



Gangliosides

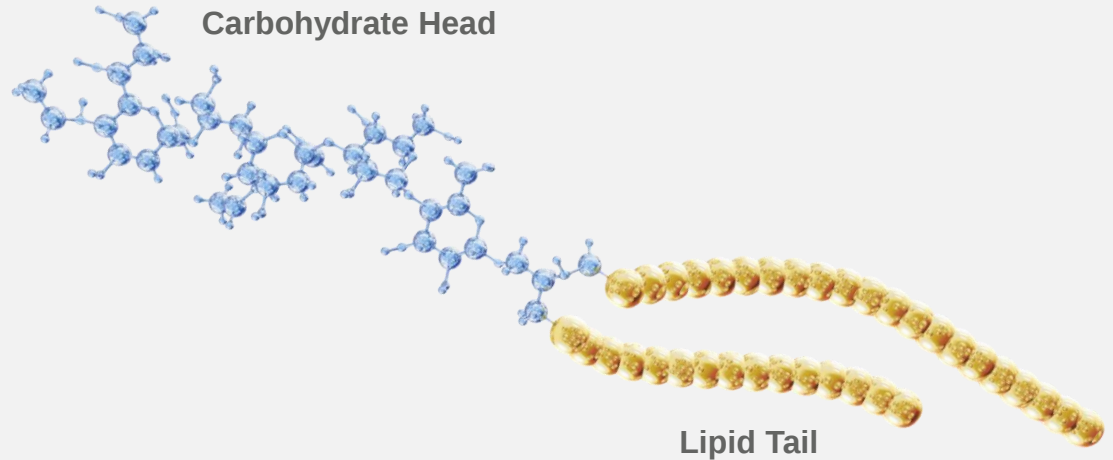
The role of biological and functional components of milk on infant development

Ryan Carvalho

Gangliosides

Structure

- Complex molecule with a unique structure composed of¹:
 - A complex carbohydrate: oligosaccharide linked to sialic acid
 - A lipid: sphingolipid (fatty acids plus sphingosine)



Molecule reconstructed

Gangliosides

GAs are also important in neurological development, memory formation, and synaptic signal transduction,

Implicated in regulating the immune system and supporting gut maturation in the newborn

McJarrow, P.; Schnell, N.; Jumpsen, J.; Clandinin, T. Influence of dietary gangliosides on neonatal brain development. *Nutr. Rev.* **2009**, 67, 451–463. [[CrossRef](#)]

Rueda, R. Gangliosides, immunity, infection and inflammation. In *Diet, Immunity and Inflammation*; Calder, P.C., Yaqoob, P., Eds.; Woodhead Publishing Ltd.: Cambridge, UK, 2013.

Sonnino, S.; Mauri, L.; Ciampa, M.G.; Prinetti, A. Gangliosides as regulators of cell signaling: Ganglioside-protein interactions or ganglioside-driven membrane organization? *J. Neurochem.* **2013**, 124, 432–435.

Geographic variation in breast milk ganglioside profiles

The average total GA (TGA) concentration measured in the UAE mothers' transitional milk (21.2 ± 11.46 mg/L) and mature milk (20.2 ± 9.8 mg/L) was not significantly different ($p > 0.05$) across the two-time points.

However, the relative distribution of ganglioside classes, GD3 and GM3, changed across the two-time points from 56% and 44%, respectively, for transition milk, to 9% and 91% respectively, for mature milk, with both GM3 and GD3 showing significant changes in concentration.

Geographic variation in breast milk ganglioside profiles – Middle East, Global data

Time Point	Gangliosides		
	GM3	GD3	Total GA
Transitional (<i>n</i> = 41)	9.47 ± 8.37 ^a (45%)	11.71 ± 9.46 ^a (55%)	21.18 ± 11.46 ^a
Mature (<i>n</i> = 40)	18.62 ± 9.69 ^b (92%) #	1.57 ± 2.24 ^b (8%) #	20.18 ± 9.75 ^a

Reference	Milk	<i>n</i>	GM3	GD3	Total GA
Giuffrida et al. [40] China	Colostrum/Transition (0–11 days)	450	3.8 ± 0.4 (47)	4.3 ± 0.9 (53)	8.1
Ma et al. [34] Malaysia	Transition	12	8.3 ± 4.8 (44)	10.6 ± 4.3 (56)	18.9 ± 6.6
This Study UAE	Transition (5–15 days)	41	9.5 ± 8.4 (45)	11.7 ± 9.5 (55)	21.2 ± 11.5
Ma et al. [34] Malaysia	Mature (6 months)	42	21.4 ± 13 (85)	4.3 ± 5.5 (15)	25.3 ± 15.7
Ma et al. [35] China	Mature (6 months)	20	21.4 ± 9.5 (93)	1.5 ± 1.4 (7)	22.9 ± 9.9
This Study UAE	Mature (6 Months)	40	18.6 ± 9.7 (92)	1.6 ± 2.2 (8)	20.2 ± 9.8

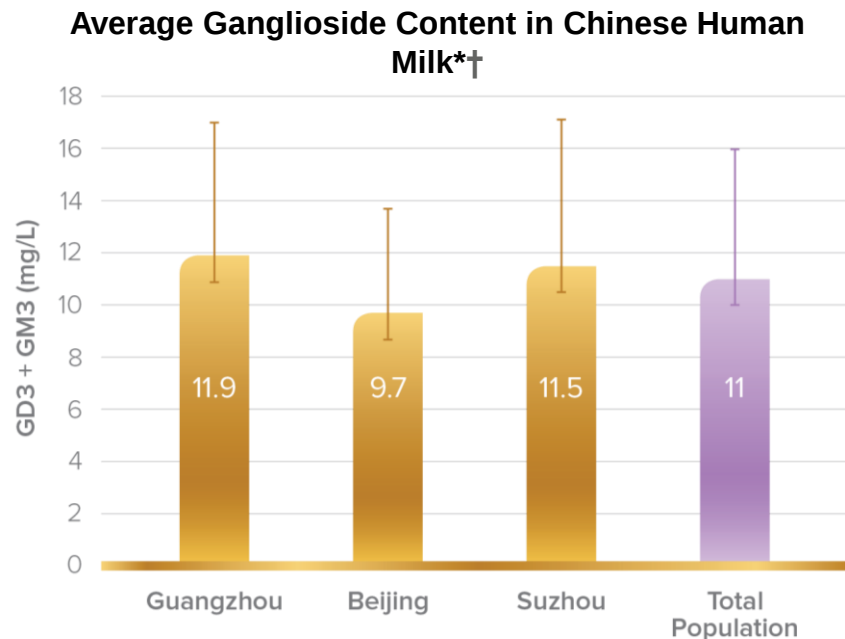
Breastmilk Naturally Contains Gangliosides

The two major gangliosides found in breastmilk are GD3 and GM3¹:

GD3 is more predominant in colostrum

GM3 is more predominant in mature milk

The average ganglioside content is approximately 11 mg/L²⁻⁴



*Mature milk (N = 345).

†Levels are comparable to min/max values from other publications.²⁻⁴

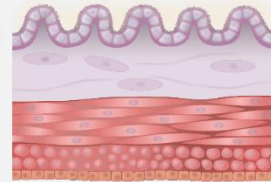
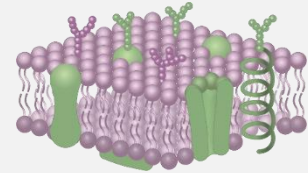
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- Complex molecule with a unique structure composed of¹:
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Location in the Body

- Widely distributed throughout the body²:
 - Integral to the structure and function of cell membranes²
 - Abundant in the brain³⁻⁶
 - Found in the intestinal wall of the gut³⁻⁸



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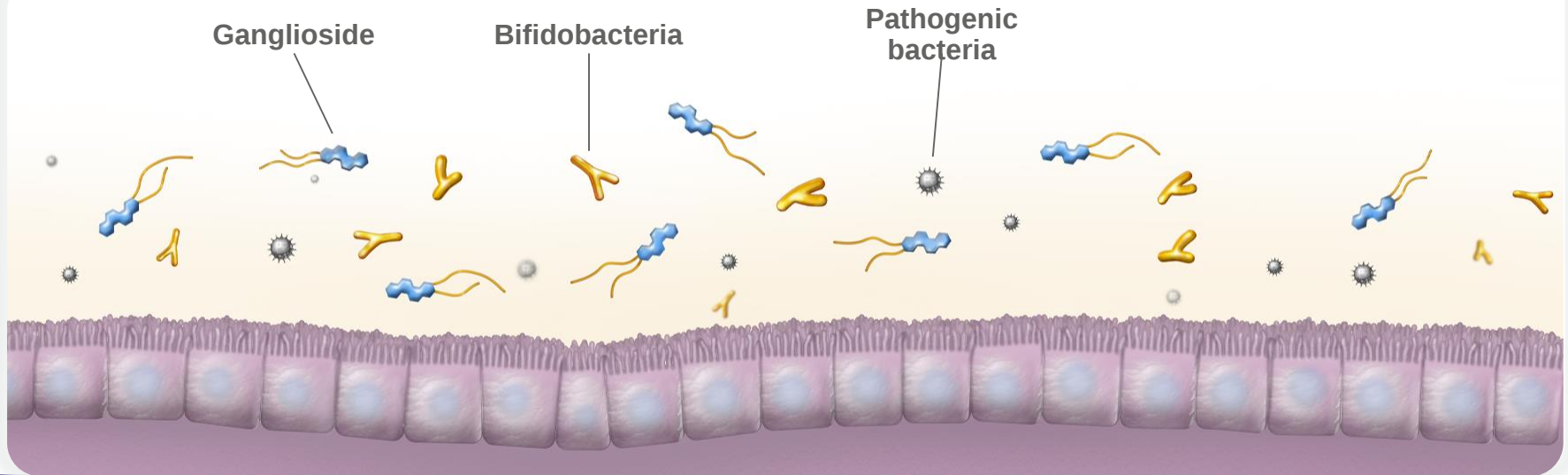
Source

- Produced endogenously (naturally by the body)^{2,9}
- Obtained from the diet, such as through breastmilk^{2,9}

Gangliosides Are Thought To Play An Important Role In Intestinal Immunity: Promote a Healthy Microbiota¹⁻⁷

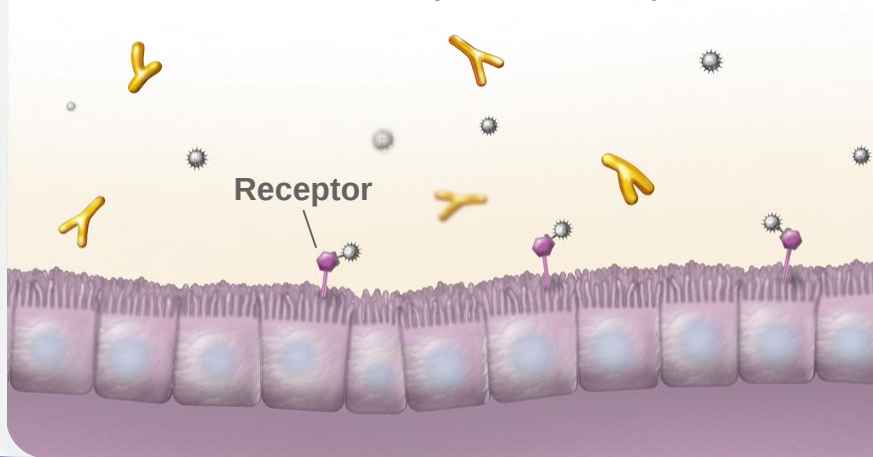
Resist digestion and reach the intestinal tract intact⁸

May guide the composition of the microbiota in the gut



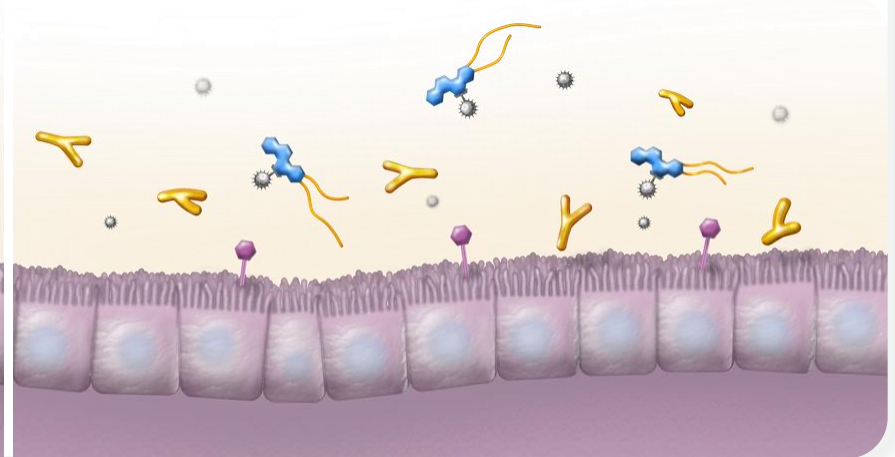
Gangliosides Are Thought To Play An Important Role In Intestinal Immunity: Prevent Pathogen Adherence¹⁻⁷

- The gut is a major site of contact with pathogens as it is a frontline barrier to limit pathogenic bacteria from invading the host⁸⁻¹⁰
- Pathogens want to attach, colonize, and invade the host—to attach, they bind to receptors in the



gut¹⁻⁵

- Gangliosides may act as decoys, as they look structurally similar to the receptors, interfering with pathogen binding¹⁻⁵



Scientific Review Papers

Several review papers have explained the potential mechanism by which gangliosides may impact gut health and immunity

Rueda (2007)

- Play a role in immunity and prevention of infection by¹:
 - Acting as a decoy and interfering with pathogen binding in the intestine
 - Modifying the gut microbiota and promoting intestinal immune development

Garrido et al. (2013)

- Guide the composition of the developing infant's intestinal microbiota by²:
 - Preventing the colonization of enteric pathogens
 - Providing a source of energy for commensal bacteria in the gut

Nilsson (2016)

- May have multiple effects, including³:
 - Influencing gut microbiota
 - Interacting with pathogens
 - Affecting mucosal epithelial and immune functions

Observational Study

An observational study of healthy term, exclusively breastfed infants found that ganglioside levels are¹:

Associated with higher bifidobacteria in infant stools

- Higher *Bifidobacterium* ($\rho = 0.37$, $P = 0.02$)*

Negatively correlated with potentially pathogenic bacteria

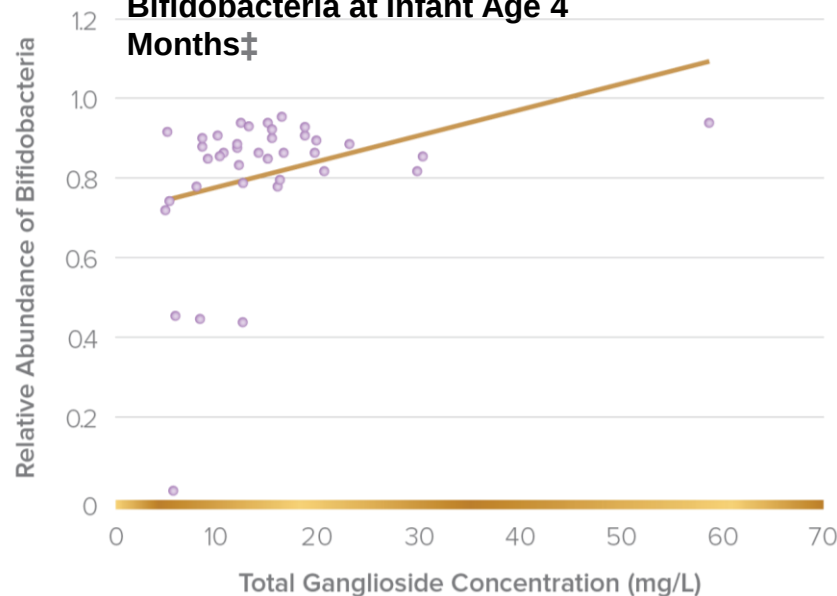
- Lower *Clostridium* ($\rho = -0.36$, $P = 0.03$)*
- Lower *Citrobacter* ($\rho = -0.34$, $P = 0.03$)†
- Lower *Streptococcus* ($\rho = -0.36$, $P = 0.02$)†

Suggests gangliosides in breastmilk play a role in modulating infant gut microbiota

*At age 4 months.

†At ages 21–26 days and 1.5 months.

Total Gangliosides Are Correlated with Bifidobacteria at Infant Age 4 Months‡

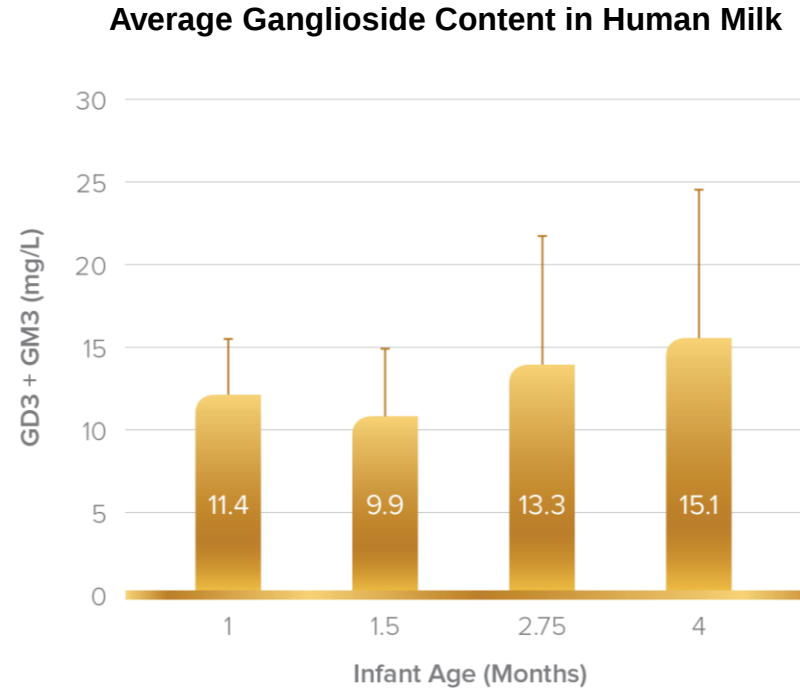


‡By Spearman's correlation coefficient, $P = 0.02$.

Observational Study

The study also found that the mean level of total gangliosides (GD3 and GM3) in breastmilk ranged from 9.9–15.1 mg/L¹

Similar to previously reported levels in breastmilk²⁻⁵



Clinical Study

A clinical study in premature infants fed formula supplemented with dietary gangliosides showed^{1,2}:

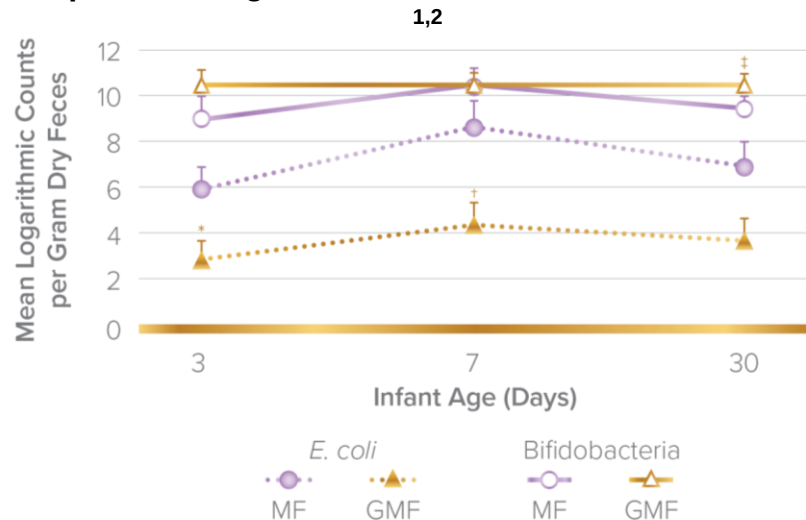
An increase in bifidobacteria

A reduction in pathogenic gut bacteria (fecal *E. coli*)

Although the fecal microbiota is known to be different in preterm infants, these results are supportive of the mechanism of action

Ganglioside supplementation similar to amount in illuma per 100 kcal

Impact of Gangliosides on Bifidobacteria and *E. coli*



Results are means $\pm$ SEM. Twenty samples were analyzed for each feeding group. Samples were collected at 3, 7, and 30 days of life.^{1,2}

MF = Milk formula; GMF = Milk formula with gangliosides 1.43 mg/100 kcal.

* $P < 0.01$ (versus MF group); † $P < 0.001$ (versus MF group); ‡ $P < 0.05$.

Summary

Gangliosides are complex bioactive lipids, naturally found in breastmilk
Gangliosides are integral to the structure and function of cell membranes
They are widely distributed throughout the body, including the gut

Gangliosides are thought to promote a healthy gut microbiota and may act as a decoy to help prevent pathogens from attaching to the intestine

These bioactive molecules are one of the ways breastmilk may support baby's inner defenses

The presence of gangliosides in infant formula brings the composition closer to that of breastmilk

More data is needed to better understand the functional benefits