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Human breast milk: A review on its composition and bioactivity

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ABSTRACT

Breast milk is the perfect nutrition for infants, a result of millions of years of evolution, finely attuning it to the requirements of the infant. Breast milk contains many complex proteins, lipids and carbohydrates, the concentrations of which alter dramatically over a single feed, as well as over lactation, to reflect the infant's needs.

In addition to providing a source of nutrition for infants, breast milk contains a myriad of biologically active components. These molecules possess diverse roles, both guiding the development of the infants immune system and intestinal microbiota.

Orchestrating the development of the microbiota are the human milk oligosaccharides, the synthesis of which are determined by the maternal genotype. In this review, we discuss the composition of breast milk and the factors that affect it during the course of breast feeding.

Understanding the components of breast milk and their functions will allow for the improvement of clinical practices, infant feeding and our understanding of immune responses to infection and vaccination in infants.

Contents

Abbreviations: Group-B streptococcus, GBS; human milk oligosaccharides, HMO; secretory IgA, SIgA; toll-like receptor, TLR; Transforming growth factor beta, TGF-β.

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1. Introduction

Breast milk is an extremely complex and highly variable biofluid that has evolved over millennia to nourish infants and protect them from disease whilst their own immune system matures. The composition of human breast milk changes in response to many factors, matching the infant's requirements according to its age and other characteristics [1,2]. Therefore, the composition of breast milk is widely believed to be specifically tailored by each mother to precisely reflect the requirements of her infant [3].

The many antimicrobial and immunomodulatory components of breast milk are suggested to compensate for the deficiencies in the neonatal immune system, and impair the translocation of infectious pathogens across the gastrointestinal tract [4]. In addition, breastfed infants are also known to possess a more stable and less diverse intestinal microbiota than formula-fed infants, but possess more than twice the number of bacterial cells [5]. This may be partially due to alterations at the level of the gut mucosa due to bioactive substances in human milk.

Demonstrating the bioactivity of breast milk, a study on shed epithelial cells in the faeces of infants has shown that gene expression in the neonatal gastrointestinal tract is influenced by breastfeeding, with differential expression found between formula-fed and breast-fed infants in genes regulating intestinal cell proliferation, differentiation and barrier function [6].

Breast milk contains bioactive factors that are capable of inhibiting inflammation, as well as enhancing specific-antibody production, including the compounds PAF-acetylhydrolase, antioxidants, interleukins 1, 6, 8 and 10, transforming growth factor (TGF), secretory leukocyte protease inhibitors (SLPI) and defensin 1 [4]. Breast milk also contains factors with the potential to mediate the differentiation and growth of B cells, including high concentrations of intracellular adhesion molecule 1 and vascular adhesion molecule 1; and lower concentrations of soluble S-selectin, L-selectin and CD14 [4].

Additionally, pattern-recognition receptors, which are crucial factors in the recognition of microorganisms in the neonatal respiratory tract and gut, are present in breast milk. Factors such as the Toll-like receptors (TLR-2 and TLR-4) provide efficient microbial recognition, working in synergy with the co-receptor CD14 and soluble CD14, which are found in high quantities in breast milk [7]. Further regulation by soluble toll-like receptor 2 (sTLR-2), which regulates cell activation via cell surface TLR-2, has also been noted in breast milk but not in infant formula [8]. Similarly, an as-yet unnamed 80 kDA protein identified in breast milk appears to inhibit TLR-2–mediated but activates TLR-4–mediated transcriptional responses in human intestinal epithelial and mononuclear cells [9]. Reduced TLR-2 responsiveness at birth has been proposed to facilitate the normal establishment of beneficial microbiota such as bifidobacteria.

Various studies have examined the influences of maternal characteristics on breast milk composition. Important factors known to influence breast milk composition—such as the gradual increase in fat concentrations throughout a feed, have well-defined effects. However, other potential influences, such as the mode of delivery and maternal BMI, have less high-quality evidence supporting their role. The difficulties in accurately assessing the composition of breast milk (e.g. sampling time) hinder efforts to elucidate the true value of these effects. Furthermore, there is a profound lack of knowledge regarding how alterations in breast milk composition may subsequently impact infant and later health outcomes.

Metabonomics, the study of multiple metabolites in biofluids, using techniques including mass spectrometry and 1H NMR spectroscopy, is capable of measuring components in extremely low concentrations. This may assist in unravelling the factors influencing breast milk composition, as well as identifying previously unidentified components and their influence on human health [10,11].

In this review, we discuss the nutritional and non-nutritional components of breast milk and the effect of breast milk components on infant colonisation with potentially pathogenic bacteria and factors which are known to influence its composition.

2. Lipid

Lipids are the largest source of energy in breast milk, contributing 40%–55% of the total energy of breast milk [12]. These lipids are present as an emulsion. The vast majority of lipids secreted are triacylglycerides, contributing towards 98% of the lipid fraction. The remainder predominantly consists of diacylglycerides, monoacylglycerides, free fatty acids, phospholipids and cholesterol. These components are packaged into milk fat lipid globules, with the phospholipids forming the bulk of the membrane of the globules and the triacylglycerols found in the core [13] (Fig. 1). These globules usually range from 1 to 10 μm across, with an average diameter in mature milk of 4 μm [14].

Breast milk contains over 200 fatty acids; however, many of these are present in very low concentrations, with others dominating. For example, oleic acid accounts for 30–40 g/100 g fat in breast milk [16]. De novo synthesis of fatty acids accounts for approximately 17% of the total fat in breast milk [17]. Long-chain polyunsaturated fatty acids, molecules with a chain length of more than 20 carbon atoms—plus 2 or more double bonds—constitute ~2% of the total fatty acids present in breast milk [18].

The positions occupied by fatty acids along the glycerol backbone are highly conserved, with the fatty acids commonly appearing in specific positions [19] (Fig. 2). For example, fatty acids present in the highest concentrations in breast milk; oleic, palmitic and linoleic acid, are commonly found at the sn-1, sn-2 and sn-3 positions, respectively [19]. Interestingly, the distribution of fatty acids along glycerol influences their availability; with palmitic acid at the sn-2 position being absorbed more readily. Significantly, this positional preference is not replicated by many artificial formulas, and has been observed to influence the infants' plasma lipid profile, including cholesterol concentration [20].

Short-chain fatty acids (SCFA) found in breast milk are also an important source of energy [22], as well as being essential for normal maturation of the gastrointestinal tract [23]. Sphingomyelins, present in the milk fat globule membrane, are especially important for central nervous system myelinisation, and have been shown to improve the neurobehavioral development of low-birth weight infants [24].

Breast milk lipids have been shown to inactivate a number of pathogens in vitro, including Group B streptococcus (GBS). This suggests

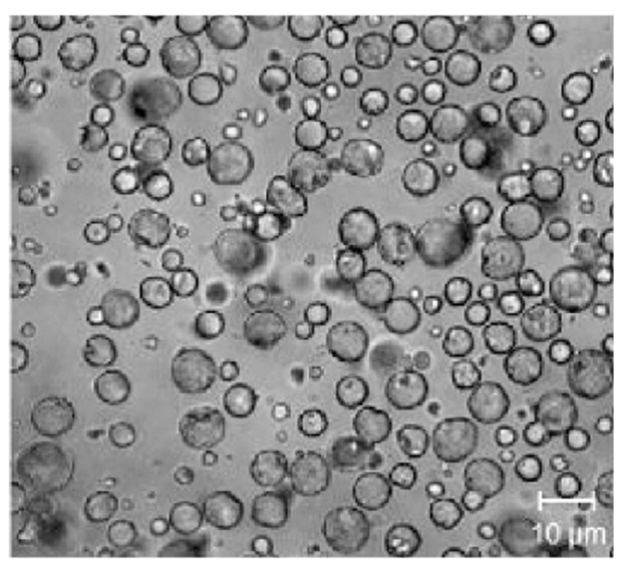

Fig. 1. An optical microscopy image of milk fat lipid globules, displaying the structure of milk. Adapted with permission from ref. [15], American Chemical Society.