

GlyCareTM LNT

Human Milk Oligosaccharides brought to you by dsm-firmenich, at the forefront of HMO innovation

Early life nutrition innovation from dsm-firmenich

Providing the best infant nutrition is vital for all families. That's why dsm-firmenich is proud to offer GlyCare™ HMOs. These compounds are developed with science-backed quality and safety at their core. As a fully integrated manufacturer with one of the broadest HMO offerings, dsm-firmenich can reliably provide ease-of-scale no matter the size of your business. Partner with us to get your products one step closer to what nature intended.

Partner with dsm-firmenich for access to our broad portfolio of products, customized solutions, and expert services aimed at supporting your entire product life cycle, from concept to consumption.

www.dsm-firmenich.com/health-nutrition-care



Human Milk Oligosaccharides (HMOs): delivering the benefits nature intended

Uniquely human

- HMOs are complex carbohydrates found in human breastmilk
- No other mammal has near the concentration and complexity of structures in their milk¹⁻⁶

Abundance and diversity in human milk

- 3rd largest component of human milk⁷
- >200 different HMOs identified in human milk, a diversity not seen in other animal milks⁴⁻⁶
- Variation occurs over lactation period, by maternal genetics, geographic region, and ethnicity^{8,9,25}

Complex structures with potential functional benefits

- Help establish a balanced early-life microbiota 10,11
- Contribute to immune system support¹²⁻¹⁶

Lacto-N-tetraose (LNT): A neutral-core HMO found in both colostrum and mature milk^{15,16}

- One of the most commonly detected and abundant HMOs in human milk^{9,17-21}
- May support the immune response²³⁻²⁴
- Stimulates the growth of beneficial bacteria, including bifidobacteria^{22,25-27}

HMO functionality is structure-specific: not all HMOs serve the same purpose^{23,24}

Potential functional benefits of GlyCare™ LNT, as demonstrated primarily in pre-clinical studie



 May benefit gut health by supporting a favorable microbiome^{22,25-27}



- Emerging evidence suggests a possible role in deflecting the adhesion of certain undesirable micro-organisms to specific human cells²⁸⁻³¹
- In vitro evidence suggests LNT may hinder the growth of the undesirable micro-organism group B Streptococcus²⁴



Breastmilk – the gold standard

Breastmilk provides nutrients that are vital for an infant's growth and development and sets the standard in infant feeding. 32,33 Human milk oligosaccharides (HMOs) are the third largest solid component of human milk after lipids and lactose and a key differentiating feature between human milk and cow's milk. The unique structure, concentration, and variety of oligosaccharides in human milk sets them apart from those found in cow's milk. 34,35 Differences in health outcomes between breastfed and formula–fed infants may partly be explained by these features. 8,34,36,37

HMOs stimulate the growth of beneficial bacteria

- When ingested, HMOs resist digestion and reach the colon mostly intact^{35,37}
- By selectively feeding the gut with beneficial bacteria, HMOs enhance the growth of helpful bacteria like bifidobacteria and limit the nutrient supplymfor undesirable organisms^{25,35,38}
- HMOs also support production of short chain fatty acids and other metabolitesmthat work to create a community of healthy microbes in the GI tract³⁹⁻⁴²

GlyCare™ DFL product information

- · 5 years of shelf life from production date
- Purity levels range from 70%
- White, homogenous, amorphous powder with a neutral to slightly sweet taste
- · Contains up to 12% lactose§
- Manufactured without contact to latex, bisphenol A, or phthalates
- · This product is free from:
- Animal derived ingredients (ADI), Allergens (except milk),§ Genetically modified organisms (GMO)*
- \$ according to EC regulation 1169/2011 annex II
 \$ according to EC regulation 1829/2003 and 1830/2003





Broad product portfolio and a leading HMO innovator



Proven, reliable supply that scales with you



Highest safety and quality standards



Largest global market access: 160+ countries*

^{*} We are continuously expanding our global approval footprint across application areas. For more details, please ask for our Regulatory Overview.

For more information, get in touch with your dsm-firmenich representative, or visit www.dsm-firmenich.com/health-nutrition-care

dsm-firmenich GlyCare™ HMOs are produced to the highest quality of certifications, approvals, and procedures











FSSC 9001:2015 22000 **SMETA**

Halal Kosher

The full GlyCare™ HMO portfolio

- GlyCare™ 2FL
- GlyCare™ LNnT

GlyCare™ 6SL

- GlyCare[™] 3SL GlyCare™ LNT
- GlyCare™ 2FL/DFL
- GlyCare™ 3FL
- GlyCare™ LNFP I

References

- T. Urashima, T. Saito, T. Nakamura, and M. Messer, "Oligosaccharides of milk and colostrum in non-human mammals," Glycoconjugate Journal, vol. 18, no. 5. Springer, pp. 357–371, 2001, doi: 10.1023/A:1014881913541.
- D. S. Newburg et al., "Milk oligosaccharides across species," Pediatr. Res., vol. 45, no. 5, pp. 745–745, May 1999, doi: 10.1203/00006450-199905010-00044.
- S. Albrecht et al., "A comparative study of free oligosaccharides in the milk of domestic animals," Br. J. Nutr., vol. 111, no. 7, pp. 1313–1328, Apr. 2014, doi: 10.1017/S0007114513003772.
- N. Tao et al., "Evolutionary glycomics: Characterization of milk oligosaccharides in primates," J. Proteome Res., vol. 10 no. 4, pp. 1548–1557, 2011, doi: 10.1021/pr1009367.
- T. Urashima, S. Asakuma, F. Leo, K. Fukuda, M. Messer, and O. T. Oftedal, "The Predominance of Type I Oligosaccharides Is a Feature Specific to Human Breast Milk," Am. Soc. Nutr. Adv. Nutr., vol. 3, pp. 473S-482S, 2012, doi: 10.3945/ an.111.001412.
- P. Gagneux et al., "Human-specific Regulation of a2-6-linked Sialic Acids," J. Biol. Chem., vol. 278, no. 48, pp. 48245–48250, 2003, doi: 10.1074/jbc.M309813200.
- Hegar, B., Wibowo, Y., Basrowi, R. W., Ranuh, R. G. Hegar, E., WIDOWO, Y., Basrowi, R. W., Kahun, R. G., Sudarmo, S. M., Munasir, Z., Atthiyah, A. F., Widodo, A. D., Supriatmo, Kadim, M., Suryawan, A., Diana, N. R., Manoppo, C., & Vandenplas, Y. (2019). The Role of Two Human Milk Oligosaccharides, 2'-Fucosyllactose and Lacto-NNeotetraose, in Infant Nutrition. Pediatric gastroenterology, hepatology & nutrition, 22(4), 330–340. https://doi.org/10.5223/pghn.2019.22.4.330
- Vandenplas, Y., Berger, B., Carnielli, V. P., Ksiazyk, J Vandenplas, Y., Berger, B., Carnielli, V. P., Ksiazyk, J., Lagström, H., Sanchez Luna, M., Migacheva, N., Mosselmans, J., Picaud, J., Possner, M., Singhal, A., & Wabitsch, M. (2018). Human Milk Oligosaccharides: 2"-Fucosyllactose (2"-FL) and Lacto-N-Neotetraose (LNTT) in Infant Formula. Nutrients, 10(9)10.3390/nu10091161
- Soyyılmaz, Buket, et al. "The Mean of Milk: A Review of Human Milk Oligosaccharide Concentrations throughout Lactation." Nutrients, 2021, doi:10.3390/nu13082737
- Berger, Bernard, et al. "Linking Human Milk Oligosaccharides, Infant Fecal Community Types, and Later Risk to Require Antibiotics." MBio, vol. 11, no. 2, 2020, pp. 1–18, doi:10.1128/mBio.03196–19.
- Bezirtzoglou, Eugenia, et al. "Anaerobe Microbiota pro Fi Le in Feces of Breast- and Formula-Fed Newborns by Using FI Uorescence in Situ Hybridization (FISH)." Anaerobe, vol. 17, no. 6, Elsevier Ltd, 2011, pp. 478–82, doi:10.1016/j anaerobe.2011.03.009
- Zhang, Bin, et al. "Human Milk Oligosaccharides and Infant Gut Microbiota: Molecular Structures, Utilization Strategies and Immune Function." Carbohydrate Polymers, vol. 276, no. October 2021, Elsevier Ltd, 2022, p. 118738, doi:10.1016/j. carbpol.2021.118738
- Zuurveld, Marit, et al. "Immunomodulation by Human Milk Oligosaccharides: The Potential Role in Prevention of Allergic Diseases." Frontiers in Immunology, vol. 11, no. May, 2020, doi:10.3389/fimmu.2020.00801.

- Derya, S. M., Spiegel, H., Hanisch, F. G., Morozov, V., Schroten, H., Jennewein, S., & Parschat, K. (2020). Biotechnologically produced fucosylated oligosaccharides inhibit the binding of human noroviruses to their natural receptors. Journal of Biotechnology, 318(November 2019), 31–38. https://doi.org/10.1016/j.jbiotec.2020.05.001
- Koromyslova, A., Tripathi, S., Morozov, V., Schroten, H., & Hansman, G. S. (2017). Human norovirus inhibition by a human milk oligosaccharide. Virology, 508(April), 81–89. https://doi.org/10.1016/j.virol.2017.04.032
- Yang, B., Chuang, H., & Yang, K. D. (2009). Sialylated glycans as receptor and inhibitor of enterovirus 71 infection to DLD-1 intestinal cells. Virology Journal, 6, 1–6. https://doi. org/10.1186/1743-422X-6-141
- Asakuma S, Urashima T, Akahori M, et al. Variation of major neutral oligosaccharides levels in human colostrum. Eur J Clin Nutr. 2008;62(4):488–494.
- Erney RM, Malone WT, Skelding MB, et al. Variability of human milk neutral oligosaccharides in a diverse population. J Pediatr Gastroenterol Nutr. 2000;30(2):181-192.
- Wang M, Li M, Wu S, et al. Fecal microbiota composition of breast-fed infants is correlated with human milk oligosaccharides consumed. J Pediatr Gastroenterol Nutr. 2015;60(6):825-833.
- Wu J, Wu S, Huo J, et al. Systematic Characterization and Longitudinal Study Reveal Distinguishing Features of Human Milk Oligosaccharides in China. Curr Dev Nutr. 2020;4(8):nzaail3.
- Austin S, De Castro CA, Bénet T, et al. Temporal Change of the Content of 10 Oligosaccharides in the Milk of Chinese Urban Mothers. Nutrients. 2016;8(6).
- Özcan E, Sela DA. Inefficient Metabolism of the Human Milk Oligosaccharides Lacto-N-tetraose and Lacto-Nneotetraose Shifts Bifidobacterium longum subsp. infantis Physiology. Front Nutr. 2018;5:46.
- Craft KM, Thomas HC, Townsend SD. Sialylated variants of lacto-N-tetraose exhibit antimicrobial activity against Group B Streptococcus. Org Biomol Chem. 2019;17(7):1893-
- 24. Lin AE, Autran CA, Szyszka A, et al. Human milk oligosaccharides inhibit growth of group B Streptococcus. J Biol Chem. 2017;292(27):11243–11249.
- Asakuma S, Hatakeyama E, Urashima T, et al. Physiology of consumption of human milk oligosaccharides by infant gut-associated bifidobacteria. J Biol Chem 2011;286(40):34583-34592
- Ruiz-Moyano S, Totten SM, Garrido DA, et al. Variation in consumption of human milk oligosaccharides by infant gut-associated strains of Bifdobacterium breve. Appl Environ Microbiol. 2013;79(19):6040–6049.
- James K, Motherway MO, Bottacini F, van Sinderen D. Bifidobacterium breve UCC2003 metabolises the human milk oligosaccharides lacto-N-tetraose and lacto-N-neotetraose through overlapping, yet distinct pathways. Sci Rep. 2016;6:38560.

- Andersson B, Dahmén J, Frejd T, et al. Identification of an active disaccharide unit of a glycoconjugate receptor for pneumococci attaching to human pharyngeal epithelial cells. J Exp Med. 1983;158(2):559-570.
- Cravioto A, Tello A, Villafán H, Ruiz J, del Vedovo S, Neeser JR. Inhibition of localized adhesion of enteropathogenic Escherichia coli to HEp-2 cells by immunoglobulin and oligosaccharide fractions of human colostrum and breast milk. J Infect Dis. 1991;163(6):1247-1255.
- 30. El-Hawiet A. Kitova EN, Klassen JS, Recognition of human milk oligosaccharides by bacterial exotoxins. Glycobiology. 2015;25(8):845–854.
- El-Hawiet A, Kitova EN, Kitov PI, et al. Binding of Clostridium difficile toxins to human milk oligosaccharides. Glycobiology. 2011;21(9):1217–1227.
- 32. Lessen R, Kavanagh K. Position of the academy of nutrition and dietetics: promoting and supporting breastfeeding. J Acad Nutr Diet. 2015;115(3):444–449.
- Johnston M., Landers S., Noble L., Szucs K., L. V. Breastfeeding and the use of human milk. Pediatrics. 2012;129(3):e827-841.
- 34. Urashima T, Taufik E, Fukuda K, Asakuma S. Recent advances in studies on milk oligosaccharides of cows and other domestic farm animals. Biosci Biotechnol Biochem. 2013:77(3):455-466
- 35. Bode L. Human milk oligosaccharides: every baby needs a sugar mama. Glycobiology. 2012a;22(9):1147–1162.
- Chouraqui JP. Does the contribution of human milk oligosaccharides to the beneficial effects of breast milk allow us to hope for an improvement in infant formulas? Crit Rev Food Sci Nutr. 2020:1-12.
- Cheng L, Akkerman R, Kong C, Walvoort MTC, de Vos P. More than sugar in the milk: human milk oligosaccharides as essential bioactive molecules in breast milk and current insight in beneficial effects. Crit Rev Food Sci Nutr. 2020:1–17.
- Kunz C. Historical aspects of human milk oligosaccharides. Adv Nutr. 2012;3(3):430s-439s.
- Schwab C, Ruscheweyh HJ, Bunesova V, Pham VT, Beerenwinkel N, Lacroix C. Trophic Interactions of Infant Bifdobacterium halli during L-Fucose and Fucosyllactose Degradation. Front Microbiol. 2017;8:95.
- Gibson GR, Wang X. Regulatory effects of bifidobacteria on the growth of other colonic bacteria. J Appl Bacteriol. 1994;77(4):412-420.
- Smilowitz JT. Lebrilla CB, Mills DA, German JB, Freeman St. Breast milk oligosaccharides: structure-function relationships in the neonate. Annu Rev Nutr. 2014;34:143-169.
- Lawson MAE, O'Neill IJ, Kujawska M, et al. Breast milk-derived human milk oligosaccharides promote Bifidobacterium interactions within a single ecosystem. Isme j. 2020;14(2):635-648.

Disclaimer
Although dsm-firmenich-firmenich has used diligent care to ensure that the information provided herein is accurate and up to date, dsm-firmenich makes no representation or warranty of the accuracy, reliability, or completeness of the information. This brochure only contains scientific and technical information for business to business use. Country or region-specific information should also be considered when labeling or advertising to final consumers. This publication does not constitute or provide scientific or medical advice, diagnosis, or treatment and is distributed without warranty of any kind, either expressly or implied. In no event shall dsm-firmenich be liable for any damages arising from the reader's reliance upon, or use of, these materials. The reader shall be solely responsible for any interpretation or use of the material contained herein. The content of this document is subject to change without further notice. Please contact your local dsm-firmenich representative for more details. All trademarks listed in this brochure are either registered trademarks, trademarks or licensed trademarks of dsm-firmenich group of companies in the Netherlands and/or other countries, unless explicitly stated otherwise.

© dsm-firmenich Nutritional Products 2022

