



## Importance of folate for pregnant women and babies

**F**olate is indispensable for the healthy development of a child. It is undisputed that women who wish to get pregnant or who are already pregnant should ingest sufficient amounts of folate. Scientific studies show that an adequate folate supply can reduce the occurrence of neural tube defects. The efficacy and safety of directly available 5-methyltetrahydrofolate (5-MTHF; in the form of Metafolin®) is well documented in these cases.

But even after birth, a good folate supply is highly important for a baby. With breast milk, the infant receives 5-MTHF, the metabolically active form of folate, which can be used immediately. The logical next step is to also add a folate source to formulae that resembles that in breast milk. Fortifying formula with Metafolin® is a natural and safe way to provide every baby with easily digestible folate.

### Folate compounds – indispensable for mother and baby

Both folic acid and folate are water-soluble vitamins and are also called vitamin B9. They are involved in the synthesis of purine and pyrimidine and thus in RNA and DNA synthesis. In the body, they play a crucial role in cellular differentiation, regeneration and formation, and are therefore indispensable for growth, blood formation and brain development.<sup>3,4</sup>

For this reason, an adequate folate supply is not only essential for women before and during pregnancy, but also for infants and young children to aid in their growth and development.<sup>2,3</sup>

Folic acid and folate differ in origin and the way they are metabolised. This is taken into account in the calculation of the D-A-CH reference

values for the recommended daily intake as well as in the EU regulation for infant formulae and follow-on formulae (EU Regulation 2016/127) and further specified under the term “folate equivalent”.<sup>4</sup>

### Folic acid – the synthetic form

Folic acid does not occur naturally. It is a synthetic compound that has no vitamin function in this form. Folic acid must be converted by the body in several steps into its bioactive form 5-methyltetrahydrofolate (5-MTHF) before its effect can unfold (see figure). Several enzymes are involved in the conversion, including dihydrofolate reductase (DHFR) and methyltetrahydrofolate reductase (MTHFR).

Some people cannot convert sufficient amounts of the synthetic form of this B vitamin into its metabolically active form. The reason for this is a restricted or limited activity of individual enzymes. If this

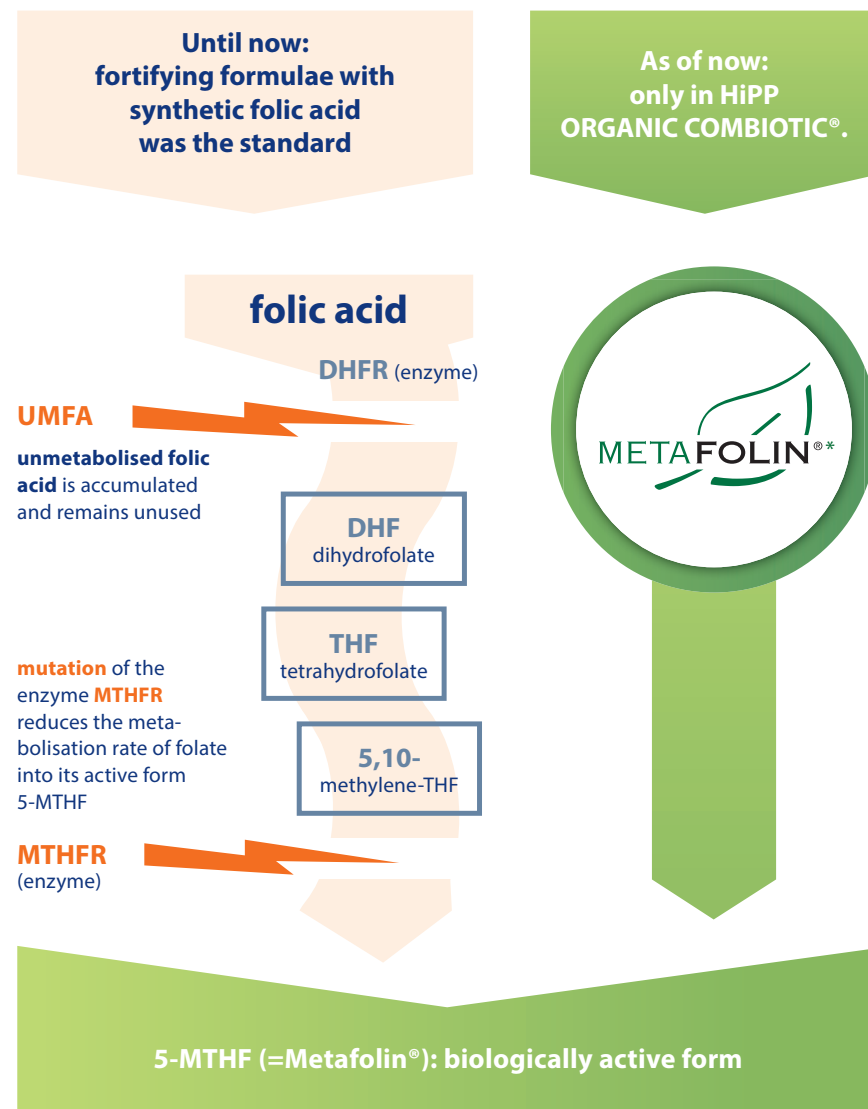


Fig. 1

**Our goal: to fully understand nature's example – breast milk**

- ✓ more than 10 years of intensive research by HiPP's Research Group on Human Milk
- ✓ in cooperation with specialists from around the world

is the case for the DHFR enzyme, the amount of unmetabolised folic acid, useless for the body, increases.<sup>11</sup> Furthermore, a genetic mutation of the enzyme MTHFR can lead to a reduction in enzyme activity of up to approximately 60%.<sup>5</sup> In cases of enzyme polymorphism, the conversion rate of folic acid into its active form is also much lower. These correlations help explain why folate levels can be too low despite an adequate folic acid intake.

**Natural folate – advantages with respect to usability**

Folate is the umbrella term for all naturally occurring compounds having the same effects of this B vitamin. 5-MTHF is the predominant form of naturally occurring folate in the blood.<sup>12</sup> Unlike folic acid, it does not need to be converted or activated and exerts its effects immediately. The main storage organ for this compound is the liver.<sup>3</sup> Breast milk also contains the metabolically active folate form 5-MTHF.<sup>14</sup>

**Studies have shown that the administration of 5-MTHF does not lead to an accumulation of unmetabolised folic acid in the serum and the possible presence of enzyme polymorphism is also of no relevance.<sup>1</sup> This means that the bioactive folate form 5-MTHF has been shown to be superior in use to synthetic folic acid.<sup>11, 13</sup>**

**Effect of folate for pregnant women well documented**

Current research shows that a low folate level in pregnant women is associated with an increased risk of several birth defects, i.e. neural tube defects (spina bifida, anencephaly

and encephalocele). It can also cause congenital anomalies of the heart, lips or palate as well as miscarriages, premature births and low birth weight.<sup>10, 16</sup>

Clinical studies demonstrate the efficacy of periconceptional folate supplementation in reducing the risk of neural tube defects.<sup>9</sup> Based on strong data, professional societies recommend a folate-rich diet and the supplementary intake of 400 µg folate per day via food supplements at the latest four weeks before conception and until the end of the first trimester.<sup>7</sup>

**Metafolin® – the better choice also for formulae**

Metafolin®, as a calcium compound of the body's own metabolically active 5-MTHF, has been used for several years as a food supplement to improve the folate levels in women who wish to have children and in pregnant women. Studies on this topic demonstrate the safety and efficacy of Metafolin® to improve folate levels.<sup>8</sup> Metafolin® ensures a faster and more even replenishment of folate stores without the accumulation of unmetabolised folic acid.<sup>8</sup> The intake of Metafolin® also leads to higher folate levels in breastfeeding women as compared to supplementation with folic acid.<sup>6</sup> Timely supplementation with this natural form of folate therefore provides optimal protection for the health of both mother and child.

Furthermore, studies show that exclusively breastfed infants receiving 5-MTHF through breast milk have low serum concentrations of unmetabolised folic acid.<sup>6</sup> Consequently, it seems prudent to add a folate form to formulae that is inspired

by nature and thus directly available. Metafolin® is a safe way to adequately provide infants with folate.

**COMBIOTIC® with Metafolin® – one step closer to nature's example**

Up to now, synthetic folic acid has been prescribed by law as the standard for formulae. To get a little closer to nature's example, HiPP has added another piece of the puzzle to its tried-and-tested COMBIOTIC® formulae: Metafolin® – a natural and directly available folate source. This calcium salt of 5-MTHF has received a positive evaluation from the European Food Safety Authority (EFSA) for use in formulae and has recently also been included in the respective legal regulations.<sup>15</sup>

A controlled study has been carried out to determine the safety of Metafolin® fortified formula. The results show that children who received this bioactive folate form showed adequate growth and

development. The folate levels in these infants (intervention group) were comparable to that of the control group.<sup>14</sup> The formula with Metafolin® was well accepted and also very well tolerated. Stool characteristics in those two groups, i.e. consistency, colour and smell, were also comparable. This means that every baby can benefit from a formula that already contains the bioactive folate form as it guarantees an adequate supply of this vitamin.

**Information:**

Legal regulations stipulate the addition of fixed amounts of folic acid to formulae. According to the current regulation for infant formulae and follow-on formulae, 15 µg folate equivalents per 100 kcal have to be added.<sup>15</sup> This 2020 amendment replaces the requirement from the previous EU Regulation of 10 µg of folic acid per 100 kcal.



\*Metafolin® is a registered trademark of Merck KGaA, Darmstadt, Germany.

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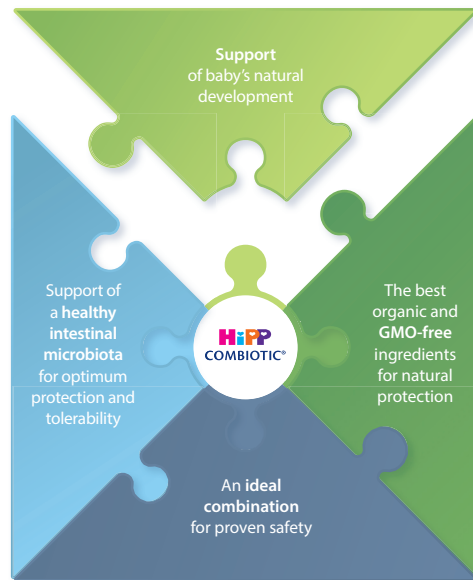


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For more information on Metafolin®, scan:



**HiPP ORGANIC COMBIOTIC® is the only formula with Metafolin®.**

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**Important notice:** Breastfeeding is best for babies. Infant formula should only be given upon the advice of paediatricians or other independent experts.

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