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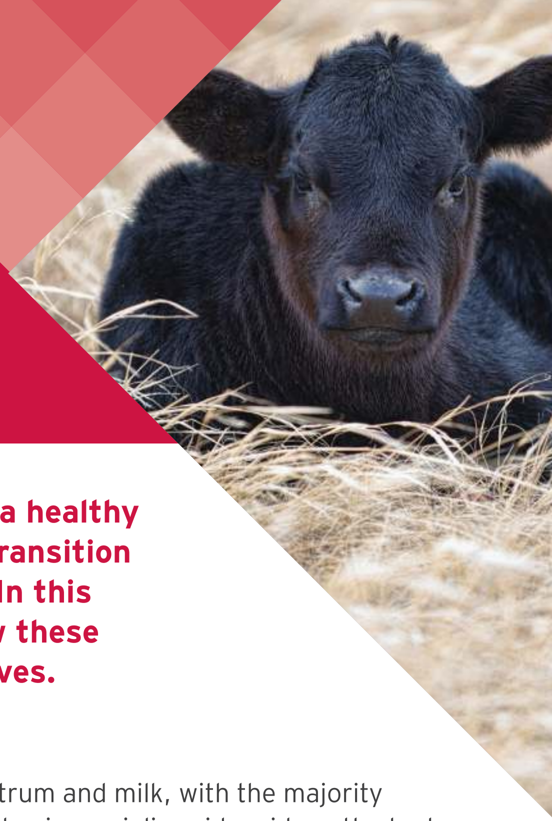
The Colostrum Counsel



Did you know other factors beyond IgG can attribute to a healthy gut in your calves? Oligosaccharides in colostrum and transition milk serve as potential mediators of a healthy calf gut. In this issue of The Colostrum Counsel, we will explain just how these factors work in optimizing the overall health of your calves.

The Colostrum Counsel: Oligosaccharides Explained

Calves rely on the timely feeding of good-quality colostrum to provide them with passive immunity, since there is no transfer of immunoglobulins from the dam to the calf in utero. Due to the importance of passive immunity, most research in bovine colostrum and transition milk has focused on the quantity and quality of IgG. Yet, colostrum is also rich in additional nutrients and bioactive factors that are necessary for the proper development and maturation of the gut. These factors are just beginning to gain popularity in the field of colostrum research. Among these bioactive factors are oligosaccharides (OS). These molecules are essentially "simple sugars" and have been hypothesized to play a key role in the development of the newborn gut. In particular, OS help establish healthy gut bacteria, inhibit pathogenic bacteria, and may also enhance the absorption of IgG from colostrum into the blood.

Structures and Concentrations in Colostrum

As mentioned previously, OS are simple-sugar compounds with lactose being the core structure of all OS. In order to create structurally different molecules, fucose (neutral charge) or sialic acid (acidic charge) residues are added onto the lactose core in the mammary gland. Approximately 40 different OS compounds have been identified in bovine colostrum and milk, with the majority (>70%) of bovine OS having a sialic acid residue attached (Tao et al., 2008; Figure 1). Bovine OS are different from OS produced by humans, as the carbon chains of human OS are longer and only a small amount (5-15%) have a sialic acid group attached (Ninonuevo et al., 2006).

The most abundant OS in bovine colostrum is 3'sialyllactose (3'SL), which is 4 times higher in colostrum compared to mature milk, followed by 6'sialyllactosamine (6'SLN) with the second highest concentration (Martin-Sosa et al., 2003; Figure 1). In contrast to IgG, the concentrations of OS do not decline as rapidly after the colostrum milking. In fact, it has been shown that 3'SL, 6'SLN and 6'sialyllactose (6'SL) have higher concentrations at 2 days after calving compared to 7 days after calving (Nakamura et al., 2003; Figure 2).

The majority of farms often feed 1-2 meals of colostrum after birth, followed immediately by an abrupt transition to milk replacer or whole milk. The elevated concentrations of OS, along with an abundance of additional bioactive molecules in transition milk (milkings 2-6) demonstrate that there is likely value in feeding transition milk to the gut health of young calves on farm.

Functions of Oligosaccharides

The majority of OS can reach the intestine quickly since they can resist the acidic pH of the stomach and cannot be broken down by any of the calf's gut enzymes. Most researchers assumed the majority of the OS would reach the large intestine in tact, however Janschter-Krenn et al. (2013) demonstrated these compounds can actually change structure and may play a role in the small intestine as well. So, what exactly are these small simple sugars doing in the small and large intestines?

Energy Source for Healthy Gut Bacteria

Several beneficial groups of bacteria in the small intestine and colon have a variety of enzymes that allow them to break down OS and utilize them as an energy source. It has been shown that the beneficial bacteria Bifidobacteria can consume 3'SL, the major OS in bovine colostrum, to promote its growth (Yu et al., 2013). Moreover, recent studies demonstrated that newborn calves have a higher amount of Bifidobacteria in the small intestine when higher concentrations of OS are provided in colostrum (Fischer et al., 2018; Malmuthuge et al., 2015).

A higher amount of Bifidobacteria in the calf intestine likely contributes to an overall healthy gut bacterial community, since they are able to produce short chain fatty acids that have positive effects on colon cells, as well as stabilize the gut mucosal barrier and improve the immune system of the gut to prevent the overgrowth of pathogenic bacteria (Picard et al., 2005; Yasui et al., 1995; Boffa et al., 1992). Additionally, another beneficial group, known as Bacteroides, can uniquely use the sialic acid portion of the OS to promote their growth and establishment in the neonatal gut (Marcobal et al., 2011).

Inhibition of Pathogenic Bacteria

In addition to promoting the growth of beneficial bacteria, OS have also been shown to prevent pathogenic bacteria from establishing themselves in the gut. In order to invade the host tissues, pathogens must bind to sugars that are structurally similar to OS, known as "host glycans", on the surface of intestinal cells. Since the structures of glycans and colostrum and milk OS are so similar, OS can act as "receptor decoys" and bind to the pathogen. This inhibits their ability to bind to the host and cause subsequent infection and disease (Zivkovic et al., 2011). Specifically, it has been demonstrated that two of the major OS in bovine colostrum and transition milk, 6'SL and 6'SLN, can block the binding of enterotoxigenic E. coli (Martin et al., 2002). Additional colostrum and milk OS can also bind to rotavirus (Huang et al., 2012), Vibrio cholera (Coppa et al., 2006), and Streptococcus pneumoniae (Andersson et al., 1986), which demonstrates their diverse capability to maintain a healthy and balanced gut microbial community.

Enhance Immune Function

As mentioned previously, beneficial gut bacteria can utilize colostrum and milk OS, which allows them to positively regulate the immune system through multiple pathways. For instance, bacteria that consume OS induce higher expressions of anti-inflammatory compounds and decrease pro-inflammatory compounds, compared to bacteria that consume an alternative energy source (Chiclowski et al., 2012). Bacteria that grow on OS can also up-regulate the amount of tight junction proteins between intestinal cells, which basically means they "tighten" the gaps so pathogenic bacteria cannot go between the intestinal cells and enter the blood stream (Chiclowski et al., 2012; Ewaschuk et al., 2008).

One fascinating aspect about the sialic acid portion of an OS is when sialic acid is bound to the intestine, it can actually enhance the binding of IgG to the intestinal cell, as well as its uptake into the cell (Gill et al., 1999). This may explain why bovine colostrum has such a high abundance of OS with sialic acid residues compared to human colostrum, in which only a small portion have sialic acid. In humans, there is passive transfer of immunoglobulins during pregnancy from the mother to the fetus, where as in bovine animals, the calf can only obtain IgG from colostrum since there is no passive transfer during pregnancy. Therefore, since the passive transfer of IgG is one of the most important factors in promoting the health and survival of the newborn calf, the high abundance of sialic acid in colostrum may actually be present to assist IgG in gaining access to the calf's blood stream¬–kick-starting the immune system.

What about mannan-oligosaccharides?

Mannan-oligosaccharides (MOS) are frequently supplemented to the calf in milk replacer (e.g. Bio-Mos®) during the first weeks of life. In contrast to bovine-derived OS, mannan-OS are derived from the cell wall of yeast, namely Saccharomyces cerevisiae. Mannan-OS have "brush-like" structures which allow them to attach to pathogenic bacteria, such as Salmonella and E. coli, thus blocking them from binding to the intestinal cell wall and causing subsequent infection. Calves fed MOS in milk replacer show a reduction in faecal E. coli counts (Jacques et al., 1994), improvements in fecal score (Morrison et al., 2010), and better growth performance (Sellars et al., 1997).

Due to the positive effects observed when supplemented in milk replacer, researchers sought out to determine if similar effects might also be seen when supplemented in colostrum or colostrum replacer. Unfortunately, a study that supplemented MOS in colostrum replacer found no effect on passive transfer at 24h of life, or on the incidence of disease (Robichaud et al., 2014).

Moreover, additional recent studies that supplemented MOS in fresh bovine colostrum actually found a negative effect on passive transfer when compared to calves fed unsupplemented colostrum (Brady et al., 2015; Short et al., 2016). The structure of an oligosaccharide is a major determinant of biological function and the calf gut is evolutionarily tailored to respond to compounds secreted by the dam into colostrum. Since bovine-derived OS are "more natural" for the newborn dairy calf, it may be possible that their supplementation during the first days of life may lead to increased passive immunity and better gut health when compared to those supplemented with MOS.

Take Home Message

The high abundance of oligosaccharides produced by the dam into colostrum and transition milk can have positive effects on gut health, specifically by acting as an energy source for healthy gut bacteria, inhibiting pathogens, and by enhancing the immune system. Therefore, feeding transition milk or milk supplemented with a quality colostrum replacer may offer increased gut protection for the newborn calf. Additional research should focus on the possibility of supplementing OS in traditional milk replacers, or even in whole milk, to ensure maximum protection of the newborn calf gut.

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Figures

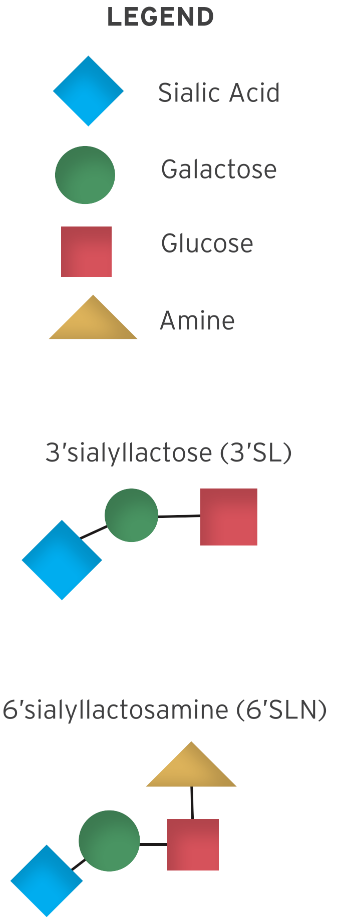

Figure 1.

The structures of the two most abundant oligosaccharides in bovine colostrum and transition milk.

Figure 2.

A study conducted by Nakamura et al. (2003) determined the concentrations of the primary oligosaccharides (3’SL, 6’SL and 6’SLN) in colostrum, transition milk, and mature milk.

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Amanda graduated from the University of Alberta with a Masters of Science, specializing in the effects of current colostrum management practices on the health of the newborn dairy calf. Amanda plays a role as an author and editor of The Colostrum Counsel and is also a research assistant at the University of Alberta with a focus on strategies to maximize the health and productivity of young dairy calves.