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Review: Mammary gland physiology and modulation during colostrogenesis in dairy goats ☆

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ABSTRACT

Newborn ruminants are highly dependent on the intake of high-quality colostrum immediately after birth to obtain energy and achieve an appropriate immunisation. Previous research indicates that poor management practices in the last months of gestation can lead to increased neonatal mortality rates by reducing colostrum quality among other factors. In ruminants, colostrum synthesis is a well-preserved mechanism which has been speculated to be regulated by the neuroendocrine system. However, this review aims to explore different approaches such as alternative dry-off management practices, the inclusion of different nutrients on prepartum diets, and the stimulation of the mammary gland immune response to modulate colostrogenesis and consequently, to enhance colostrum quality. Ensuring correct dry-off practices combined with controlled dietary supplementation can support mammary gland reorganisation and potentially modulate colostrogenesis. Despite positive effects on colostrum yield, the bioactive composition of colostrum seems to be irresponsive to prepartum energy, protein, and fat supplementation in dairy goats. On the other hand, mastitis has obvious negative effects on animal health; however, an experimentally induced local inflammation seems to trigger helpful modifications on the blood-milk barrier, enhancing the concentration of some immune components (i.e., immunoglobulin G and M) in goat colostrum. Yet, most research has focused on dairy cattle, leaving a significant knowledge gap on colostrogenesis in small ruminants. Therefore, future studies should focus on developing novel dry-off and dietary strategies to not only promote a healthy lactation but also to guarantee a successful colostrum synthesis.

Implications

Adequate management practices during the dry period are essential to ensure a successful colostrum synthesis. Newer approaches based on reducing milking frequency before the dry period and increasing energy supply or applying melatonin implants during the last month of gestation, combined with an induced immune response within the mammary gland seem to be effective strategies to enhance colostrum quality and yield. Increased colostrum quality will improve the transfer of passive immunity from dams to newborns, increasing the health status and performance of the offspring, which in turn will promote a better performance in their adult life.

Introduction

The dairy goat industry faces important challenges such as reduced feed sources and pastures caused by droughts, the rise of feed prices or the widespread infectious diseases. All these aspects have considerable negative effects on animal performance. However, dairy goat producers have also identified neonatal mortality as a major economic and welfare issue (Rätsep, 2020). Goat kid mortality within the first week of life is commonly associated with the presence of pneumonia, diarrhoea, or starvation among other health issues. Despite the timing of kid mortality still not being well-defined, most losses have been observed in animals with birth BW < 2.5 kg and within the first days of life (Bajhau and Kennedy, 1990), as those animals often show reduced blood immunoglobulins concentrations within the first 84 h of life (Zamuner et al., 2023a, b; Argüello et al., 2004). Consequently, these animals have greater susceptibility to infections, which in turn increases mortality rates. Several studies reported preweaning goat kid mortality across the world ranging between 4.3 and 57.7%

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(Table 1). This mortality rate is highly influenced by multiple factors such as management system, dam health, birth BW, litter size, season (i.e., low ambient temperatures), and successful immunisation after colostrum intake (Chowdhury et al., 2002; Mota-Rojas et al., 2022; Perez-Razo et al., 1998; Robertson et al., 2020). However, literature regarding neonatal mortality in the dairy goat sector across Europe is scarce, making it difficult to assess and compare results among countries.

Unlike other mammals, ruminants do not transfer enough maternal immune components to their offspring during gestation (Bigler et al., 2022; Green et al., 2021). As a result, newborn ruminants are strictly dependent on colostrum intake, not only as a source of nutrition but also for acquiring essential immune components. During the first hours of life, foetal enterocytes allow a non-specific absorption of macromolecules (Weström et al., 2020). However, these cells will be gradually replaced by mature enterocytes which leads to reduced intestinal permeability, also known as gut closure (Castro-Alonso et al., 2008; Moretti et al., 2012, 2013). Additionally, enterocyte proliferation and apoptosis are regulated by growth factors (i.e., insulin-like growth factors, transforming growth factors-β) and hormones (i.e., leptin, ghrelin) present in colostrum, proving its role in the development of the intestinal tract (Godlewski, 2011). Thus, good colostrum quality must be fed shortly after birth to promote a successful transfer of passive immunity (**TPI**).

As colostrum is one of the main factors affecting goat kid mortality, several studies have been conducted to define its quality. Colostrum quality can be primarily determined by its immunoglobulin G (**IgG**) concentration, which is considered the main parameter responsible for a correct TPI. Literature describes several techniques used to measure IgG concentration in colostrum, including laboratory assays such as radioimmunoassay, electrophoresis, radial immunodiffusion, and enzyme-linked immunosorbent assay (Weaver et al., 2000). Additionally, on-farm practical estimation methods such as colostrometers (Bartier et al., 2015), optical or digital refractometers (Castro et al., 2018; Pérez-Marín et al., 2023) and visual colour assessments (Argüello et al., 2005) are also available. These approaches provide both, precise analyses and accessible on-farm tools enabling researchers and farmers to effectively evaluate colostrum quality.

Despite most colostrum research on dairy ruminants has been performed on dairy cows, there is no clear definition of colostrum quality in this species as it differs significantly between species and breeds (Nowak and Poindron, 2006; Stelwagen et al., 2009; Wheeler et al., 2007). A similar situation has been showed on colostrum research performed on dairy goats (Agradi et al., 2023; Kessler et al., 2019; Torres et al., 2013). Currently, cut-off values to define good quality colostrum have been set as ≥ 50 mg/mL of IgG in cattle (Weaver et al., 2000), and ≥ 20 mg/mL of IgG in goats (Argüello et al., 2005; Castro et al., 2005; Kessler et al., 2021). Yet, no cut-off values have been stablished for sheep colostrum IgG concentration. Defining clear thresholds, analogous to those in dairy cattle has become essential for improving colostrum management practices in small ruminants, which have been reviewed by Castro et al. (2011b) and Fischer-Tlustos et al. (2021). In calves, IgG and serum total protein concentrations ≥ 10 mg/mL and ≥ 6.2 g/dL, respectively, and ≥ 15 mg/mL and ≥ 4.6 g/dL in lambs and goat kids have been widely accepted as cut-off values for successful passive transfer of immunity (Lombard et al., 2020; Weaver et al., 2000; Zamuner et al., 2023a, 2024), whereas concentrations below these thresholds generally indicate a failure of TPI. Additionally, different cut-off values for some on-farm tools such as Brix refractometry have been described as these values are highly correlated with colostrum and serum IgG concentrations (Kessler et al., 2021). According to the literature, colostrum Brix values ≥ 22° in cattle (Chigerwe and Hagey, 2014), ≥ 26° in sheep (Hamer et al., 2023) and ≥ 20° in goats (Kessler et al., 2021) are considered indicative of good quality colostrum. To summarise, the acquisition of a correct TPI (i.e., > 10 mg/mL of IgG in calves and > 11.4 mg/mL of IgG in goat kids; Weaver et al., 2000; Zamuner et al., 2023a) strictly depends on colostrum quality, timing of colostrum intake and intestinal permeability.

Colostrum also contains essential nutrients such as lactose and triglycerides that can be metabolised to produce energy and induce thermogenesis. Indeed, it has been demonstrated that rectal temperature in newborn calves increases within the first hours after colostrum consumption contributing to their survival under harsh environmental conditions (Kirovski, 2015). Colostrum also provides diverse bioactive molecules (i.e., immunoglobulins, growth factors, peptides, enzymes and hormones) which are either absorbed or act within the gut lumen during the first hours of life.

Table 1
Goat kid mortality rates before weaning.

Region/Country	Mortality rate, %	Breed	Management system	Reference
Africa				
Ethiopia	31 – 42	Arsi-Bale & Borana	Extensive	(Hailu et al., 2006)
Ghana	10	West African Dwarf	Intensive	(Turkson et al., 2004)
Morocco	16	Beni Arouss & Northen Morocco	Extensive	(Bahri et al., 2021)
South Africa	8.6–16.5	Angora	Extensive	(Snyman, 2010)
America				
Canada	20 – 30	Saanen & Alpine	Intensive	(Rätsep, 2020)
USA	10–14	n/s	n/s	(USDA, 2012)
Asia				
India	8.92–57.7	Sirohi & LB	Semi-intensive	(Chauhan et al., 2019) (Perumal et al., 2019)
Jordan	13	Crossbred Shami	Extensive	(Aldomy et al., 2009)
Sri Lanka	23.7–32.2	South Indian & LB	Extensive	(Ranatunga, 1971)
Europe				
Germany	16.1–24.1	Alpine & Saanen	n/s	(Balasopoulou et al., 2022)
Netherlands	4.3	n/s	Intensive	(Dijkstra et al., 2023)
Spain	21	MG & MG × Boer	Intensive	(Fernández et al., 2021)
Oceania				
Australia	20	Boer & Kalahari Red	n/s	(Robertson et al., 2020)
New Zealand	5.9–20.5	n/s	Intensive	(Todd et al., 2019)

Abbreviation: n/s = not specified; LB = local breed; MG = Murciano-Granadina.

These components are vital to ensure newborn survival, and its concentration depends on multiple factors such as species, breed, dam nutrition, and health status (Hernández-Castellano et al., 2016; Soufleri et al., 2021). Besides its effects on passive immunity, colostrum also promotes gastrointestinal tract development and health of newborn ruminants. According to Kargar et al. (2020) and McCarthy et al. (2024), an extended colostrum feeding during the first 2 weeks of life can increase daily weight gain and reduce diarrhoea and pneumonia susceptibility in dairy calves, whereas these effects in goat kids still need to be addressed. This time-sensitive process underlines the vital role of prompt colostrum intake to ensure the health status of newborn ruminants.

For all the above, low-quality colostrum can result in the failure of TPI, thereby increasing the risk of morbidity and mortality in newborn ruminants. This issue can be strongly linked to inadequate management practices in the last 2 months of gestation (Caja et al., 2006; Castro et al., 2011b; Weaver et al., 2021). During this period, also known as the dry period, the mammary gland ceases milk production and starts an involution which ultimately ends in colostrum synthesis, also known as colostrogenesis. This dry period is essential to not only ensure an optimal subsequent lactation but also the health status of the offspring. Therefore, this review aims to address the different factors that influence colostrogenesis during the dry period as well as summarise some novel approaches on colostrogenesis modulation which can impact colostrum quality in dairy goats.

Colostrum synthesis and the role of its bioactive components

Colostrum components are secreted by different mechanisms. The passage of components from blood into the mammary secretion can be either through cells mediated by vesicles, or paracellularly between cells (Lascelles, 1979). In goat colostrum, immunoglobulins represent approximately one-third of colostrum total proteins, mainly IgG (90.3%), immunoglobulin M (**IgM**; 6%) and immunoglobulin A (3.7%) (Rudovsky et al., 2008). There are two subclasses of IgG (i.e., IgG_1 and IgG_2), being IgG_1 the most abundant and representing between 95 and 98% of the total IgG concentration in colostrum (Micusan and Borduas, 1976). This subclass is present in blood and transferred into colostrum selectively by specific receptors such as the neonatal Fc receptor (**FcRn**; Lu et al., 2007; Sasaki et al., 1976, Sasaki et al. (1977)). However, another source of IgG besides blood appears to be present during colostrogenesis as total IgG in colostrum represents seven times the mass that is present in the individual cow blood (Baumrucker and Bruckmaier, 2014). Therefore, there is still some controversy about the origin of immunoglobulins in colostrum, as the mechanisms that regulate the transfer and local synthesis are still unknown. Other blood components can also reach colostrum through leaky tight junctions between epithelial cells (i.e., leukocytes; Wheeler et al., 2007). Plasma cells and lymphocytes in the mammary gland are able to synthesise and secrete immunoglobulins, cytokines, and enzymes with immunomodulatory activity (Hagiwara et al., 2008). For instance, the enzyme chitotriosidase synthesised by macrophages is capable of hydrolysing chitin present in the cell wall of fungi and nematodes (Hollak et al., 1994; Renkema et al., 1995) as well as activating other immune cells such as Helper T cells and eosinophils (Wiesner et al., 2015). Interestingly, this enzyme has a greater activity in goat colostrum and blood after parturition compared to the following days postpartum (Argüello et al., 2008; Castro et al., 2011a) having a possible role in protecting both the dam and the newborn animal around parturition (Argüello et al., 2008). Other locally synthesised components such as oligosaccharides, lactoferrin, active peptides, and hormones can be also secreted into colostrum and seem to have a role in the protection of the newborn animal. For instance, colostrum oligosaccharides can promote the growth of beneficial bifidobacteria and improve gut health in calves, enhancing nutrient utilisation and ultimately, weight gain (Bunyatratchata et al., 2021). In fact, Marziali et al. (2018) described a decrease of oligosaccharides concentration in goat colostrum from 2.4 to 0.7 mg/mL during the first 4 days postpartum agreeing with previous studies performed in beef and dairy cows (Fischer-Tlustos et al., 2020). A similar trend is observed for lactoferrin, with significantly higher concentrations found in goat colostrum (i.e., 387–582 μg/mL) compared to whole milk (10–28 μg/mL; Hiss et al., 2008; Segura et al., 2024). This iron-binding glycoprotein is capable of binding soluble ferric ions with sufficient affinity to make it unavailable for bacterial growth, acting as a natural antimicrobial agent (Schanbacher et al., 1993). The greater concentrations of these bioactive molecules highlight the crucial role of colostrum in newborns' immunity and survival.

Additionally, new studies have focused on milk and colostrum exosomes (Sedykh et al., 2020). They are also known as extracellular vesicles and are considered mediators of cell-to-cell communication as they contain mainly signalling and transcription factors such as RNA and proteins (Doyle and Wang, 2019; Narang et al., 2022). Castro et al. (2024) and Ma et al. (2023) have studied exosomes in goat colostrum finding greater expression of microRNAs involved in cell proliferation, bone homeostasis, and nervous system development in neonates. It seems that the combined effects of these bioactive components may be responsible for the important benefits of colostrum on growth, gut development, and other important physiological functions for the newborn (Fischer-Tlustos et al., 2021). Yet, studies on goat colostrum bioactive components and its effects on the health and performance of the offspring are currently scarce.

Onset of colostrogenesis

In cattle, the onset of colostrogenesis occurs approximately 3–4 weeks before parturition (Brandon et al., 1971, 1975). During this period, about 40% of the total mass of IgG present in colostrum is transferred from blood to the secretion (Gross et al., 2014). Similarly, circulating IgG concentrations are reduced by 39.7% from the third month of gestation to 15 days before parturition in dairy goats (Castro et al., 2006), which supports the progressive transfer of maternal immune components from blood into colostrum. While multiple studies have investigated the physiological changes occurring during colostrum synthesis (Davis et al., 1979; Fleet et al., 1975; Fleet and Peaker, 1978), the specific molecular mechanisms regulating these changes have not been fully elucidated. During the dry period, there is an accumulation of nutrients and bioactive components that involve coordinated molecular mechanisms in which the neuroendocrine system plays an important role. Although endocrine pathways regulating colostrogenesis are not completely understood in ruminants, it seems that there is not a specific hormone controlling this process. Instead, colostrogenesis might be tightly regulated by several hormones which act in different stages of colostrum synthesis. It seems that the main factor contributing to the onset of colostrogenesis is the progressive reduction of circulating progesterone 2 or 3 weeks before parturition (Barrington et al., 2001). The decrease of progesterone concentrations occurs simultaneously with the increase of certain galactopoietic hormones (i.e., prolactin and placental lactogen) and oestrogens, which promote the transfer of IgG_1 into colostrum by increasing the FcRn receptor activity (Smith et al., 1971; Davis et al., 1979; Barrington et al., 2001). In fact, non-pregnant dry cows treated with a combination of oestrogen and progesterone for a week can synthetise a similar fluid in composition to bovine colostrum (Smith et al., 1971), suggesting that these hormones play a crucial role in initiating colostrogenesis, even in the absence of gestation. However, it must be considered that the isolated or combined role of certain hormones is not enough to fully trigger all physiological mechanisms involved in colostrum synthesis. Increased oxytocin before parturition also induces the impairment of tight junctions between mammary epithelial cells, enhancing the transfer of other immune components into colostrum (Wall et al., 2016). Additionally, the growth hormone has been also proposed to influence this process (Hadsell et al., 1993; Barrington et al., 2001) although the mechanism underlying this regulation is still not well-understood. Certainly, these hormones can regulate colostrogenesis through multiple pathways, not only through the modulation of receptors' activity but also through the activation of different transcription factors within the mammary epithelial cells (Topper and Freeman, 1980). The complex interaction between hormones, transcription factors, receptors, intracellular intermediates, and extracellular signalling molecules within the mammary gland is likely to trigger the molecular mechanisms responsible for colostrum synthesis (Akers, 2006; Groner, 2002).

As parturition approaches, colostrum becomes more liquid and edible due to the increase of prolactin concentrations (Gross et al., 2014; Lacasse et al., 2016) which leads to a greater uptake of glucose and a progressive increase of lactose synthesis contributing to the water accumulation in the mammary secretion (Davis et al., 1979; Bigler et al., 2023). Colostrogenesis will cease with the increase of hormones such as prostaglandin F2α and prolactin during the last days of gestation which are likely to determine the end of colostrum synthesis and the onset of milk production (Bigler et al., 2023; Gross et al., 2014). In fact, the induction of parturition using prostaglandin F2α analogues can result in reduced colostrum immunoglobulin concentrations in dairy cattle and goats (Field et al., 1989; Castro et al., 2011a). Similarly, the administration of glucocorticoids within 6–8 weeks before expected parturition in dairy cows can cease completely the IgG transfer to colostrum (Brandon et al., 1975).

In addition to the endocrine mechanisms influencing colostrogenesis, parity and litter size have been also associated with some changes in colostrum yield and composition in goats. Colostrum yield in multiparous goats is higher than in primiparous goats (Knight and Peaker, 1982), which is also supported by Peris et al. (1999) who demonstrated that multiparous goats have greater udder volume and secretory tissue than primiparous goats. This agrees with other dairy species such as cattle and ewes (Adegoke et al., 2016; Fernandez et al., 1995; Walsh et al., 2007). Although no effects of parity and litter size on colostrum yield and composition were reported in Majorera dairy goats (Argüello et al., 2006), Romero et al. (2013) found higher protein and lactose percentages in colostrum from primiparous and single-birth *Murciano-Granadina* goats. In addition, colostrum fat, IgG, interferon-gamma, and interleukin-2 concentrations can be higher in twin-birth goats than in single-birth goats (Zhou et al., 2023). These findings suggest that parity and greater litter size can be associated with increased colostrum yield and a possible dilution of components.

Colostrogenesis modulation

Understanding the mechanisms regulating colostrogenesis has opened new paths to develop novel management strategies to enhance colostrum quality. Hereunder are highlighted some of the most novel approaches to modulate colostrogenesis in small ruminants which includes the implementation of alternative management strategies during the dry-off period, different dietary approaches in late gestation and the induction of a local immune response within the mammary gland at parturition.

Dry-off management

The dry period, also known as the period between two consecutive lactations, promotes the mammary gland to recover from months of intense milk production. During this period, there is an active reorganisation of the mammary gland, preparing the organ for the next lactation. Dairy animals (i.e., cows, ewes and goats) have been selected to produce milk above the nutritional requirements of the offspring. Since reproductive management practices in intensive systems result in lactation and gestation overlapping, these animals are unable to naturally cease milk production. The omission of the dry period reduces colostrum IgG concentrations due to a partial inhibition of the mammary gland involution and a continuous milking that prevents the IgG accumulation (Annen et al., 2007; Caja et al., 2006; Safayi et al., 2010). Therefore, it is necessary to modulate the metabolic activity of the gland to reduce milk production and ensure a 2-month dry period.

Traditionally, dry-off strategies in dairy cows, sheep and goats have consisted in a progressive reduction of the amount of energy in the diet by reducing cereal grains, a reduction in milking frequency and the application of preventive mastitis treatments (Anniss and Mcdougall, 2002; Bertulat et al., 2015; Petridis and Fthenakis, 2019). However, this last practice tends to be applied occasionally and selectively to prevent unnecessary antimicrobial use and to reduce costs. In addition to the common dry-off strategies, dopamine agonist treatments such as cabergoline have been used in dairy cows (Bach et al., 2015; Boutinaud et al., 2016; Hernández-Castellano et al., 2023), sheep (Caja et al., 2020) and goats (Lacasse et al., 2016) to reduce prolactin concentrations in blood and consequently milk yield. Nevertheless, due to the negative effects of these drugs in dairy cows (i.e. hypocalcemia, hypothermia, ataxia, diarrhoea and in some cases death), this product was banned by the European Medicines Agency in 2019. In dairy sheep and goat, the use of melatonin implants has become a common practice to stimulate oestrus and ovulation (Elhadi et al., 2022). Moreover, melatonin also promotes an efficient mammary gland reorganisation during the dry period and increases milk yield in the subsequent lactation in both species (Avilés et al., 2019; Misztal et al., 2018) although the effect of these implants on colostrum quality remains unknown. Therefore, future studies should focus on developing novel and efficient dry-off strategies to not only promote healthy lactation but also to guarantee a successful colostrum synthesis.

Nutrition management

The development of the mammary gland begins before parturition, a period in which the uptake of blood-derived molecules will progressively increase and accumulate in the udder. Consequently, the uptake of nutrients during the dry period can impact colostrum yield and composition (Hare et al., 2023). Indeed, a nutrient restriction during gestation causes reduced colostrum yield in dairy cows and sheep without affecting IgG concentration (Logan, 1977; Banchero et al., 2006; Zarrin et al., 2021). Although the effects of feed restriction on goat colostrum have not been addressed yet, a similar yield reduction is expected. In contrast, exceeding energy requirements in dairy cows during colostrogenesis does not affect colostrum yield (Daneshvar et al., 2020; Fischer-Tlustos et al., 2021) nor IgG concentrations (Dunn et al., 2017; Springer et al., 2008), although Mann et al. (2016) described reduced IgG concentrations in colostrum from cows fed above the metabolisable energy requirements prepartum. Similarly, feeding dairy ewes and goats above the energy requirements during the last month of gestation does not affect either colostrum yield or immunoglobulin concentrations (Celi et al., 2008; Gallo et al., 2020). However, Ramírez-Vera et al. (2012) found greater colostrum yield and lactose percentage in grazing goats that were supplemented with corn starch 12 days before the expected parturition.

Although limited data are available in goats, dietary supplementation, or inclusion of different sources of protein and fat in late gestation does not seem to influence colostrum yield and composition. According to Shabrandi et al. (2019), a prepartum metabolisable energy and metabolisable protein supplementation (i.e., 10% of NRC recommendations) can cause greater mammary gland development in dairy goats, although colostrum yield is not affected. Similar results were observed in dairy ewes supplemented with 116.5 g CP and 84.6 g metabolisable protein/kg DM compared to the control group that received 99.4 g of CP and 70.5 g metabolisable protein/kg DM (Mousavi et al., 2016). However, results across studies remain inconsistent as some authors have found higher protein concentrations in ewe colostrum after protein supplementation during late gestation (Amanlou et al., 2011). Differences among these studies might be caused by the source and type of protein (i.e., rumen degradable vs undegradable protein) and length of supplementation (i.e., 3 vs 6 weeks before expected parturition date). Prepartum fat supplementation has been also tested in ruminants. In dairy cows, prepartum fat supplementation increases colostrum IgG and fatty acids concentrations but does not affect colostrum yield (Ricks et al., 2020). Unlike in cattle, the supplementation with conjugated linoleic acid from the third month of gestation does not increase colostrum IgG concentration in dairy goats (Castro et al., 2006). Similarly, Moreno-Indias et al. (2014) found that supplementing pregnant dairy goats with 5 g/day of *Chlorella pyrenoidosa* as a source of unsaturated fatty acids and essential aminoacids (Chen et al., 2022; Kouřimská et al., 2014) does not have any effect on yield, fatty acids profile and immune components in colostrum. However, Cattaneo et al. (2006) described that 1.1% fish oil supplementation during the last 3 weeks before parturition increases long-chain n-3 polyunsaturated fatty acids, mainly eicosapentaenoic and docosahexaenoic acid, in dairy goat colostrum. In ewes, fish oil supplementation during the dry period has a negative impact on colostrum yield as well as on fat, protein, and IgG concentrations (Annett et al., 2009). The differences observed among studies might be associated with factors such as nutrient source, timing and length of supplementation, breed and management system that can directly influence the degree of response to the dietary supplementation. Although increasing certain macro- and micronutrients during the last weeks of gestation seems to positively impact colostrum yield and composition in dairy goats, future studies need to characterise the effects of different dietary strategies in both colostrum chemical composition and less abundant bioactive compounds.

Colostrogenesis and intramammary health

The epithelial cells and connective tissue forming the alveoli in the mammary gland create a structure known as the blood-milk barrier (**BMB**) which regulates the transfer of components between blood and milk. Linzell and Peaker (1971) carried out the first studies on mammary gland permeability in lactating goats, describing that the differences between colostrum and milk composition could be caused by structural changes in the tight junctions between epithelial cells during late gestation. It seems that the mechanisms underlying changes in the BMB permeability are complex and could be associated with hormonal changes that induce modifications in the mammary tight junctions. During inflammation, the BMB becomes permeable allowing the passage of immune cells and factors such as lymphocytes, neutrophils, and antibodies from blood to the lumen of the alveoli and consequently into milk (Burton and Erskine, 2003; Wellnitz and Bruckmaier, 2021.). The recruited immune cells secrete IgG_1, IgG_2, IgM and cytokines enhancing pathogen phagocytosis, which in turn increases the somatic cell count in milk (Wall et al., 2018; Wellnitz et al., 2015). No changes have been detected in colostrum immunoglobulin concentrations from either primiparous or multiparous Holstein cows with naturally occurring mastitis (Maunsell et al.,1998; Enger et al., 2021). However, Bruckmaier and Wellnitz (2017) observed blood-derived constituents in milk (i.e., serum albumin, lactate dehydrogenase and IgG) after inducing an experimental mastitis in dairy cows. Cell-wall components such as lipopolysaccharides (**LPS**) from gram-negative bacteria (*Escherichia coli*) as well as lipoteichoic acid (**LTA**) or peptidoglycans (**PGN**) from gram-positive bacteria (*Staphylococcus aureus*) have been widely used to mimic sterile mastitis in experimental conditions (Kusebauch et al., 2018; Wellnitz et al., 2013), observing different immune components in milk from cows treated with LPS compared to those treated with either LTA or PGN. Although the induction of udder inflammation has been mainly used to assess the mammary immune response to determine better approaches to treat mastitis in dairy cows, some studies have also assessed its impact on milk and colostrum composition. Danielsen et al. (2010) described changes in the milk proteome profile of dairy cows in response to an intramammary LPS challenge (i.e., 200 mg *Escherichia coli* serotype O111:B4) reporting an upregulation of acute phase proteins, immunoglobulins and complement factors as well as an increase of α-, β-, and k-caseins after 7 h of the LPS challenge. Similarly, higher protein and lower lactose percentages have been reported in milk from *Murciano-Granadina* dairy goats challenged with 10 μg of intramammary LPS (*Escherichia coli* serotype O55:B5; Salama et al., 2020). Aiming to assess these effects on colostrum composition, González-Cabrera et al. (2024a) showed that the intramammary infusion of 2 mL of saline containing 50 μg of LPS (*Escherichia coli* serotype O55:B5) in each half udder at parturition caused increased IgG and IgM concentrations in colostrum without any sign of local inflammation or discomfort. In agreement with these findings, Alcindo et al. (2023) also reported higher colostrum IgG concentrations in response to a natural infection in dairy goats. These strategies are of special interest in goats producing low-quality colostrum, as it has been demonstrated that the absorption capacity of macromolecules (i.e., immunoglobulins) in the newborn animal can be already saturated when providing high-quality colostrum (González-Cabrera et al., 2024b; Saldana et al., 2019). In addition, feeding newborn goat kids with colostrum derived from LPS-treated goats is safe as no signs of disease has been reported (González-Cabrera et al., 2024b). In support of these findings, Samarasinghe et al. (2020) showed that the administration of LPS (i.e.,12 μg/kg of BW) in milk did not induce any acute inflammatory response in 1-month-old Holstein calves, suggesting that oral intake of LPS has no detrimental effects on the health status of the animals. However, it should be considered that these molecules (i.e., LPS, LTA or PGN) could be absorbed if the intestinal permeability is impaired (i.e., leaky gut), causing a systemic immune response that may compromise animal health. Besides this, modulation of the BMB permeability through an induced immune response might still have remarkable applications. For instance, increased permeability combined with the vaccination against certain pathogens could enhance the transfer of specific antibodies from blood to colostrum and milk, promoting a better immunisation of the offspring. Therefore, and despite mastitis has evident detrimental effects on performance and health in dairy animals, inducing a moderate and local immune response within the udder might be used to positively modulate colostrum quality.

Conclusions

In ruminants, colostrogenesis is a well-preserved mechanism. However, multiple factors such as dry-off management practices, the inclusion of different nutrients on prepartum diets, and udder inflammation can also impact colostrogenesis and consequently, be used strategically to enhance colostrum quality. However, there is still the need to deeply assess the effects of macro– and micronutrients supplementation in late gestation to develop better nutritional strategies to modulate and promote colostrum yield and composition in dairy ruminants. Inducing a mammary gland immune response seems to trigger helpful modifications on the blood-milk barrier enhancing colostrum immune composition. Future studies should focus on developing optimal management and nutritional strategies during late gestation to enhance colostrum quality and consequently, offspring health and performance.

Ethics approval

Not applicable.

Data and model availability statement

Not applicable. Information can be made available from the authors upon request.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) did not use any AI and AI-assisted technologies.

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Declaration of interest

None.

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