSRI/SNRI-Treated Patients with Depression Using Second-Generation Antipsychotics or L-Methylfolate as Adjunctive Therapy. *J Manag Care Pharm.* 20(1):76-85



Cytoplan celebrates 25 years in the field of food-based supplementation and from the moment of conception to the present day we have promoted the philosophy that nutrients are best delivered to the body "in the same form as food".

The philosophy and message of Cytoplan was founded on the simple logic that our bodies are designed to eat food and utilise its components for the maintenance of life. The ultimate goal of Cytoplan is to 'improve the health of the nation' by supplying supplements in a bio-effective form for optimal absorption and utilisation.



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