

Safety is our most important ingredient

HiPP ORGANIC COMBIOTIC®
Rounded off with Metafolin®



Science and nature
hand in hand

Information for healthcare professionals



Safety through research, innovation and experience

Our milestones in developing our formulae:

- **2002:** pioneering use of **probiotic lactic acid cultures** originally obtained from human milk**
- **since 2011:** development of **HiPP ORGANIC COMBIOTIC®** — with a unique combination of *Limosilactobacillus fermentum* and GOS
- **2021:** Only from HiPP — **HiPP ORGANIC COMBIOTIC®** — rounded off with **Metafolin®**



UNIQUE

a unique composition of pro- and prebiotics inspired by nature



TRIED-AND-TESTED

a concept to support intestinal microbiota, tried-and-tested for 10 years



ROUNDED OFF

with a bioactive folate form that is also found in human milk



Research Group
on Human Milk

HiPP Research Group on Human Milk: understanding nature's example.

- Running for over 15 years
- In partnership with specialists from around the world
- 2007: pre- and probiotics identified as key factors influencing intestinal health

For more information, including reports from the research group, visit hcp.hipp.com

Section: Studies

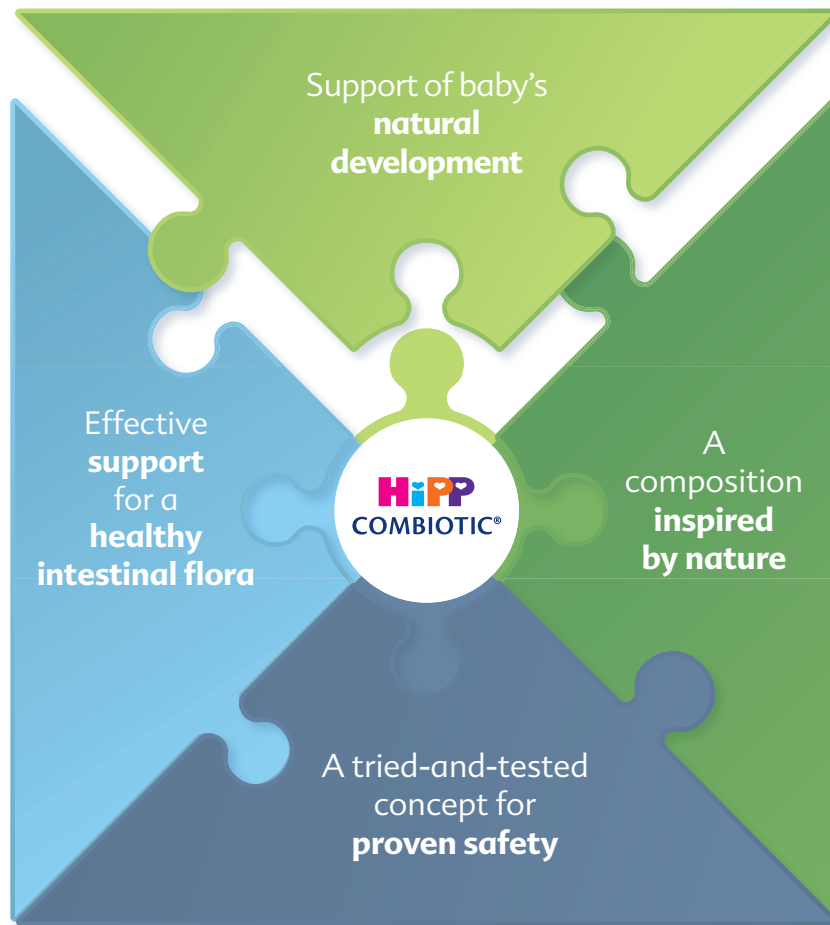


* Metafolin® is a registered trademark of Merck KGaA, Darmstadt, Germany.

** Human milk contains a large number of natural lactic acid cultures that can vary from mother to mother.

A safe and proven composition

HiPP ORGANIC COMBIOTIC®
Science and nature hand in hand



Support of baby's
natural
development

HiPP
COMBIOTIC®



The safe next step in our human milk research

Folate: crucial for cell division and tissue growth¹ ...



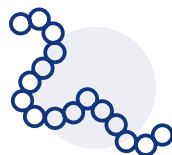
DNA synthesis



Cell division



Blood formation



Protein synthesis

... and therefore indispensable, especially in the early stages of development!



While trying to get pregnant and during pregnancy

Ideal folate form: 5-MTHF

- it does not need to be metabolised
- it is immediately available to the body



While breastfeeding

Birth

Preventing neural tube defects:
5-MTHF supplementation

Ideal infant development:
5-MTHF in human milk

HiPP ORGANIC COMBIOTIC® with Metafolin®

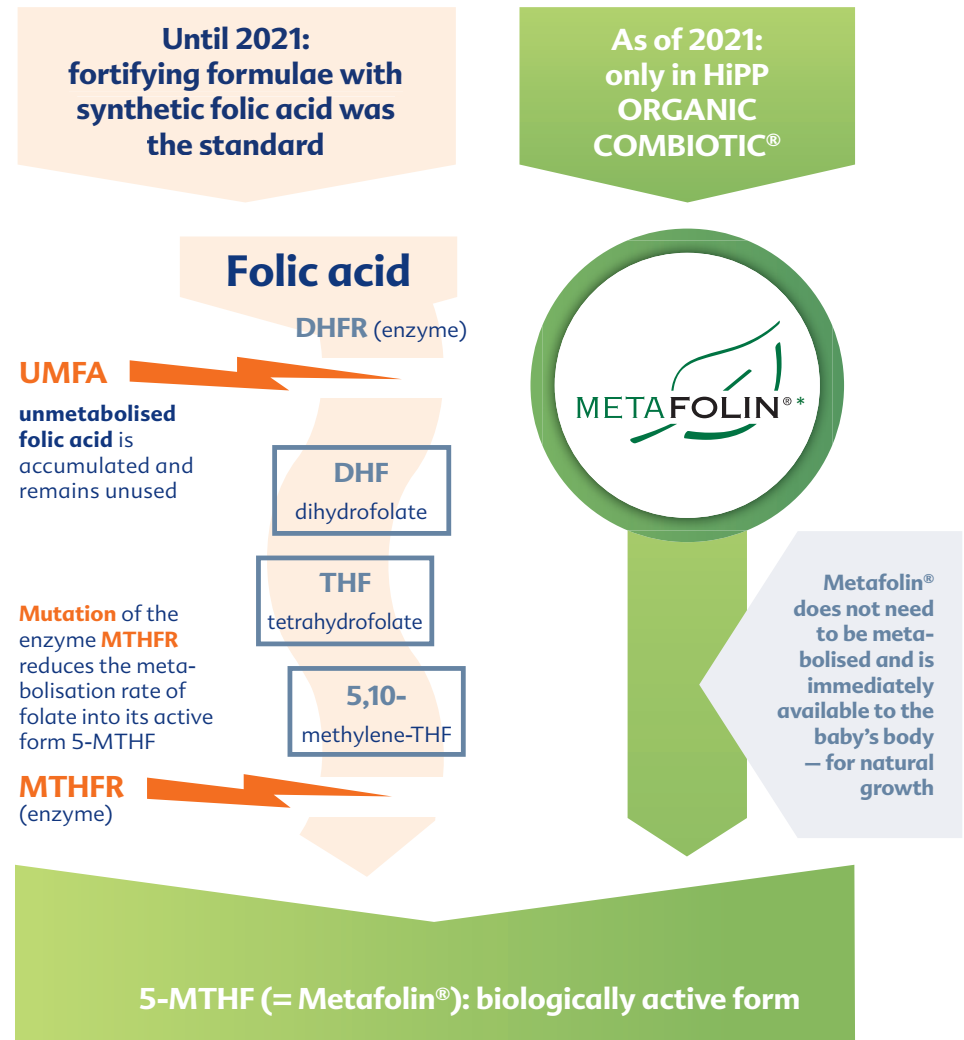
Natural folate form (5-MTHF) as found in human milk: immediately available and safe.

Safety is the top priority at HiPP: Metafolin® is safe for use in formula²!

For our HiPP ORGANIC COMBIOTIC® we use the most advanced folate form – Metafolin®:

- ✓ a calcium salt of 5-MTHF
- ✓ it is a bioactive form of folate
- ✓ it corresponds to the main folate form in human milk, making it ideally suitable for use in formula³

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For more information on Metafolin®, scan:



The safe choice for a healthy intestinal microbiota

Building up the intestinal microbiota from day one is vital, as over 80% of immunocompetent cells are located in the intestine.

A well-developed intestinal microbiota provides optimum protection:

- promotes the development of the immune system^{4,5}
- protects against intestinal infections⁴

What influences the intestinal microbiota?

- type of birth (vaginal or caesarean section)
- whether the child is breastfed or bottle-fed
- composition of formula (standard, prebiotic, probiotic or synbiotic)

As a natural, synbiotic substance, human milk provides your child with everything they need for an ideal composition of their intestinal microbiota.

Caesarean-born infants had an intestinal microbiota that more closely resembled the maternal skin microbiota rather than the maternal vaginal flora.⁶



A safe and effective composition

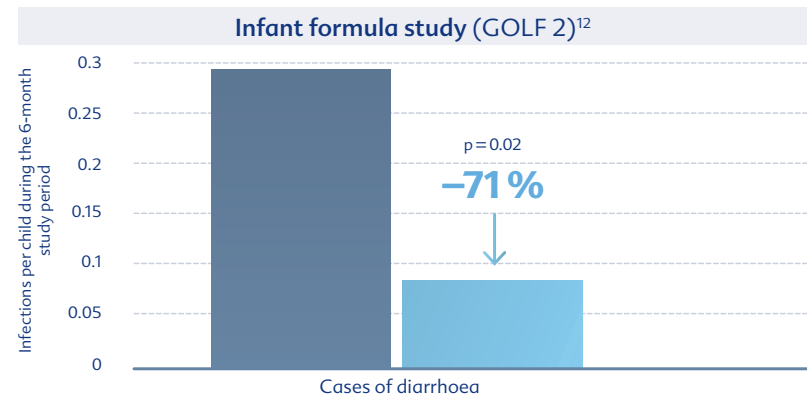
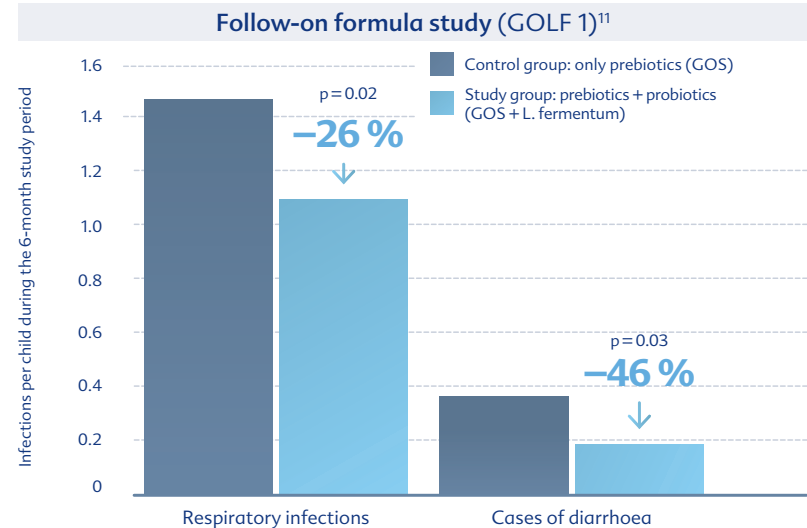
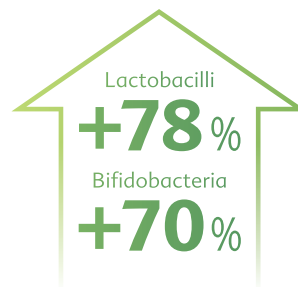
HiPP ORGANIC COMBIOTIC®

with its synbiotic composition of pre- and probiotics – galacto-oligosaccharides (GOS) and *Limosilactobacillus fermentum* – promotes a healthy intestinal microbiota and increases tolerability.



The prebiotic GOS supports the developing digestive system and leads to:⁷⁻¹⁰

- less colic
- increased stool frequency
- softer stool consistency and a stool colour similar to that of breastfed children



Clinical studies prove that the synbiotic combination of prebiotics and probiotics in HiPP ORGANIC COMBIOTIC®:

- ✓ increases the number of beneficial bacteria in the intestine¹¹
- ✓ significantly reduces gastrointestinal infections^{11, 12}
- ✓ is significantly better than only using prebiotics (GOS)^{11, 12}

Definitely the ideal combination

Natural probiotic

- Limosilactobacillus fermentum hereditum® CECT5716
- unmodified natural lactic acid culture from human milk^{13–15}
- a primary coloniser of the intestine¹⁶
- supports a healthy intestinal flora²⁹
- contributes to a modulation of immune response^{18, 19}

Probiotics

Proven prebiotic: GOS

- galacto-oligosaccharides obtained from organic lactose
- stool consistency and frequency similar to breastfed children^{7–10, 17}
- promotes the growth of beneficial intestinal bacteria^{7–9, 17}
- proven to be safe²⁰

Prebiotics



Metafolin® — a bioactive folate form for natural development

Appropriately low protein content

- < 2.0 g/100 kcal, tailored to physiological needs²¹
- obtained from high-quality organic milk and organic whey

Protein

HiPP ORGANIC COMBIOTIC® supplies all the key, high-quality macro- and micronutrients in the appropriate quantities.

Fatty acid spectrum inspired by nature

valuable fatty acids

Important palmitic acid

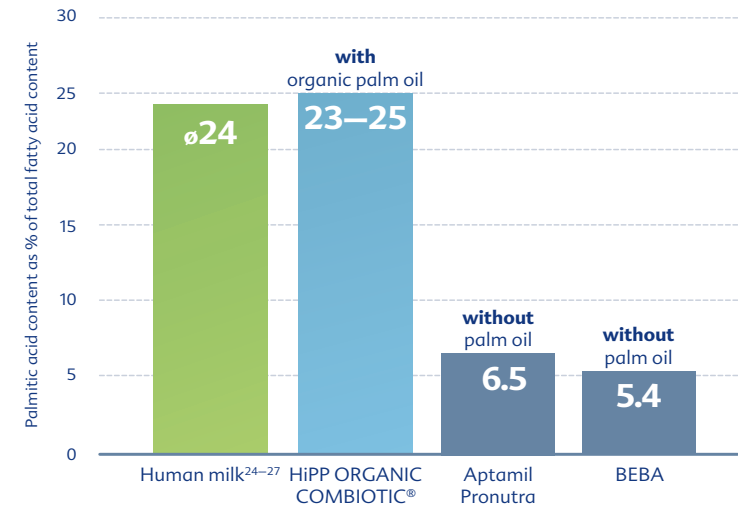
- the predominant saturated fatty acid in human milk
- important for good tolerability of formula²²
 - ▶ less watery and more yellowy stools (similar to those of breastfed children)

Omega-3 and omega-6 LCPs

- evidence-based and recommended²³
- important for brain and nerve tissue development, as well as visual development
- optimum ratio of omega-3 and omega-6 LCPs (DHA and ARA)

Our unique mixture of fats in HiPP ORGANIC COMBIOTIC® is made from sustainable and organic sunflower, palm and rapeseed oil in order to produce a fatty acid spectrum close to that of human milk.

C16:0 palmitic acid content in various infant formulae



Analyses of powdered Pre formulae conducted by independent laboratories.
Information as of February 2022.

Why use palm oil in formulae?

- ✓ Palm oil is the best source of palmitic acid.
- ✓ The aim is to achieve a palmitic acid content similar to that of human milk.
- ✓ ESPGHAN* confirms that palm oil is suitable for use in formulae.²⁸

* ESPGHAN – European Society für Pediatric Gastroenterology, Hepatology and Nutrition

Babies' safety and wellbeing come first

Multiple studies over a number of years prove that HiPP ORGANIC COMBIOTIC® represents the highest quality:

- long-term studies demonstrate that the combination of GOS + L. fermentum is safe²⁹
- proven tolerability of the combination of GOS + L. fermentum
- with Metafolin® – a bioactive folate source that is inspired by nature

PROVEN BENEFICIAL EFFECT		STUDY
Natural probiotic L. fermentum	can colonise the human intestine	Severin AL et al. 2004 ³⁰ ; Martín R et al. 2005 ¹⁴ ; Olivares M et al. 2007 ¹⁸
	strengthens the integrity of the intestinal mucosa	Peran L et al. 2006 ³¹ ; Olivares M et al. 2006 ³²
	protects against intestinal infections	Olivares M et al. 2006 ³²
	contributes to modulation of immune response	Olivares M et al. 2007 ¹⁸ ; Perez-Cano FJ et al. 2010 ¹⁹
Proven prebiotic GOS	promotes the growth of Bifidobacteria and Lactobacilli (bifidogenic effect)	Ben XM et al. 2004 ⁷ und 2008 ¹⁷ ; Fanaro S et al. 2009 ⁸ ; Sierra C et al. 2015 ⁹
	helps produce stool consistency and frequency similar to breastfed children	Sierra C et al. 2015 ⁹ ; Fanaro S et al. 2009 ⁸ ; Ben XM et al. 2004 ⁷ und 2008 ¹⁷ ; Ashley C et al. 2012 ¹⁰
	helps reduce the stool pH value	Sierra C et al. 2015 ⁹
	has a beneficial effect in preventing infant colic	Giovannini M et al. 2014 ³³
Proven prebiotic GOS	Natural probiotic L. fermentum	positively influences the microbiota by promoting the growth of Lactobacilli and Bifidobacteria
		helps reduce the frequency of infections compared to prebiotic (GOS) alone (diarrhoea and/or respiratory problems)
Bioactive folate form Metafolin®		Metafolin® is safe for use in formulae. Compared to formulae with synthetic folic acid, infants with Metafolin® develop equally well.

i For more information, see our scientific dossier or visit hcp.hipp.com

A safe and ideal composition



Appropriately
low protein
content

< 2.0 g/100 kcal, tailored to physiological needs²¹

Proven prebiotics:
GOS from organic
lactose

Safety assessment by FDA (GRAS)²⁰
(Food and Drug Administration: GRAS status)

Natural probiotic
L. fermentum

Safety assessment by EFSA (QPS)³⁴
and FDA (GRAS)³⁵
(EFSA: European Food Safety Authority,
QPS: Qualified Presumption of Safety)

Omega-3 and
omega-6 LCP
fatty acids

Docosahexaenoic acid (DHA) and
arachidonic acid (ARA) as per current
scientific recommendations²³

Metafolin® for
natural
development

Safety confirmed by clinical study²
and EFSA/EU.³⁶

A tried-and-tested
concept for
proven safety

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Important information

Breastfeeding is best for a baby. A balanced diet during pregnancy and after birth promotes lactation. Women who do not wish to breastfeed should be informed that it is difficult to reverse that decision. It is important for women to know that the complementary feeding of formula could compromise their breastfeeding success.

Infant formulae should only be given upon the advice of independent experts. Advise parents on how to prepare the formula and note the important information and instructions on the packaging. Incorrect preparation of formula can be harmful to babies' health.

References:

- ¹ Bailey LB et al. J Nutr. 2015; 145: 1636–1680.
- ² Troesch B et al. PLoS ONE 2019 14(8): e0216790.
- ³ Page R. et al. Am J Clin Nutr. 2017 May; 105(5): 1101–1109.
- ⁴ Houghteling PD et al. J PGN 2015; 60(3): 294–307.
- ⁵ Gensollen T et al. Science 2016; 352(6285): 539–544.
- ⁶ Dominguez-Bello MG et al. PNAS 2010 107 (26) 11971–11975.
- ⁷ Ben XM et al. Chinese Medical Journal 2004; 117(6): 927–931.
- ⁸ Fanaro S et al. J Pediatr Gastroenterol Nutr. 2009; 48: 82–88.
- ⁹ Sierra C et al. Eur J Nutr 2015; 54(1): 89–99.
- ¹⁰ Ashley C et al. 2012 Nutrition Journal 2012; 11: 38.
- ¹¹ Maldonado J et al. J Pediatr Gastroenterol Nutr 2012; 54(1): 55–61.
- ¹² Gil-Campos M et al. Pharmacol Res 2012; 65(2): 231–238.
- ¹³ Martin R et al. J Pediatr 2003; 143(6): 754–758.
- ¹⁴ Martin R et al. J Hum Lact 2005; 21(1): 8–17.
- ¹⁵ Lara-Villoslada F et al. Br J Nutr 2007; 98(suppl 1): 96–100.
- ¹⁶ Blaut M & Loh C in: Bischoff SC: Probiotika, Präbiotika und Synbiotika; Thieme 2009; 2–23.
- ¹⁷ Ben XM et al. World J Gastroenterol 2008; 14(42): 6564–6568.
- ¹⁸ Olivares M et al. Nutr 2007; 23(3): 254–260.
- ¹⁹ Perez-Cano FJ et al. Immunobiology 2010; 215(12): 996–1004.
- ²⁰ FDA. 2008; GRAS Notices GRN No. 236.
- ²¹ Koletzko B et al. Am J Clin Nutr 2009; 89(6): 1836–1845.
- ²² Lloyd B et al. Pediatrics 1999; 103(1): e7.
- ²³ Koletzko B et al. Am J Clin Nutr 2020; 111: 10–16.
- ²⁴ EFSA. The EFSA Journal 2014; 12(7): 3760.
- ²⁵ Breastfeeding: A Guide for the Medical Profession, 8th edition. Elsevier, Saunders, Mosby, Churchill, 2016.
- ²⁶ Nutrition in Pediatrics: Basic Science, Clinical Applications. Volume 1, 2016.
- ²⁷ Lee et al. Front Pediatr. 2018; 6: 313.
- ²⁸ Bronsky J et al. J Pediatr Gastroenterol Nutr 2019; 68: 742–760.
- ²⁹ Maldonado-Lobón JA et al. Pharmacol Res 2015; 95-96: 12–19.
- ³⁰ Severin et al. FEMS Microbiol Rev. 2004; 28(4): 405–440.
- ³¹ Peran L et al. Int J Colorectal Dis 2006; 21(8): 737–746.
- ³² Olivares M et al. J Appl Microbiol 2006; 101(1): 72–79.
- ³³ Giovannini M et al. J Am Coll Nutr 2014; 33(5): 385–393.
- ³⁴ EFSA: The EFSA-Journal 2007; 587: 1–16.
- ³⁵ FDA. 2015; GRAS Notices GRN No. 531.
- ³⁶ COMMISSION DELEGATED REGULATION (EU) 2021/571 of 20 January 2021. Official Journal of the European Union, 8 April 2021. EFSA Journal, doi: 10.2903/j.efsa.2020.5947.