Breast Milk: the Gold Standard

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Top 7 Components of Human Milk

1. Oligosaccharides
2. Antibodies
3. Anti-oxidants
4. Lactoferrin
5. Osteopontin
6. White blood cells
7. Stem cells.
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Human Milk Oligosaccharides (HMOs)

- Indigestable complex carbohydrates
- Synthesized in the mammary glands
- Oligosaccharides are highly resistant to hydrolysis in the gastrointestinal tract.
- Most HMOs will enter colon. A few is absorbed in the neonatal small intestine.
Human Milk Oligosaccharides (HMOs)

HMOs are the third most predominant component in human milk.

* An estimate. Oligosaccharide content varies over time and between individuals.
Human Milk Oligosaccharides (HMOs)

Table 1: Total and sialylated oligosaccharides in human milk, bovine milk, and infant formulas based on cow's milk.

<table>
<thead>
<tr>
<th>Oligosaccharides</th>
<th>Human colostrum (&lt;7 days)</th>
<th>Mature human milk (30–120 days)</th>
<th>Bovine colostrum</th>
<th>Mature bovine milk</th>
<th>Infant formulas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total oligosaccharides</td>
<td>13,300–23,000 mg/L</td>
<td>3,500–14,000 mg/L</td>
<td>~1,000 mg/L</td>
<td>300–500 mg/L</td>
<td>400–8,000 mg/L</td>
</tr>
<tr>
<td>Sialylated (acidic) oligosaccharides</td>
<td>1,000–3,300 mg/L</td>
<td>135–2,150 mg/L</td>
<td>230–1,500 mg/L</td>
<td>10–195 mg/L</td>
<td>14–288 mg/L</td>
</tr>
<tr>
<td>6'-sialyllactose</td>
<td>250–1,300 mg/L</td>
<td>170–500 mg/L</td>
<td>30–243 mg/L</td>
<td>17–88 mg/L</td>
<td>3.8–4.6 mg/L</td>
</tr>
<tr>
<td>3'-sialyllactose</td>
<td>90–350 mg/L</td>
<td>76–300 mg/L</td>
<td>354–1,250 mg/L</td>
<td>30–119 mg/L</td>
<td>17–19 mg/L</td>
</tr>
</tbody>
</table>

*Products include formulas supplemented with galacto-oligosaccharides and/or fructo-oligosaccharides.
Human Milk Oligosaccharides

- > 100 different HMOs in breast milk
- **Neutral HMOs:**
  - galacto-oligosaccharides, fructo-oligosaccharides
- **Acidic HMOs:**
  - sialyllactose, other sialylated milk oligosaccharides
HMOs: potential effects

1 - Development of microbiota:
   - Stimulation of outgrowth of specific bifidobacteria and lactobacilli.

2 - Gut maturation:
   - Regulation of EGF-receptor activation 
   - Epithelial differentiation
   - Adhesion of maternal IgG to infant intestinal epithelium

3 - Resistance to gut pathogens:
   - Competition for pathogen binding sites on epithelium (decoy activity/preservation of adhesion)
   - Reduction of pH in lumen of colon
   - Mucin composition

4 - Resistance to respiratory tract pathogens:
   - Increase of pathogen phagocytosis
   - Mucin composition

5 - Immune function and inflammation:
   - Enhancement of endocytosis by DCs
   - Induction of immune regulation by SA-receptors on immune cells
   - Reduction of leukocyte adhesion to endothelium
   - Induction of T cell skewing
   - Reduction of inflammation in IBD
   - Involvement in reduction of NEC

6 - Brain and cognitive development:
   - Incorporation of SA in brain gangliosides (learning ability)

Potential effects of SL and sialylated oligosaccharides

Nutrition Reviews; 72(6): 377-389
HMOs: potential effects

1. Development of microbiota & Resistance to gut pathogens
   - Limit pathogenic microbes (e.g. E. coli) by blocking the binding of microbe to infant’s mucosal receptors.
   - Oligosaccharide-mucosal receptor complex allows specific attachment of B. bifidum to the intestinal mucosa, competitively inhibiting the attachment of pathogenic organisms.
   - ↑ Growth on non-pathogenic commensal microbe (Bifidobacterium bifidus)
HMOs: potential effects

1. Development of microbiota & Resistance to gut pathogens

- Gut microbiota produce SCFA (short chain fatty acids).
- SCFA
  - Barrier against pathogens
  - Antidiarrheal agents (↑ sodium and water absorption)
  - Nutrient absorption
  - Immune development
HMOs: potential effects

2. Gut maturation

- Regulation of EGF (epidermal growth factor) – receptor activation → epithelial differentiation
- Adhesion of maternal IgG to infant epithelium
HMOs: potential effects

3. Resistance to respiratory tract pathogens:
   - ↑ pathogen phagocytosis
   - Mucin composition (sialic acid)
Newton ER. Lactation and Breastfeeding in Obstetrics: Normal and Problem Pregnancies
4. Immune function and inflammation

- Anti-inflammatory properties by ↓ proinflammatory cytokines (IL-8, TNF-a, etc.)
- ↓ risk of NEC (necrotizing enterocolitis) in preterms
- May prevent inflammatory bowel disease in adulthood.
HMOs: potential effects

5. Brain and cognitive development

- Sialic acid is mostly found in brain’s grey matter (gangliosides, glycoproteins) → cell-to-cell communication
- Breastfed babies have 32% more protein-bound SA in brain tissue.
- Brain disorders e.g. retardation, psychosis, alzheimer’s disease associated with lower SA content of the brain.
HMOs: potential effects

Ear
- Breastfed infants have a lower risk of developing otitis media than formula-fed infants
- Common pathogens of otitis media are inhibited by HMOS and/or HMGs

Stomach
- HMOS inhibit *Helicobacter pylori* binding to gastric mucosal receptors

Kidney, ureter, and bladder
- Breastfed infants have a lower risk of developing urinary tract infections than formula-fed infants
- HMOS inhibit adhesion of uropathogenic *Escherichia coli* to bladder epithelium

Lungs
- Breastfed infants have a lower risk of developing respiratory infections than formula-fed infants

Small intestine
- Breastfed infants have a lower risk of developing antinomic infections and autoimmunity than formula-fed infants
- HMOS and HMGs inhibit binding of antipathogens to mucosal receptors
- HMOS suppress mucosal inflammation

Large intestine
- Breastfed infants have a lower risk of developing severe antinomic infections and autoimmune disease than formula-fed infants
- The microbiota of breastfed infants contains abundant, beneficial *bifidobacteria*
- HMOS support the growth of *bifidobacteria* and their production of organic acids
- HMOS and HMGs inhibit the binding of antipathogens to mucosal receptors
- HMOS suppress mucosal inflammation
Top 7 Components of Human Milk

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Stem cells in breastmilk: theory becomes reality

Breast milk-derived cells
Neuro Res Int 2014

Mammary stem cells (red/blue) and differentiated adult mammary cells (green) isolated from breast milk.
Stem Cells 2012;30:2164-2174
"Internal Repair System"

- Develop into many different cell types in the body during early life and growth.
- Hassiotou et al. studied on cell culture of pump-expressed mature breastmilk.
Human milk stem cells

Stem Cells 2012;30:2164-2174
Human milk stem cells-derived neural stem cells

Neurons and astrocytes

Oligodendrocytes

Neurology Research International 2014