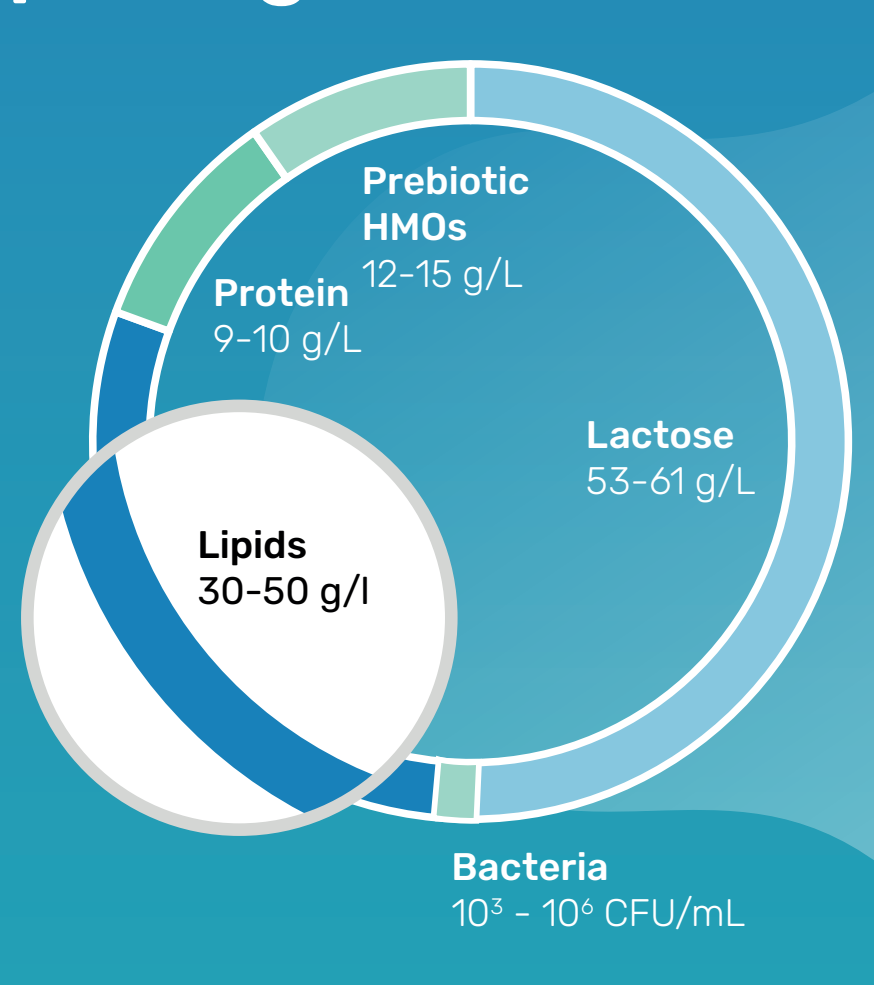
Structural organization of milk lipids determines effective lipid digestion in infants

Lipids are the second-largest group of macronutrients in breast milk.[1]



The lipid fraction is an essential component in breast milk due to its importance in **ensuring optimal growth and development in infancy.**[1-3]

Triglycerides constitute 98%–99% of breast milk lipids and act as the major energy source for infants.

These contribute to **approximately 50%** of the energy requirement of infants.[4]

Other breast milk components include:

Phospholipids
Essential for brain and cognitive development[5]

Sphingolipids
(mainly sphingomyelins)
Important for optimal functioning of the central nervous system and cognitive development[6,7]

Glycolipids
(including gangliosides)
Crucial for signal transduction, brain growth and maturation, immune function and infection prevention[5]

Essential fatty acids
(linoleic acid, alpha-linolenic acid, arachidonic acid, docosahexaenoic acid)
Important for infant's neuronal development and sensory qualities[8,9]

Cholesterol
Necessary for neurological development and is the basis for certain enzymes[10]

Efficient lipid absorption is crucial for infant growth, since lipids are the dominant energy source for infants.[11]

Notably, the type of enzymes, enzymatic activity, bile salt concentrations and digestive conditions differ significantly between infants and adults.[11–13]

Pre-birth: Glucose-dominant phase

Birth: Lipid-dominant phase

Milk-based diet

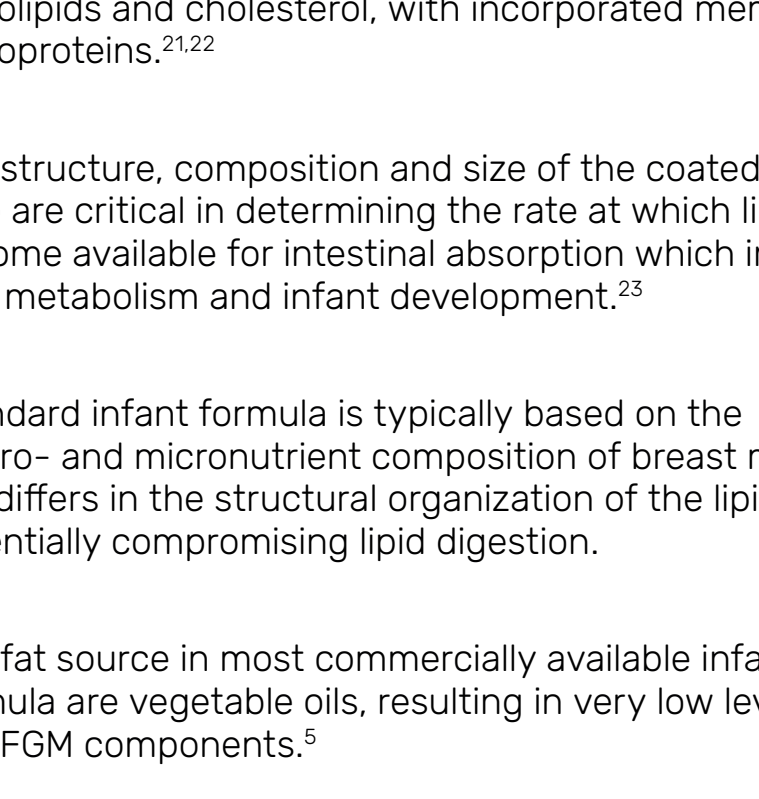
Lipid digestion in infancy
Lipid digestion in infants is characterized by:

- Decreased lipid digestion capacity[11,14]
- Higher gastric pH levels[15]
- Reduced bile acid levels[11,16]
- Immature gut barrier[18]
- Developing gut microbiota community[17]

Breast milk lipid characteristics enhance lipid digestion

Breast milk triglycerides are stored in the core of large **Milk Fat Globules (MFG)**, surrounded by a unique triple-layer membrane, known as the **Milk Fat Globule Membrane (MFGM)**.[19,20]

These lipid globules have a MODE DIAMETER ~4 μm.[9]



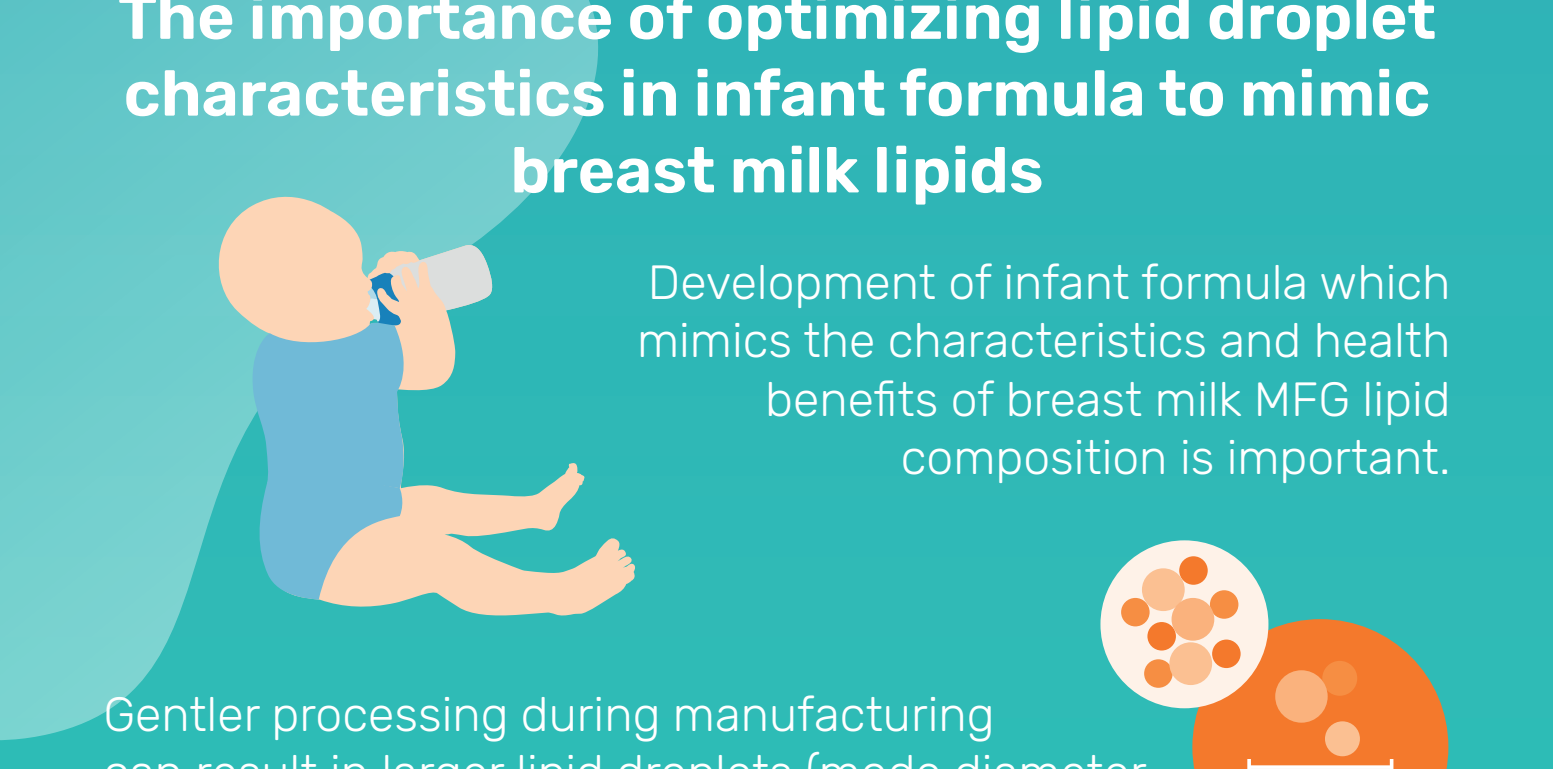
The inner MFGM monolayer is rich in phospholipids, while the outer bilayer contains phospholipids, sphingolipids, glycolipids and cholesterol, with incorporated membrane glycoproteins.[21,22]

The structure, composition and size of the coated MFG are critical in determining the rate at which lipids become available for intestinal absorption which impacts lipid metabolism and infant development.[23]

Standard infant formula is typically based on the macro- and micronutrient composition of breast milk but differs in the structural organization of the lipids, potentially compromising lipid digestion.

The fat source in most commercially available infant formula are vegetable oils, resulting in very low levels of MFGM components.[5]

Even in infant formula enriched with MFGM components, the manufacturing processes typically result in the loss of the original large lipid droplets and MFGM structure.



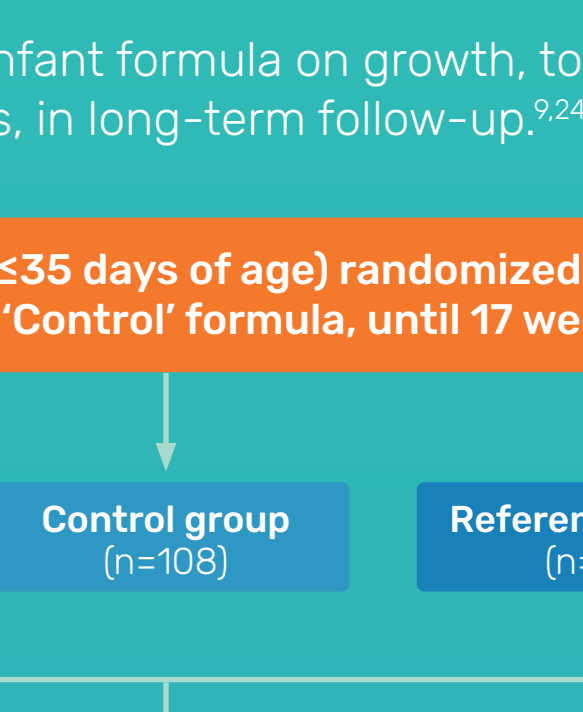
The importance of optimizing lipid droplet characteristics in infant formula to mimic breast milk lipids

Development of infant formula which mimics the characteristics and health benefits of breast milk MFG lipid composition is important.

Gentler processing during manufacturing can result in larger lipid droplets (mode diameter 3–5 μm), resembling breast milk MFG.

MODE DIAMETER 3–5 μm

This unique concept formula, containing large, milk phospholipid-coated lipid droplets, has shown promise in supporting adequate growth in healthy infants.[9,24,25]



MERCURIUS study:

The effect of a unique infant formula on growth, tolerance and safety in healthy infants, in long-term follow-up.[9,24,25]

Healthy, term infants (≤35 days of age) randomized to receive either a 'Concept' or a 'Control' formula, until 17 weeks of age

- **Concept group** (n=115)
- **Control group** (n=108)
- **Reference group** (n=88)

Concept and Control infant formula:

- **Protein** (1.3 g/100 mL)
- **Lipids** (3.4 g/100 mL)
- **scGOS/lcFOS prebiotic mixture** (9:1, 0.8 g/100 mL)

Concept
Vegetable (52%) and dairy lipids (48%) & 3-fold increase of sn-2 palmitic acid with lipid droplets having a mode diameter of 3–5 μm

Control
Vegetable oil-based lipid droplets (no dairy lipids) of mode diameter ~0.5 μm

Reference
Breastfed

Equivalent daily weight gain with Concept formula vs. Control formula

No relevant differences in adverse events

Long-term follow-up of 3, 4 and 5 years

Follow-up study outcomes[9,20]

BMI

- Lower in Concept group vs Control group (statistically significant at 1 year of age).
- BMI trajectory in Concept group was highly similar to that in the breastfed group, up to 5 years.

CHILDHOOD BLOOD PRESSURE

- Lower mean diastolic and arterial blood pressure at 5 years, in the Concept group vs the Control group.
- A lower percentage of children in the Concept group had elevated blood pressure.

COGNITIVE OUTCOMES

- Higher in the Concept group vs the Control group.
- DCCS scores (executive function tests, NIH Toolbox Early Childhood Cognition Battery) were higher in the Concept group vs the Control group.

Conclusion:

Optimizing the lipid composition and lipid droplet structure improves lipid digestion and utilization in early life and is associated with healthy infant growth and neurocognitive development, closer to that observed in breastfed infants.[9,24,25]

BMI, body mass index; BSSL, bile salt-stimulated lipase; DCCS, dimensional change card sort; lcFOS, long-chain fructo-oligosaccharides; MFG, milk fat globule; MFGM, milk fat globule membrane; NIH, National Institutes of Health; PTL, pancreatic triglyceride lipase; PRPL2, pancreatic lipase-related protein 2; scGOS, short-chain galacto-oligosaccharides.

References:
1. Koletzko, B. Ann. Nutr. Metab. 2016; 6(2):27-40.
2. Demmelmair H & Koletzko B. J Clin Endocrinol Metab. 2018;32(1):57-68.
3. Hageman JH et al. Int. Dairy J. 2019;92:37-49.
4. Ramiro-Cortijo D, et al. Nutrients. 2020 Feb; 12(2): 534.
5. Brink LR, Lönnerdal B. J Nutr Biochem. 2020 Nov:85:108465.
6. Albi E et al. Front Biosci (Landmark Ed). 2022 Aug 17;27(8):247.
7. Schneider N et al. eNeuro. 2019 Jul-Aug; 6(4): ENEURO.0421-18.2019.
8. K. D. Guiding principles for complementary feeding of the breastfed child. 2003.
9. Schipper L et al. Front Nutr. 2023; 10: 1215199.
10. The Breastfeeding Network, United Kingdom. Raised cholesterol and breastfeeding. Available at: https://www.breastfeedingnetwork.org.uk/factsheet/cholesterol/. Accessed February 2024.
11. Lindquist S, Hernell O. Curr Opin Clin Nutr Metab Care. 2010 May;13(3):314-20.
12. Zhao P et al. Food Hydrocoll. 2023;142:108859.
13. Bourlieu C, et al. Crit Rev Food Sci Nutr. 2014;54(11):1427-57.
14. Hamosh, M., et al., J Clin Invest, 1981. 67(3): p. 838-46.
15. Abrahamse, E., et al., Food Dig, 2012. 3(1-3): p. 63-77.
16. Ménard, O., et al., Food Chemistry, 2018. 240: p. 338-345.
17. Wopereis, H., et al., Pediatr Allergy Immunol, 2014. 25(5): p. 428-38.
18. Kaye, J.L., nt J Clin Pharm, 2011. 33(1): p. 20-4.
19. Gallier S et al. Colloids Surf B Biointerfaces. 2015 Dec 1:136:329-39
20. Delplanque B et al. J Pediatr Gastroenterol Nutr. 2015 Jul;61(1):8-17.
21. Gallier S et al. J Agric Food Chem. 2010 Apr 14;58(7):4250-7.
22. Lopez C, Ménard O. Colloids Surf B Biointerfaces. 2011;83(1):29-41.
23. Cohen K et al. Nutrients. 2020;13(1):199.
24. Breij LM et al. Am J Clin Nutr. 2019;109(3):586-596.
25. Abrahamse-Berkeveld M et al. Am J Clin Nutr. 2024 Jan;119(1):87-99.