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SIALIC ACID

Sialic acid is a general term for a family of 9-carbon monosaccharides. The most common form in humans is N-Acetylneuraminic Acid (Neu5Ac) abbreviated as NANA. Other forms are found in nature.

Sialic acid is not often found on its own. It is commonly bound to oligosaccharides and glycoconjugates such as glycoproteins and glycolipids.

Sialic acid is not generally found in invertebrates, plants, and prokaryotes. Most frequently identified in vertebrates, it is present in a number of tissues and secretions. In humans, it is found in the brain, body fluids, (e.g. serum, saliva, milk, urine) and other tissues. Sialic acid can be synthesized in the liver from sugar precursors. [1, 5]

1. Sialic acid and the human brain

The adult human brain contains concentrations of sialic acid that are 2 to 4 fold higher than those of other mammals. Neural cell membranes contain 20 times more sialic acid than other types of membranes. [2, 5]

- Brain gangliosides are especially rich in sialic acid. Gangliosides are complex glycolipids distributed in tissues, body fluids and especially neural tissues. They make up 10% of the lipid mass of the brain. They are located on neuronal and especially synaptic membranes. They are thought to play a role in the structural and establishment of synaptic pathways. [5]

- In addition, it is thought some brain glycoproteins containing sialic acid are involved in memory formation. [5]

2. Sialic acid and human milk

Sialic acid appears to be important during pregnancy and lactation. Serum levels increase during the late stage of pregnancy. There is also a high content of sialic acid in colostrum. The total sialic acid level in human milk decreases over time (by 70% over the first 3 months of lactation). There appears also to be a great variability of sialic acid content in human milk between mothers. Accordingly, sialic acid appears to be one of the most variable components of human milk. [2]

Sialic acid is found mostly bound to oligosaccharides in human milk [2]:

- 69-79% bound to free oligosaccharides
- 21-28% bound to glycoproteins
- 3% in free form

It is to be noted that sialic acid is found in lower concentration in cow's milk and that 5 to 35% of the sialic acid found in cow's milk is of a different form than NANA. In addition, sialic acid is mainly bound to glycoproteins rather than oligosaccharides. [2]

Because of its presence in the human brain and human milk, sialic acid is thought to be a potentially important element, among others, for the infant brain development. In addition, it is postulated that infants may not be able to sufficiently or efficiently synthesise sialic acid because of the immaturity of their liver.

3. Infants' ability to synthesise sialic acid

Livers of all mammals have the capacity to synthetise sialic acid from sugar precursors. However, some elements tend to suggest infants may not be able to synthetise sufficient sialic acid important for the rapid growth of the brain. [2]

The results of a study carried out by Tram et al (1997), showed higher levels of sialic acid in the saliva of breast fed infants compared to formula fed infants. This study tends to suggest that supplementary sialic acid from breast milk was assimilated by breastfed infants where formula fed infants neither had sufficient sialic acid from their dietary intake nor were they able to produce similar levels endogenously. [3]

In young rats, it has been shown also that the activity of a key enzyme in the production of sialic acid is initially low. Other animal studies tend to indicate enzyme activity is correlated with age and development stage. [5]

4. Absorption of exogenous sialic acid

Free sialic acid has been shown to be well absorbed in rats (90% absorbed, 30% retained in the body and 3-4% in the brain after 6 hours). It has been shown that exogenous sialic acid administered orally and intraperitoneally increases brain ganglioside sialic acid. [2, 5]

Timing appears to be critical because studies in older animals do not show a similar level of incorporation after acute dosing of sialic acid. [2]

The study by Tram et al (1997) suggests also that dietary sialic acid, which is mainly bound to oligosaccharides and glycoproteins in breast milk, is absorbed by infants.

However, the mechanisms for its release and absorption when bound to oligosaccharides and other glyconconjugates are not well known yet. [5]

Oligosaccharides resist digestion in the small intestine and are fermented in the colon. Sialic acid occupies the terminal position of milk oligosaccharides, and the bond may be cleaved by sialidase even if the remainder of the chain resist digestion. However, some studies in vitro did not show the release of sialic acid when oligosaccharides where incubated with pancreatic and mucosal enzyme mixtures. [5]

5. Sialic acid roles and functions

Sialic acid is a structural element of complex molecules such as oligosaccharides and glycoconjugates which have a wide range of functions and roles. Sialic acid may not just be a structural element; it may also have specific functions.

- As mentioned in previous paragraphs, sialic acid is an important structural and functional component of the brain gangliosides. [5]

- Sialic acid is a structural component of oligosaccharides and glycoconjugates which have a wide range of functions:
    - some oligosaccharides and glycoproteins can prevent bacterial agents from binding to cell surfaces. They are important in preventing infections. [1, 5]
    - some glycoproteins can bind with vitamins (e.g Vitamin B12), making them more bioavailable. [1]
    - some glycoconjugates on cell surfaces play a role in cellular recognition.[1]

- In addition, cell surface sialic acid may be important in protecting against bacterial colonisation due to its ability to modulate cell aggregation and attachment. [1]

- It may play a role in the regulation of synthesis of glycoproteins and appears to function in immune modulation. [1]

KEY POINTS

1. Sialic acid is present in human milk.
2. Sialic acid is found in high concentrations in brain gangliosides which are thought to be important structural and functional elements of the human brain.
3. It is hypothesised that infants may not be able to sufficiently or efficiently synthetise sialic acid because of the immaturity of their liver. Consequently, supplementary sialic acid from the diet may be important in providing sufficient amounts important for the development of infants.

However, there are still a number of questions to be answered. Further studies are required to better understand absorption mechanisms, metabolic fate and nutritional importance. Sialic acid may be associated with a number of important functions which are still currently unknown or not well understood.

References:

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