
HiPP
COMBIOTIC®
Safety is our most important ingredient
HiPP ORGANIC COMBIOTIC®
Rounded off with Metafolin®
ONLY FROM
HiPP
METAFOLIN®*
Science and nature hand in hand
HiPP COMBIOTIC® 10 YEARS
Information for healthcare professionals
* Metafolin® is a registered trademark of Merck KGaA, Darmstadt, Germany.

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

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

HiPP Research Group on Human Milk

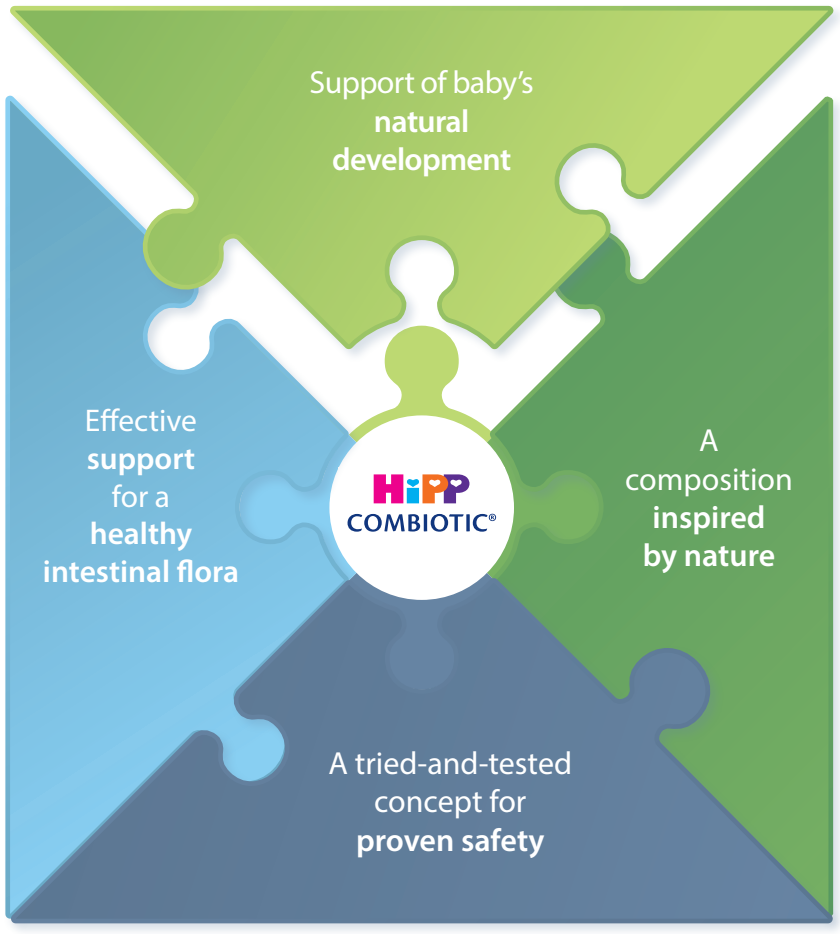
HiPP Research Group on Human Milk: understanding nature's example.

- Running for over 10 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

A safe and proven composition

HiPP ORGANIC COMBIOTIC®
Science and nature hand in hand



HiPP COMBIOTIC®

ONLY FROM HiPP METAFOLIN®*

The safe next step in our human milk research

Folate: crucial for cell division and tissue growth[1] ...

DNA synthesis · Cell division · Blood formation · Protein synthesis

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

Ideal folate form: 5-MTHF
- it does not need to be metabolised
- it is immediately available to the body

While trying to get pregnant and during pregnancy → Birth → While breastfeeding

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 formula[2]!

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 formula[3]

Until 2021: fortifying formulae with synthetic folic acid was the standard

As of 2021: only in HiPP ORGANIC COMBIOTIC®

Folic acid

DHFR (enzyme)

UMFA

unmetabolised folic acid is accumulated and remains unused

DHF dihydrofolate

THF tetrahydrofolate

Mutation of the enzyme **MTHFR** reduces the metabolisation rate of folate into its active form 5-MTHF

5,10-methylene-THF

MTHFR (enzyme)

METAFOLIN®*

Metafolin® does not need to be metabolised and is immediately available to the baby's body – for natural growth

5-MTHF (= Metafolin®): biologically active form

For more information on Metafolin®, scan:

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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 infections[4]

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)

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

Effective **support** for a **healthy intestinal microbiota**

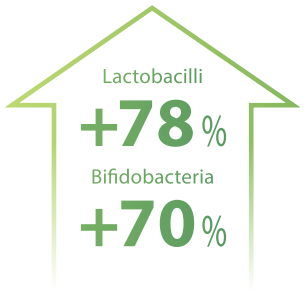
As a natural, synbiotic substance, human milk provides your child with everything they need for an ideal composition of their intestinal microbiota.

A safe and effective composition

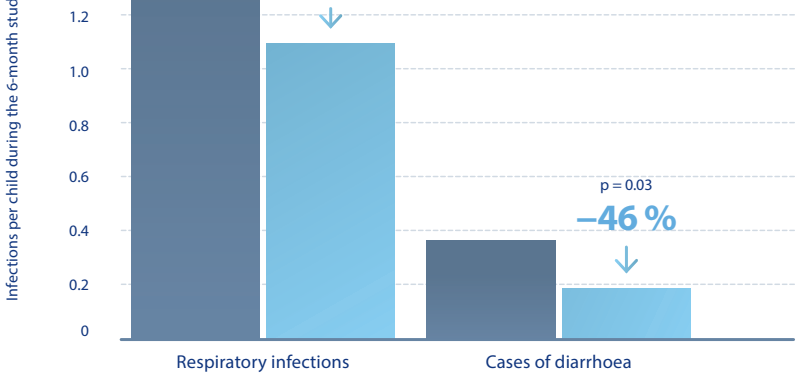
HiPP ORGANIC COMBIOTIC®
with its synbiotic composition of pre- and probiotics – galacto-oligosaccharides (GOS) and Limosilactobacillus fermentum – promotes a healthy intestinal microbiota and increases tolerability.

The prebiotic GOS supports the developing digestive system and leads to:[7–10]

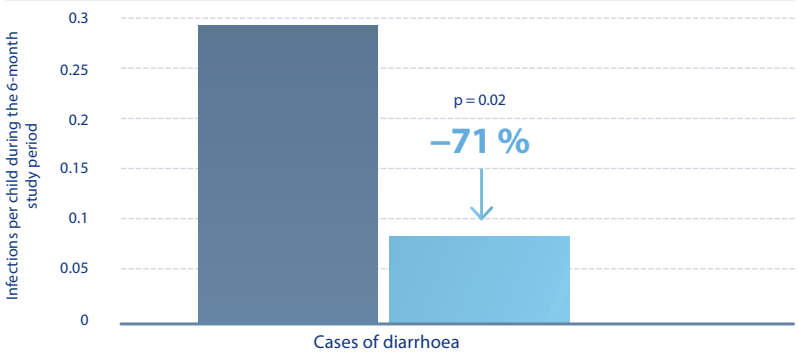
- less colic
- increased stool frequency
- softer stool consistency and a stool colour similar to that of breastfed children



Follow-on formula study (GOLF 1)[11]



Infant formula study (GOLF 2)[12]



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

- ✓ increases the number of beneficial bacteria in the intestine[11]
- ✓ 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 intestine[16]
- supports a healthy intestinal flora[29]
- contributes to a modulation of immune response[18, 19]

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 safe[20]

Probiotics + Prebiotics

METAFOLIN®*

Metafolin® – a bioactive folate form for natural development

Appropriately low protein content

Protein

- < 2.0 g/100 kcal, tailored to physiological needs[21]
- obtained from high-quality organic milk and organic whey

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

A composition **inspired by nature**

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Fatty acid spectrum inspired by nature

valuable fatty acids

Important palmitic acid

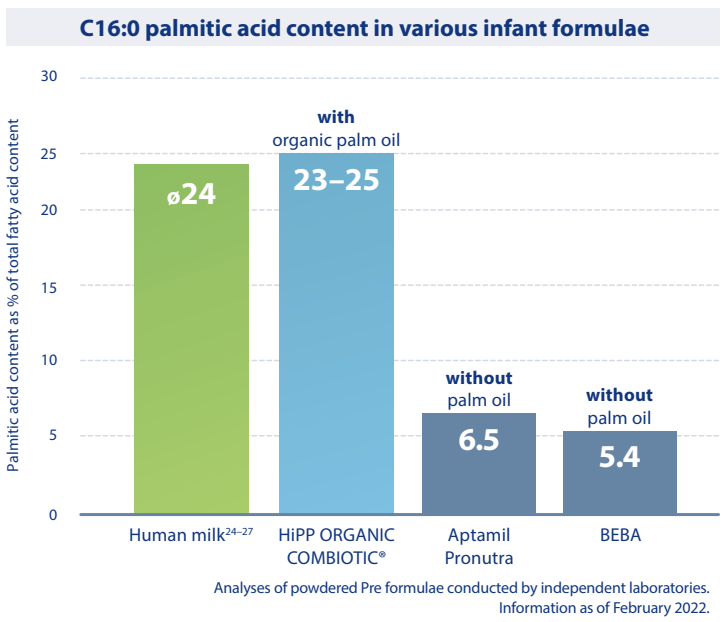
- the predominant saturated fatty acid in human milk
- important for good tolerability of formula[22]
  - less watery and more yellowy stools (similar to those of breastfed children)

Omega-3 and omega-6 LCPs

- evidence-based and recommended[23]
- 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 safe[29]
- 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 probiotc 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	GOLF 1 (follow-on formula) Maldonado J et al. 2012[11]
	helps **reduce the frequency of infections** compared to prebiotic (GOS) alone (diarrhoea and/or respiratory problems)	GOLF 1 (follow-on formula) Maldonado J et al. 2012[11]; GOLF 2 (infant formula) Gil-Campos M et al. 2012[12]
Bioactive folate form Metafolin®	**Metafolin® is safe for use in formulae.** Compared to formulae with synthetic folic acid, infants with Metafolin® develop equally well.	Troesch B et al. 2019[2]

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

A safe and ideal composition

High-quality protein	< 2.0 g/100 kcal, tailored to physio-logical needs[21]
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 recommendations[23]
Metafolin® for natural development	Safety confirmed by clinical study[2] and EFSA/EU.[36]

A tried-and-tested concept for **proven safety**

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HiPP COMBIOTIC®

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.

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