Exogenous melatonin: effects on lactation and colostrogenesis in small ruminant livestock

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SUMMARY

Melatonin is a neuroendocrine hormone involved in numerous functions in animals, most studies have focused on the ability to control reproduction in species that are sensitive to photoperiodicity. Recently, however, the number of studies on the effects of melatonin on productive aspects of small ruminant livestock has increased. This review summarizes recent published studies on the effects of exogenous melatonin on lactation and colostrogenesis in small ruminants. The melatonin membrane receptors MT1 and MT2 are in the epithelial cells of the mammary glands, which suggests that melatonin might influence milk yield and composition. Furthermore, melatonin exhibits anti-inflammatory, antibacterial, and immune properties, and might regulate udder health. Research has shown that melatonin influences the immune system by affecting the synthesis of IgG; however, the precise pathway through which melatonin influences lactation and colostrogenesis in small ruminants is not fully understood. Variability in the effects of exogenous melatonin on lactation and colostrogenesis occurs because of differences in administration routes, dosing protocols, and environmental conditions.

KEY WORDS

Melatonin, dairy small ruminants, milk yield, milk composition.

INTRODUCTION

Melatonin (N-acetyl-5-methoxy-triptamine) is a neuroendocrine hormone derivative of tryptophan, which is an amino acid that is produced in the pineal gland, primarily (1,2). From the bloodstream, an amino acid tryptophan is metabolized through four successive intracellular steps that are enzymatically catalyzed by tryptophan hydroxylase, aromatic amino acid decarboxylase, arylalkylamine-N-acetyltransferase, and hydroxyindole-0-methyltransferase (3,4).

Melatonin was first isolated in 1958 from the bovine pineal gland (5), and research in several species has shown that it is secreted in other organs, tissues, and cells, particularly, the gastrointestinal tract of the rainbow trout (6) and rat (7), vertebrates' retina (8), mouse and human bone marrow (9), human skin (10), and mouse oocytes (11). At the cellular level, mitochondria are the main sites of melatonin synthesis (12) and, therefore, all cells appear to have the ability to synthesis melatonin.

Circadian variations in the secretion of melatonin from the pineal gland are mediated by photoperiod (13). At night (the dark phase), melatonin is synthesized and released and, during the day, the pineal gland's secretory activity is reduced (14). The fetal pineal gland does not produce melatonin and, therefore, fetal circulating melatonin is of maternal origin (15). In rats, sheep, and humans, the pineal gland starts producing melatonin postnatally (16, 17, 18).

In the last 60 years, the actions of melatonin in domestic animals have been studied extensively (19). For example, we now know that melatonin modulates circadian and seasonal timing (20, 21, 22), oxidative stress (23, 24), immune (25) and cardiovascular systems (26), fetal system nervous center level (15), neuroendocrine (26), reproduction (27, 21), pregnancy and parturition (28, 29), and corpus luteum function (30).

Melatonin is a multitasking molecule that exhibits remarkable versatility in the diversity of its physiological actions (31). For that reason, its effects on livestock have been the subject of several bibliographical reviews. Studies have investigated the role of melatonin on the immune system (32,33,34), cardiovascular system (35), brown adipose tissue (19), hair follicles (36), the physiology and behavior of ungulates (37), and lamb neonatal mortality (38). Moreover, male reproduction (39, 40), sperm in farm animals (41), seasonality in sheep (42, 43), ovary activity (44), control of reproduction in goat and sheep (45, 46, 47, 48) and other farm animals (49, 50, 51, 52), embryo establishment and viability in sheep (53, 54), and production and preservation of mammalian gametes and embryos (55).

Most research and review articles on melatonin in the 30 yrs since the hormone was discovered have focused on the ability to control reproduction in species that are sensitive to photoperiodicity (47). In those photoperiod-influenced animals, melatonin mediates the transfer of photoperiodic information to the endocrine system, which induces ovulatory activity and dictates the precise timing of reproduction (56,57). Although extensive research has identified the wide range of roles that

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melatonin plays, a compilation of research on the effects of melatonin in other aspects of animal science has not been published. It is important to know the effects of exogenous melatonin supplements on small ruminants within various management scenarios because that might identify the effects of melatonin on production practices. An analysis of the effects of melatonin within a variety of contexts can aid in assessing the suitability and effectiveness of its use in various livestock farming systems. In this review, we describe the main effects of exogenous melatonin associated with lactation and colostrogenesis in small ruminant livestock. For an overview, studies on these effects are summarized in Table 1 (sheep) and Table 2 (goats).

LACTATION

Milk Yield

Although melatonin is known primarily for its role in regulating reproductive processes, it plays a role in the regulation of mammary gland development and subsequent milk production in ruminants. Furthermore, there is immunohistochemical and molecular evidence of the melatonin membrane receptors MT1 and MT2 in the epithelial cells of the mammary glands in lactating dairy goats (58). As such, at the level of mammary tissue, melatonin has a regulatory effect on cell proliferation (mammogenesis) and milk production (galactopoiesis). It is unknown, however, the specific role of melatonin in the mammary gland as a target tissue (59,58), and the results of studies on its effects in ruminant species have been contradictory (56). A wide variety of factors including species-specific differences (60,61), dosages (62), and melatonin release characteristics (63) can cause differences in milk production in response to melatonin.

Several studies have shown that high melatonin circulations are associated with reduced milk production in dairy ruminants (63). Melatonin supplements reduce prolactin secretion, which can reduce milk yield (64). Most of the research that has shown a reduction in milk yield has involved Longwool Poland ewes, which are not typical dairy animals and exhibit distinct seasonality in reproduction. Molik et al. (2013) (65) demonstrated that the subcutaneous implantation of exogenous melatonin twice (57 d and 147 d before lambing) under long-days conditions significantly reduced (15.6%) milk yields in the milking period. Two other studies have shown that implanting sheep with melatonin (18 mg) twice (6 wk before and after lambing, in spring and autumn, resp) reduced milk yield, which occurred under long-photoperiod conditions in the lamb-nursing period and after lamb weaning (from day 57 until the end of lactation) (66,67). In another study, Cashmere goats exhibited similar responses to having received one (18 mg) melatonin implant in lactation (7 wk and 16 wk) (63).

Studies have shown that melatonin implants administered in the dry period increased milk production in the subsequent lactation in small ruminants. In nursing creole Mexican goats, two melatonin implants (36 mg) inserted seven weeks before kidding (summer solstice) increased milk production by > 20% in the suckling and milking period (short day) (61). One (18 mg) or two (36 mg) melatonin implants administered six weeks before lambing increased milk yield in early lactating (90 d in milk) dairy Assaf ewes (68). Similarly, Karagouniko ewes that received their last melatonin implant six weeks before lambing showed an increase in milk production in early lactation (40 d) (69).

Studies on the use of melatonin that did not detect an effect on milk yield have been reported, and most of those have involved ewes specialized in milk production in lactation. Elhadi et al. (2022) (70) and Cosso et al. (2021) (62) reported that melatonin implants (18 mg) in early lactation (35 d or 60 d after lambing) under short-day conditions did not affect milk yield in Manchega, Lacaune, and Sarda ewes. Similarly, melatonin treatment during late lactation (fourth-seventh month) in spring (long days) did not affect total milk and the pattern of milk production in Lacaune and Assaf ewes lambed in autumn and winter, respectively (56).

Milk Quality

To encourage dairy farmers to produce high-quality milk, the dairy industry has established a variable payment structure that is based on specific economic and health factors, which rewards high fat and protein content and penalizes elevated somatic cell counts (SCC) and bulk milk total bacterial count (71). Lactose content was not included in the payment structure because, historically, it was considered a low-value component of milk. Recently, however, it has gained economic interest, internationally (72). Although the effects of melatonin on those milk parameters have been the subject of considerable research, limited information is available on the effects of exogenous melatonin on milk components and results have differed among studies (62,70).

Lipids are the most significant components of milk in terms of cost, nutrition, and the physical and sensory characteristics that they impart to dairy products (73). For that reason, milk fat content is an important criterion for assessing milk quality and is one of the main target traits of dairy breeding (74). Research has shown that melatonin is a key modulator of fat synthesis and adipose differentiation (75,76). A recent study of the dairy cow metabolome revealed that melatonin treatment reduced most of the metabolites associated with lipid oxidation, which suggests an increase in fat accumulation. Fat accumulation might alter the concentration of milk fat (77). Nevertheless, the regulatory role of melatonin in fat synthesis remains unclear and warrants further study (74,78).

Subcutaneous melatonin implants are promising means of increasing milk fat gain in ewes, which appears to offer consistent benefits among breeds and the reproductive and productive cycle (pregnancy, dry period or lactation). Dairy ewes that received melatonin supplements in gestation exhibited increases in milk fat concentrations at the beginning of lactation; specifically, two melatonin implants administered 40 d before lambing, increased milk fat concentrations at 15 d and 90 d in milk (68). Rasa Aragonesa dams that had received subcutaneous melatonin treatments (18 mg) at lambing showed an increase in milk fat content, particularly near the end of lactation (78). In addition, Polish Longwool ewes that had received an implant either in lactation or dosages in pregnancy and lactation, exhibited an increase in milk fat concentrations (79, 67).

In many countries, total protein is one of the main quality criteria for sheep and goat milk payments (80,81). Genetics and non-individual factors such as stage of lactation, season, age, and influence total protein content (82). Studies have demonstrated that exogenous melatonin can affect the synthesis of milk proteins and, therefore, the quality of milk. A study of the effects of exogenous melatonin in dairy sheep has found an increase in milk protein. Thus, Molik et al. (2020) (67) reported that milk protein content increased 15% in Polish Longwool ewes that had been given a melatonin implant (18 mg) in mid-lactation in spring.

Lactose, which is synthesized from glucose in the mammary gland, is the main carbohydrate in sheep and goat milk. It is vital in maintaining osmotic balance between the bloodstream and the alveolar cells of the mammary gland during milk synthesis, and it is secreted into the alveolar lumen and the duct system of the udder (83). Lactose has the most effect on milk osmolality, which exhibits low variability (72), and most research on the effects of exogenous melatonin in small ruminants has not found an effect on lactose concentrations in goat and sheep milk. Furthermore, the absence of an effect has been observed in studies that implanted melatonin in animals that differed in physiological state, dosing regimen, or breed. For example, one (18 mg) or two (36 mg) melatonin implants in late pregnancy (110 d or 120 d) did not significantly affect lactose in the milk of dairy and meat ewes (68, 84). Bouroutzika et al. (2021) (85) reported similar results in dual-purpose sheep that had received melatonin implants (18 mg/each) every 40 d in gestation; in another studies, after lambing, a single implant in early (1 d) or mid-lactation (30 or 35 d) did not affect milk lactose content in meat and dairy ewes (62, 70). In Creole goats, melatonin (18 mg) implanted into dams 49 d before kidding did not have a significant effect on lactose content (61). Similarly, an effect was not apparent in Verata and Cashmere dams that had received a single (18 mg; 3 d) or repeated (2 mg/kg; 50 and 110 d) implants in lactation (86, 63). Some, however, have reported that exogenous melatonin administered at day 57 of lactation, either subcutaneously via an implant or orally through rumen-by-pass granules, reduced milk lactose in Polish Longwool dairy ewes (79).

An absence of effects of exogenous melatonin on milk components (fat, protein and lactose) in dairy ewes and goats has been reported. In several breeds of dairy sheep (Manchega, Lacaune, and Sarda) and goats (Creole and Verata) that differ in levels of milk production, exogenous melatonin in a subcutaneous implant combined with naturally occurring endogenous melatonin under short-day photoperiod conditions did not affect milk components (70, 62, 61, 86).

Milk Composition

SCC is used to assess milk quality. In ruminants, the SCC estimates the quantities of the cell types present in milk, including immune-related lymphocytes (white blood cells) and mammary epithelial cells (87). Although SCC differs markedly among dairy ruminants, it is an important indicator of udder health and raw milk quality (88,89). In dairy animals, an increase in SCC, often referred to as subclinical mastitis, can be an indicator of inflammation or infection in the udder (90).

Studies have shown the effects of melatonin in reducing inflammation in multiple ways. It reduces oxidative stress by eliminating the highly toxic hydroxyl radical (-OH), peroxynitrite anion (ONOO-), and hypochlorous acid (HOCl) (91). In addition, it reduces the amount of TNF- , TNF- , IL-6, and increases the expression of IL-10 and TGF- (92). Xia et al. (93) showed that melatonin can increase gene expression of anti-inflammatory enzymes and reduce gene expression of proinflammatory enzymes. Studies have shown that melatonin supplements reduced elevated milk SCC that had been induced by *Staphylococcus aureus* or *Escherichia coli* infections (94). The antibacterial effects of melatonin might act through its ability to reduce intracellular substrates, lipid levels, and metal binding, which are required for bacterial growth (95,96). Given the anti-inflammatory and antibacterial properties of melatonin, several studies have evaluated its effects on SCC in dairy sheep and goats. The beneficial effects of melatonin on mammary health through lowering of the SCC have been reported in sheep that had received melatonin implants in lactation or gestation. Cosso et al. (62) reported that melatonin implanted in the second month of lactation reduced SCC in Sardinian sheep, which was evident 6 wk after implantation and persisted in subsequent samplings. In addition, Canto et al. (2022) (68) detected a decrease in SCC at 45 d after implantation in Assaf dairy sheep, although melatonin was administered in the last third month of gestation. Furthermore, apparently, the duration of the reduction in sheep SCC and melatonin dosage are strongly correlated. For example, two melatonin implants (36 mg) prolonged the reduction in SCC one month longer than did one implant (18 mg) (68). A single study has shown that melatonin implants reduced SCC in the milk of Verata goats (a dual purpose breed). Jiménez et al. (2009) (86) observed that the application of melatonin implants at the start of lactation reduced SCC at 60 d and 90 d in milk (DIM) in goats. Furthermore, they reported that melatonin positively influences the activity of antioxidant enzyme GSHPx, leading to a more efficient antioxidant system, more capable to protect neutrophils against oxidative damage.

COLOSTROGENESIS

Colostrum is the first substance secreted by the mammary gland before parturition and is formed through colostrogenesis, which is a complex process that is a pre-partum transfer of substances, primarily immunoglobulin G (IgG), from the maternal bloodstream into mammary secretions within a specific, limited period (97). Colostrum differs from milk, physically and chemically, including differences in density, color, and composition (98). In sheep and goats, it provides a source of passive immunity in newborns because of the high concentration of immunoglobulins, which do not get into the fetus's bloodstream (99). In addition, colostrum contains proteins, fats, lactose, and minerals, and is the first source of nutrition to the newborn (100).

Thus, in ruminant species, colostrum quality significantly affects the passive immune transfer to the newborn and the growth and muscle development of offspring (101). Many factors such as breed, lactation period, length of lactation, health, and management, but, especially, nutrition have an effect on colostrum quality (102, 103). In addition, hormones such as melatonin can influence immune function and colostrum quality in ruminants.

Several studies (33) have shown that melatonin can regulate the immune system (innate and adaptive) and influences the synthesis of IgG, directly. In ruminants, evaluations of the effects of melatonin on IgG and colostrum composition have focused on the ovine species. The transfer of prepartum components from the maternal circulation into colostrum occurs in the last third of gestation and some studies have focused on melatonin administered in this period. One study indicated that melatonin implants (18 mg/implant) increased IgG in Rasa Aragonesa meat ewes. Specifically, a single melatonin implant (18 mg) administered in the fourth month of pregnancy in-

Table 1 - Experimental studies of productive responses to exogenous melatonin in sheep.

Reference	Methods	Melatonin dose/timing	Effect of melatonin in animal production parameters
56	**Exp 1.** 188 lactating Lacaune ewes lambed between Sep and Nov (one lambing/year). Artificial rearing **Exp 2.** 124 lactating Assaf ewes lambed between Nov and Jan (three lambing/two years). Weaned at 20 d. Milk yield: monthly	Subcutaneous melatonin implant (18 mg of melatonin) to lactating ewes In Mar (Exp 1) and Feb (Exp 2) ewes assigned to one of two groups that had similar milk production: M: Implanted group C: Non-implanted group	Exp 1 and 2. No changes in milk production
79	60 Polish Longwool ewes mated in Sep. Lambs were reared with mothers for 56 d. On day 57 (long day), the ewes were milked twice daily and divided into three groups. Milk yield: every 10 d Milk composition: every 28 d	The ewes were implanted s.c. with melatonin (18 mg of melatonin/implant) at day 57 of lactation. Treatments Group I: natural day length Group II: natural day length and implanted subcutaneously with melatonin (18 mg of melatonin) Group III: exposed to an artificially **short** photoperiod	- Increased milk fat concentration - Decreased lactose level after only 30 d of lactation
65	60 Polish Longwool ewes were assigned to one of three equal groups (n=20) postweaning (57th day of lactation) **Rearing period:** lambs were weaned at 56 d of lactation. Milk production was estimated based on the lamb's weight gain from 2 d to 28 d of age. **Milking period:** from day 57 of lactation to the dry period (milk yield was less than 50 ml/ewe/day) Milk yield: at 10-day intervals	Melatonin implants (18 mg of melatonin) were inserted into each ewe twice, at 90-d intervals. **LDC:** natural long-day control group **LDM**: natural long-day melatonin-treated group. **ASD:** artificial short-day with 16 h of dark and 8 h of light	In LDM compared with the LDC group: - Shorter length of lactation and milking days. - Milking period: decreased milk yield.
66	36 Polish Longwool sheep (rearing twins). Mating Sep and Jan. After weaning (from the 57th day of lactation), all ewes were milked twice a day. Milk production: every 10 d.	**SD treatment**: Lambed in Jan. **LD treatment**: **LDM treatment:** lambed in Jun and treated with the subcutaneous melatonin implanted (18 mg) in third month of pregnancy and the second implant after 90 d.	- Decreased milk yield. - Increases number of milking days.
104	60 pregnant Rasa Aragonesa mated in Jun were allocated to one of three groups Colostrum quality (IgG, %Fat, %Protein): immediately after lambing	Ewes were implanted s.c. with melatonin (18 mg). Treatments Control: non-implanted 3M: melatonin implant at the third month of pregnancy 4M: melatonin implant at the fourth month of pregnancy	- 4M increased IgG in colostrum - 3M increased % fat in colostrum - No difference in % protein in colostrum
69	68 Karagouniko ewes were allocated to one of two groups 16 d before mating. All pregnant ewes were exposed to heat stress (first 100 d of pregnancy) Milk: 5, 10 and 40 d	Ewes were implanted s.c with melatonin (18 mg): before mating and in pregnancy every 40 d (in total, 4 melatonin implants; 72 mg). Treatments M: implanted C: non-implanted	- Increased milk yield
67	60 Polish Longwool ewes (rearing twins) Mating Sep and Jan. Rearing period: 0-56 d of lactation. Milk production estimated based on weight gain of the lambs. Milking period: From day 57 to dry period (milk yield < 50 mL of milk/d) Milk yield: every 10 d and milk quality Milk composition: every 28 d.	Subcutaneous melatonin implanted (18 mg) in third month of pregnancy and the second implant repeated after 90 d. G1: lambing in Feb G2: lambing in Jun G3: lambing in Jun + one melatonin implant	- Decreased milk yield in rearing and milking period - Higher content of dry matter, protein, and fat
78	**Exp. 2:** 55 Rasa Aragonesa lambs born in Oct reared by their dams. Milk composition: 15 d, 30 d, and 45 d post-lambing	Subcutaneous melatonin (18 mg) in the base of the ear 24 h after lambing (dam or lamb). **Exp 2:** cC: control group cM: implanted dams mC: implanted lambs mM: implanted dams and lambs	**Exp. 2:** - Ewes: Increased milk solids and fat content - No difference in milk protein and lactose
85	31 Karagkouniko ewes were allocated to one of two groups 16 d before mating. All pregnant ewes were exposed to heat stress (first 100 d of pregnancy). Colostrum: at lambing, 24 h, and 48 h after lambing Milk composition: 5, 10 and 40 d	Ewes were implanted s.c. with melatonin (18 mg): before mating and in pregnancy every 40 d (in total, 4 melatonin implants; 72 mg). Treatments MEL: implanted CON: non-implanted	- Increased fat and protein content in colostrum - No difference in colostrum IgG - No difference in milk composition

Reference	Methods	Melatonin dose/timing	Effect of melatonin in animal production parameters
62	100 lactating Sarda dairy sheep lambing between Dec and Jan. On 1 Mar, allocated to one of two groups Milk yield and composition: every 15 day	One subcutaneous implant (18 mg) of melatonin to dairy ewes on 1 Mar (~ two month of lactation) Treatments M: Melatonin implanted C: Non-implanted	- No effect in milk yield, fat, protein and lactose concentration - Reduced SCC in 3rd, 4th, and 5th samplings - No changes in cytokines levels
68	715 Assaf pregnant ewes from five sheep farms. Ewes were allocated to one of three groups 40 d before lambing. Milk yield and quality (%fat, %protein, % lactose and SCC (n=715): 15, 60 and 90 DIM	Ewes were implanted s.c with melatonin 40 d before lambing. Treatments C: Control (non-implanted) 1M: One melatonin implant (18 mg)	- Increased milk yield 2M increased % of milk fat - No change in milk protein and lactose - Reduced SCC - Increased colostrum IgG - No change in the % of fat, protein and lactose in colostrum
70	72 dairy ewes of two breeds (Manchega; n=36 and Lacaune; n=36) lambed in autumn (short-day photoperiod). After the weaning of the lambs (28 d), the ewes were distributed in 12 balanced groups of 6. Milk yield: daily Milk composition: 32, 50, 65, 80, and 110 DIM.	One melatonin implant (18 mg/ewe) at 35 d of lactation (SDPP). Treatments **MN CO:** non-implanted Manchega. **MN MEL:** implanted Manchega. **LA CO:** non-implanted Lacaune. **LA MEL:** implanted Lacaune.	- No changes in milk yield and composition - Decreased prolactin in MN ewes
84	50 Rasa Aragonesa ewes were assigned to one of four groups 30 d before lambing. Lambs were weaned at 42 d of age Milk: 2, 4, and 6 wk postpartum	Ewes were implanted s.c with melatonin (18 mg). Treatments M-0: melatonin implant 30 d before lambing 0-M: melatonin implant at lambing M-M: melatonin implant 30 before lambing and at lambing. 0-0: non implanted	- M-0 Increased colostrum protein and lactose - No difference in IgG - No difference in milk composition

creased IgG concentrations (78); however, in another study, if melatonin was implanted in pregnant ewes three times (at 20 d, 60 d, and 100 d gestation), it did not affect colostral IgG concentrations (85).

In addition to IgG, colostrum provides fat, protein, and lactose, and the effects of exogenous melatonin on those components are less predictable. Ewes that had received melatonin implants at 90 d of pregnancy or that had received their last melatonin implant at about 100 d (two previous doses) produced colostrum that had higher fat concentrations (104, 85). In addition, melatonin administered at gestation increased protein concentrations at 20 d, 60 d, and 100 d gestation) (85).

CONCLUSIONS

Exogenous melatonin has generated significant interest in the last three decades because of its possible impacts on ruminant livestock, and its effects have been evaluated on animals at various physiological stages and doses, mainly administered orally or subcutaneously; however, some of the results from research on its effects on milk yield and milk quality in sheep and goats have been contradictory. A variety of factors such as routes of administration, dosage protocols, and environmental conditions appear to have contributed to those contradictions. In sheep and goats, ruminal fermentation might affect the

Table 2 - Experimental studies of productive responses to exogenous melatonin in goats.

Reference	Methods	Melatonin dose/timing	Effect of melatonin in animal production parameters
86	60 Verata breed (dual purpose) goats were allocated to one of two groups on the third day after kidding. Kids were separated from their mothers 72 h after birth Blood samples: 3 d after kidding and at monthly intervals for 4 mos. Milk samples: 3 d, 30 d, 60 d, 90 d and 120 d in milk.	Goats were implanted s.c with melatonin (18 mg/goat) on the third day after kidding Treatments Control: non-implanted Implanted: melatonin implanted	- Decreased SCC in milk. - No difference in milk composition.
61	25 Creole does were kept under natural long-day conditions. At dry period, does were assigned to one of two groups. Suckling period: 21 d postpartum, milk yield was estimated by suckle-weigh-suckle method. Milking period: 22-91 d postpartum. Milk yield: estimated by hand milking each week. Milk composition: every milk yield evaluation.	Two subcutaneous melatonin implants (36 mg of melatonin/doe) at the dry period (49 d before kidding). Implants were removed at kidding Treatments CONT: non-implanted group MEL: melatonin implanted group and the milking period	- Increased milk yield during the suckling - No difference in milk composition
63	24 Inner Mongolian cashmere goats and their kids (single-female) were assigned to one of two groups at day 50 of lactation (spring). Dams Milk yield and composition: 0, 2, 4, 6, and 8 weeks of lactation	Ewes were implanted s.c with melatonin (2 mg/kg live weight) on day 50 and day 110 of lactation. MEL: implanted CON: non-implanted	Dams - Decreased milk yield - Increased fat milk concentration - No difference in milk protein (%), lactose (%) and SCC

bioavailability of melatonin, which reduces the suitability of oral administration. Furthermore, some studies have overlooked animal weight when calculating the dosage. To understand fully the effects of exogenous melatonin those factors must be considered. Further research is needed to fully elucidate the molecular mechanisms and pathways by which melatonin exerts its effects on various physiological processes that impact animal productivity directly. In addition, exploring the potential uses of melatonin in veterinary medicine and animal production is essential and includes economic analyses to assess the benefits of melatonin supplements in various livestock farming systems.

Authorship statement

FC: writing, review and editing; JAA: conceptualization and supervision, review and editing.

Acknowledgements

We thank Bruce MacWhirter for the English revision of the manuscript. F. Canto was funded by the National Agency for Research and Development (ANID)/ Scholarship Programme / Doctorado Becas Chile/ 2020 - 72210031.

Conflicts of interest

The authors declare no conflict of interest.

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