SOUTH ASIA PEDIATRIC ASSOCIATION

Lactation to Health: The Role of Human Milk Bio-Actives

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Human Milk Bioactives & Infant Health

Human milk bioactives are biologically active molecules that extend breastfeeding benefits beyond basic nutrition.

Human milk is uniquely adapted to meet infants' nutritional and immunological needs. Human milk contains various bioactive compounds, in addition to proteins, lipids, carbohydrates, and cellular components, which actively influence the infant's development, immunity, and overall health.

These bioactives are critical during the neonatal period, a time of rapid growth and immune development, conferring lifelong benefits. Formula milk falls short in replicating the complexity and functionality of human milk. More and more research is conducted to mimic bioactives, but only a small proportion of them have been found and replicated to certainty.

Key Types of Human Milk Bioactives

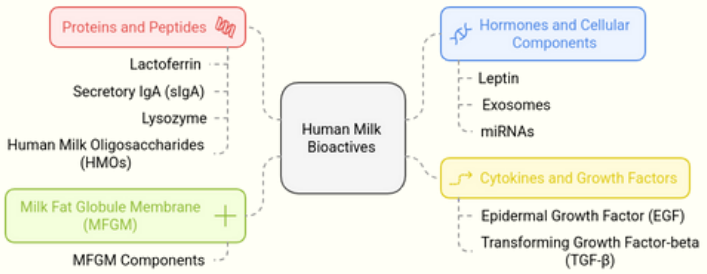

Fig 1: Key Types of Human Milk Bioactives

Proteins and Peptides

- **Lactoferrin:** An iron-binding glycoprotein that inhibits pathogen growth by depriving bacteria of free iron, directly disrupting bacterial membranes, and modulating the immune system by promoting dendritic cell maturation and enhancing NK cell activity [1].
- **Secretory IgA (sIgA):** The predominant immunoglobulin in human milk, coating the gastrointestinal mucosa to prevent pathogen adhesion, neutralize toxins, and provide immune protection without triggering inflammation [2].
- **Lysozyme:** A bacteriolytic enzyme that synergizes with lactoferrin to combat microbial infections and maintain gut microbiome health [3].

Carbohydrates

- **Human Milk Oligosaccharides (HMOs):** Uniquely tailored for neonates, they provide prebiotic support, pathogen defense through decoy receptor activity, and immune modulation. Unlike general prebiotics, HMOs also serve as anti-pathogenic agents, making them essential in infant nutrition [4]. Table 1: Comparison of HMOs and Mainstream Prebiotics in Infant

Feature	Human Milk Oligosaccharides (HMOs)	Mainstream Prebiotics
Targeted Bacteria	*Bifidobacteria infantis*, specific to neonates	Broad spectrum (*Bifidobacteria*, *Lactobacillus*)
Dual Functionality	Prebiotic + Decoy receptor	Prebiotic only
Structural Diversity	Over 200 types	Limited (FOS, GOS, inulin)
Immune Modulation	Direct and indirect	Indirect via SCFAs
Tailored for Neonates	Yes	No (Designed for general use)

Table 1: Comparison of HMOs and Mainstream Prebiotics in Infant

Milk Fat Globule Membrane (MFGM)

- **MFGM Components:** Containing bioactive proteins and lipids such as mucins and gangliosides, MFGM supports cognitive development and immune defense [4] [5].

Cytokines and Growth Factors

- **Epidermal Growth Factor (EGF):** Facilitates intestinal development and repair by enhancing epithelial cell proliferation and barrier function [5].
- **Transforming Growth Factor-beta (TGF-β):** Promotes immune tolerance by inducing regulatory T-cell differentiation, reducing allergy risk [5].

Hormones and Cellular Components

- **Leptin:** Regulates energy balance and metabolic programming, lowering the risk of childhood obesity [6].
- **Exosomes and miRNAs:** Present in human milk, exosomes transfer genetic material that modulates immune and developmental pathways, while live immune cells (macrophages, neutrophils, lymphocytes) contribute to immune defense [6].

The Mechanism of Action of Human Milk Bioactives

1. **Immune System Activation**
   - sIgA coats the infant's gut lining to block pathogen adhesion.
   - Lactoferrin binds free iron, inhibiting bacterial growth and promoting immune cell development.
2. **Gut Microbiome Development**
   - HMOs act as selective substrates for Bifidobacteria, promoting their growth and activity by providing a nutrient source that other gut microbes cannot efficiently use.

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- This mechanism fosters the development of a healthy gut microbiota by enhancing the dominance of beneficial bacteria, thereby contributing to gut health.
- Decoy receptors mimic cell surfaces, trapping pathogens.

3. **Neural and Cognitive Growth**
   - MFGM (Milk Fat Globule Membrane) and HMOs (Human Milk Oligosaccharides) both play crucial roles in promoting myelination and supporting cognitive development [9].
4. **Long-Term Health Programming**
   - Leptin regulates appetite and metabolism, reducing obesity risk.
   - TGF-β fosters immune tolerance, preventing allergies.

Benefits of Bioactives on Infant Health

Human milk bioactives play a critical role in shaping the health outcomes of infants. Formula-fed infants, who lack access to many of these bioactives, may experience significant health implications across multiple dimensions. Fig 2: Benefits of Bioactives on Infant Health

1. **Immune Protection**
   - IgA (sIgA) and lactoferrin are critical in the first year of life, when the infant's immune system is immature, to prevent infections and inflammation [10].
2. **Gut Health**
   - HMOs in human milk Reduced Pathogen Colonization, Enhancing Immune Regulation and Function [3].
3. **Long-Term Health**
   - Modulatory bioactives such as TGF-β and leptin reduce the risk of developing chronic ailments later in life, like allergies, obesity, and metabolic disorders [5][6].

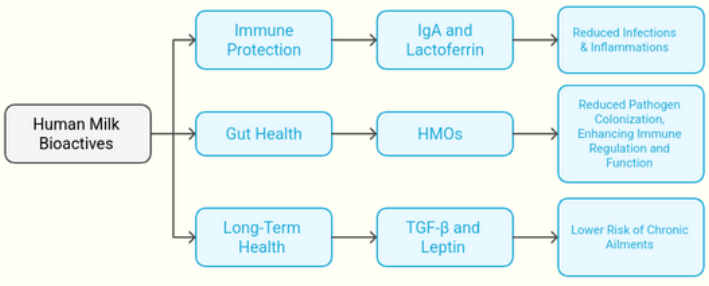

Fig 2:Benefits of Bioactives on Infant Health

Challenges in Replicating Bioactives

Formula milk strives to mimic the nutritional content of human milk but faces significant challenges in replicating its complex bioactive components, including HMOs, proteins, MFGM, cytokines, and cellular elements. These challenges arise from the following factors:

1. **Structural Complexity**
   - **Human Milk Oligosaccharides (HMOs):** Formula milk includes a limited selection of synthetic HMOs (e.g., 2′-FL, LNnT, 3′-FL, LNT, and 6′-SL), offering some functional benefits but representing only a fraction of the 200+ structurally distinct HMOs in breastmilk [7].
2. **Bioactive Proteins**
   - **Lactoferrin:** Formulas use bovine-derived lactoferrin, which has reduced bioactivity compared to human lactoferrin due to differences in glycosylation and post-translational modifications, affecting iron-binding and immune modulation [8].
   - **Secretory IgA (sIgA):** Synthetic replication of sIgA's complex structure is currently unfeasible [8].
3. **MFGM, Cytokines, and Growth Factors**
   - **MFGM:** Premium formulas include MFGM components, but their concentrations and interactions are suboptimal compared to natural human milk [7].
   - **TGF-β and EGF:** These cytokines are absent in formula milk [7].
4. **Exosomes and miRNAs**
   - These components are absent in formula due to the inability to preserve cell viability and exosome integrity in commercial production [1].

Summary

HHuman milk is a remarkable source of bioactive components that enhance infants' health and development, providing essential immunological protection against infections. Key bioactives include human milk oligosaccharides (HMOs), which support a healthy gut microbiota and modulate immunity, as well as immunoglobulin A (IgA) and lactoferrin. Additionally, components like transforming growth factor-beta (TGF-β) and leptin regulate metabolism and lower the risk of chronic disease. While infant formula has made advances, it cannot replicate the complexity and multifunctionality of the bioactives in human milk, highlighting the benefits of breastfeeding for optimal infant health.

For References Scan the QR code