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Human Milk Oligosaccharides: A practical approach for toddlers & children



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Outline

- HMOs
 - Background
 - Maternal influences
 - Role & mechanism
 - Safety
 - GOS / FOS vs HMOs
- Formulas / supplements
- Using HMOs in clinical practice
- Case studies

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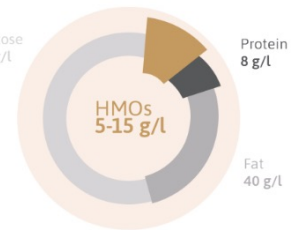
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What are HMO's

- Diverse group of over 150 complex indigestible sugars
- Bioactive, Prebiotic glycans
- Pass undigested in the large intestine
- Oligosaccharides produced by the mammary gland
- Third most abundant component of breast milk
 - 20-25g/L in colostrum
 - 5-15g/L in mature milk



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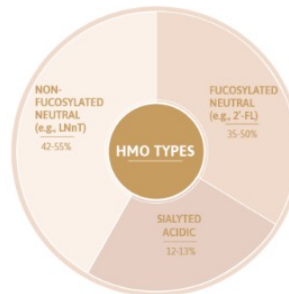
What are HMO's

• HMO types and quantities

• Fucosylated	Neutral	(35-50%)	2'FL
• Non-fucosylated	Neutral	(42-55%)	LNT
• Sialylated	Acidic	(12-14%)	3'SL

• Genetics and HMO production

- Lewis gene and secretory status
- Mirrors blood group expression



More than *breast milk*
150 HMOs

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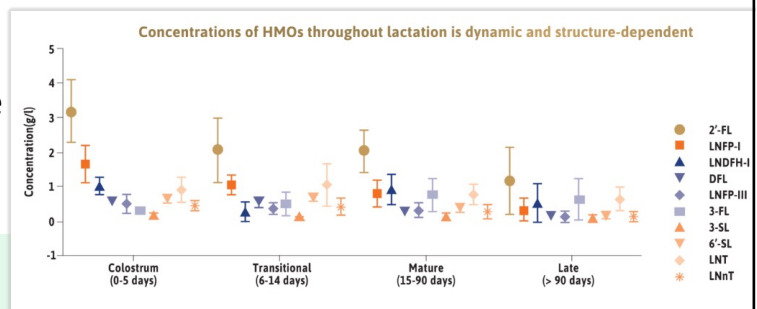
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Maternal influencers of HMO's

- High level of variation in HMO profile between mothers
 - Genetics
 - Geography
 - Environment
- But each mothers individual profile of HMO's is relatively constant over days and weeks
- Over months some HMO's decrease and others increase



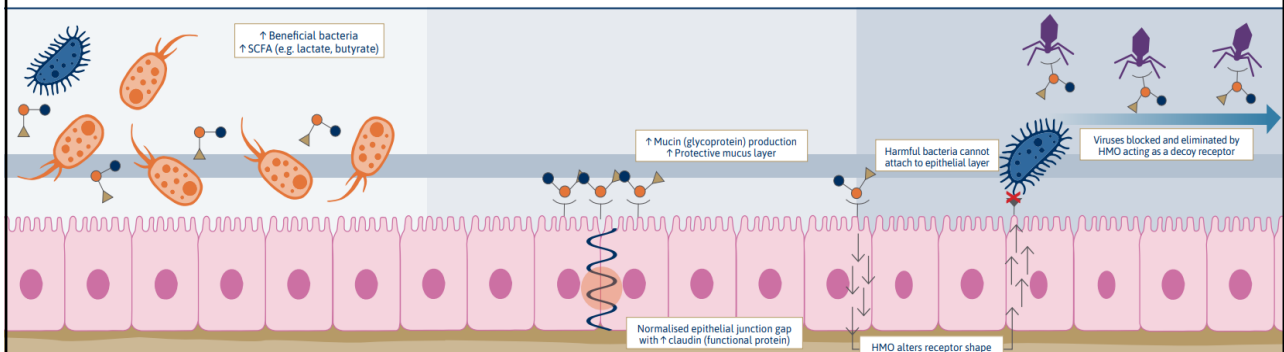
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Role / Mechanism of HMO's

- HMOs
 - Promote the growth of Bifidobacterium species
 - Reduce pathogen adhesion
 - Improve digestive function
 - Directly modulate the immune system



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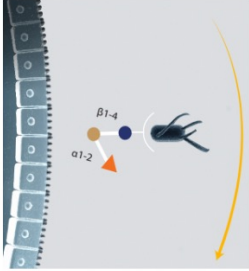


Jan 2020, 12, 266

Article
Human Milk Oligosaccharides: Health Benefits, Potential Applications in Infant Formulas, and Pharmacology
 Michał Wiciński¹, Ewelina Sawicka^{1,4}, Jakub Gębalski¹, Karol Kubiak² and Bartosz Malinowski¹

Role / Mechanism of HMO's

- HMOs contribute to the development of microflora & immune system
- HMO potential is larger than GOS/FOS
- Protect against infections
 - Anti-adhesion of pathogens
 - Support microbiota development
 - Antiviral – decrease infection risk
- Immune system development
 - Modulating
- NEC
 - HMOs (specifically DSLNT) now thought to contribute to the protective effect of breast milk against this significant cause of mortality and morbidity for premature infants





HMO acts as a decoy receptor for pathogens

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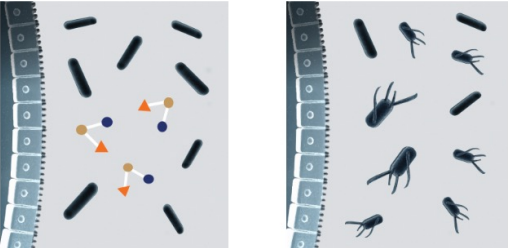


MDPI

Review
Human Milk Oligosaccharides: A Comprehensive Review towards Metabolomics
 Children 2021, 8, 804. <https://doi.org/10.3390/children8090804>

Role / Mechanism of HMO's

- Functions
 - Prebiotic effect
 - Increase gut barrier function
 - Brain development
 - Development of the immune system
 - Reduce allergy risk
 - Protect against infections
 - Protect against NEC



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ORIGINAL ARTICLE: NUTRITION



OPEN

Effects of Infant Formula With Human Milk Oligosaccharides on Growth and Morbidity: A Randomized Multicenter Trial

*Giuseppe Puccio, †Philippe Alliet, *Cinzia Cajozzo, †Elke Janssens, *Giovanni Corsello, ††Norbert Sprenger, †Susan Wernimont, ‡Delphine Egli, ††Laura Gosoni, and †Philippe Steenhout




Infant Formula With a Specific Blend of Five Human Milk Oligosaccharides Drives the Gut Microbiota Development and Improves Gut Maturation Markers: A Randomized Controlled Trial

Miroslava Bosheva¹, Istvan Tokodi², Aleksander Krasnow³, Helle Krogh Pedersen⁴, Oksana Lukjancenko⁴, Aron C. Eklund⁴, Dominik Grathwohl⁵, Norbert Sprenger⁶, Bernard Berger⁶, Colin I. Cercamondi⁷ and 5 HMO Study Investigator Consortium[†]


Nutrients. 2022 Jul; 14(13): 2625. PMID: PMC9268- PMCID: 35807-
 Published online 2022 Jun 24. doi: [10.3390/nu14132625](https://doi.org/10.3390/nu14132625)

Growth and Gastrointestinal Tolerance in Healthy Term Infants Fed Milk-Based Infant Formula Supplemented with Five Human Milk Oligosaccharides (HMOs): A Randomized Multicenter Trial

John Lasekan, *Yong Choe, Svyatoslav Dvoretzkiy, Amy Devitt, Sue Zhang, Amy Mackey, Karyn Wulif, Rachael Buck, Christine Steele, Michelle Johnson, and Geraldine Baggs

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HMO's vs GOS / FOS

- Benefits of GOS / FOS as prebiotic oligosaccharides remain but they are no longer the BEST oligosaccharide choice available
 - Bifidogenic but a non-specific action to increase bacteria in the microbiota
 - Support immune health
 - Reduced infections and reduced incidence of atopic dermatitis
- However they
 - Structurally different and less varied and less complex than HMOs
 - Non-specific action unlikely to provide the same level of health benefit as HMOs
 - Reduced Short-chain Fatty acid production compared to HMO
 - Give increased cytokine/inflammatory response compared with breast milk and HMO formula

HMO > GOS / FOS > no added oligosaccharides

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HMOs in formula & supplements

- Through scientific advances structurally identical HMOs 2'FL and LNnT now approved in Australia For use as:
 1. Addition to infant formula (0-12 months)
 2. Supplement for children over 12 months
- Since 2016 HMO containing formulas have been on the market in Europe and USA

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HMOs in formula & supplements

- European Union - EFSA (2015)
 - 2'FL and LNnT
 - 1.2g/L of 2'FL alone or in combo with LNnT at 2:1 ratio for 0-12 months in infant and follow on formula
 - 1-3 yr olds approved as safe as food supplements 2'FL and LNnT
 - Not to exceed 0.6g/L LNnT
 - Not to exceed 1.2g/L 2'FL
 - 4-8 yr olds approved as safe as food supplements 2'FL and LNnT
 - Not to exceed 1.5g/L LNnT
 - Not to exceed 3g/L 2'FL

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HMOs in formula & supplements

- United States America - FDA (2015)
 - GRAS - 2'FL, 3'SL and LNnT in infant formula 0-12months
 - 2.4g/L of 2'FL
 - 0.6g/L LNnT
 - 0.23g/L 3'SL
 - 12-24month olds 3'SL approved as GRAS 3.1g/serving in foods

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HMOs in formula & supplements

- Australia
- FSANZ Standard 2.9.1 (infant formula products)
 - 2'FL and LNnT
 - for 0-12 months in infant formula
 - Up to max 2.4g/L of 2'FL
 - Up to max 0.6g/L of LNnT
 - Must not contain GOS / FOS if it contains HMO
- TGA permissible ingredients
 - Not for use under 12months
 - 1-3 yr olds approved as safe as food supplement 2'FL
 - Not to exceed 1.2g/day 2'FL
 - 4-17 yr olds approved as safe as food supplement 2'FL
 - Not to exceed 2g/day 2'FL
 - 18yr old and over approved as safe as food supplement 2'FL
 - Not to exceed 5g/day 2'FL

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HMO clinical use

- These products can be used in the general paediatric population
- Any child who
 - Is not breast-fed and can consume dairy / intact protein
 - Wants stronger immune health and gut microbiome more similar to a breast fed infant

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HMO clinical use

- 0-12months
 - Safe and well tolerated from birth
 - Formulas with HMO's added should be preferentially used from the time formula is used
 - Future directions will include personalised individual plans and likely supplementation in a wider range of formulas
- Supplement from 12months
 - Palatable (no taste) white fine powder 1.2g dose. Mixes with water, milk, formula, yoghurt, fruit mash
 - Suggest to all children who would benefit from stronger immune health and gut microbiome more similar to a breast fed infant
 - Targeting those who have had less lifetime exposure to HMOs (shorter duration of Breastfeeding)
 - Targeting those with gut microbiome development more at risk eg frequent illness, digestive disorders, atopic, ex premature infants

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Case Study 1

- 4 months old
- Healthy infant with Mo wanting to transition from breast milk and asking the optimal formula
 - Lower protein
 - Containing HMO (in preference to GOS/FOS)
 - DHA

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Case Study 2

- 5 weeks old, irritable, poor sleep
- Mucous + 1-2 x week blood in stools + GORD – likely CMPA.
- Has been having extensively hydrolysed formula for 3 weeks, nil improvement
- Growth now suboptimal
- ? Amino acid based formula
- ? HMO supplemented formula when available

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Case Study 3

- 14 months old
- Weaned from breast milk at 12 months
- Started kindy and parents concerned about illness
- Optimise iron
- Increase dietary fibre quantity and diversity
- Consider adding a HMO supplement 1.2g/day

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Case Study 4

- 20 months old
- Non-IgE Dairy allergy persists and multiple intolerances with symptoms of bloating, irritability, significant distress on passing soft stool
- Weaned from breast milk at 14 months
- Digestive symptoms not improving with age
- Meet calcium requirements
- Work with family to identify and limit triggers
- Consider adding a HMO supplement 1.2g/day

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HMO's Future research

- Use in optimising growth and body composition
- Food allergy moderation
- Cognitive development
- Non-secretor phenotype
- Other HMO's to be synthetically produced and their targeted supplementation
- How does maternal health eg diabetes impact HMO profile
- Specific HMO to match specific clinical situation
- Bedside HMO profiling – personalised supplementation

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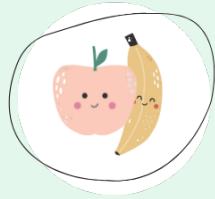
- HMOs are >150 Prebiotics produced by humans and some are now able to be produced synthetically
- Benefits to immune and digestive health are significant
- Infants given HMO consistently have stooling and health markers closer to human milk fed infants
- These have now superseded the role of GOS / FOS



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Thank you

Q and A

