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Effect of ecbolics in enhancing bovine reproductive capacities

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Abstract

Bovines' reproductive systems undergo major physiological changes during the postpartum period, which is crucial for attaining effective dairy output. The restoration of normal ovarian function, endometrial rejuvenation, and the uterus returning to its pre-conception state are important processes. Lochia and fetal membranes are expelled from the uterus by effective contractions that occur after calving. Each of the three layers that make up the uterine structure the endometrium, myometrium, and perimetrium contributes to contractions. During parturition, the majority of uterine smooth muscle activity shifts from prolonged contractures to strong contractions required for cervical dilatation and calf expulsion. Contractions help remove the placental membrane after calving and start the crucial process of uterine involution, which can take 25 to 50 days. Myometrial behavior is greatly influenced by variables including intracellular calcium levels and dietary state. Notably, hypocalcemia and poor nursing conditions can reduce postpartum uterine contractility, which can result in problems like retained fetal membranes. Although they are frequently used in veterinary procedures, ecboic drugs that cause uterine contractions may rely more on custom than on scientific analysis. Oxytocin and prostaglandin PGF_{2α} are often used ecboic that improve uterine function during the postpartum phase. Since uterine contractility and involution have a direct impact on calving intervals, reproductive success, and overall farm productivity, it is essential to comprehend these dynamics in postpartum dairy cows. The interplay between biological processes and veterinary procedures emphasizes how crucial it is to preserve ideal uterine health in order to reduce reproductive difficulties in dairy production.

Keywords: Bovine, contractions, endometrium, ecbolics, postpartum, uterine involution

1. Introduction

Reproduction is necessary for dairy production to be productive and efficient (Crowe *et al.*, 2018) [7]. Bovines go through a lot of physical and hormonal changes during the postpartum phase, making it the most crucial time for them (Raj *et al.*, 2026) [15]. One of the most significant physiological elements of the postpartum period is the full biological and functional transformation of the reproductive organs.

- The uterus returns to its pre-conception state
- Endometrial rejuvenation
- Regaining normal ovarian function.

The purpose of these activities is to guarantee that the uterus regains the proper conditions for the subsequent pregnancy (Rizzo *et al.*, 2018) [16]. Specifically, the restoration of appropriate contraction of the uterus is crucial. In view of a potential subsequent conception and pregnancy, the physiological processes that occur during the initial postpartum phase are particularly interesting. During the initial hours and days following calving, the primary purpose of a normal uterine contraction is to remove the contents of the uterus, including lochia and fetal membranes (Simoes *et al.*, 2021) [19].

Layers of the Uterus

The endometrium, myometrium, and perimetrium are the three general tissue layers that make

up the uterus.

Endometrium: The endometrium, as the name suggests, is the innermost layer that covers the uterine canal. It is made up of a covering of columnar pseudostratified or stratified epithelial cells and connective tissue underneath made up of spongiosum standard and stratum compactum.

Myometrium: The Stratum vasculare separates the thick inner circular and thin outer longitudinal layers of smooth muscle that make up the myometrium. The circular muscle fibers are concentric to the uterine longitudinal axis, while the longitudinal muscle fibers are parallel to it. Blood vessels and nerve fiber bundles make up the stratum vasculare.

Perimetrium: The serosa, a vascular layer that continues the wide ligament, is the outermost layer of the uterus. As pregnancy progresses, uterine smooth muscles undergo hypertrophy and hyperplasia. The size can expand by three to five times compared to the non-gravid condition at the end of gestation. Uterine contractions both during and after parturition are mediated by the uterine myometrium (Skjerven, 1956) ^[20].

Phases of Physiological Uterine Contractility

As the term draws near, the Myometrial Activation Phase the uterus becomes activated in response to uterotropins, such as estrogen. This phase is characterized by increased expression of a contraction-associated proteins, CAPs (including myometrial receptors for prostaglandins and oxytocin), activation of specific ion channels, and an increase in connexin-43 (a key component of gap junctions). An increase in gap junction formation between adjacent myometrial cells leads to electrical synchrony within the myometrium and allows for effective coordination of contractions. In Stimulatory Phase Uterotonic agonists, such as the stimulatory prostaglandins E2 and F2 α and oxytocin, can activate a "primed" uterus and cause it to contract. Oxytocin is the primary mediator of the uterine involution that takes place during phase 3 following delivery.

Control of the Nerves in Uterine Contractions

Sympathetic nervous system innervates the smooth muscles of the uterus. Final thoracic and first lumbar segments of the spinal cord are the source of the postganglionic sympathetic nerves that innervate the myometrium. The preganglionic nerves synapse with the so-called short postganglionic neurons that supply the uterine muscle at the pelvic plexus, which they reach via the hypogastric nerve. Both α (excitatory) and β (inhibitory) adrenoceptors are found in the smooth muscle cells of the uterus. Noradrenaline, which primarily works on α -adrenoceptors in the bovine uterus, mediates the stimulation of the myometrial cells by the postganglionic nerve fibers. Adrenaline stimulates the β -adrenoceptors (Latini *et al.*, 2008) ^[12].

Function of Uterine Contractions

Parturition

Uterine cervix is effaced and dilated during parturition due to a rise in myometrial function or, more accurately, a shift in the myometrial contractility pattern from the term "contractures" (long-lasting, low frequency activity) to "contractions" (high intensity, high frequency activity). The uterus, which was dormant throughout the entire pregnancy, begins to contract during parturition, and the

cervix, which had been tightly contracted, relaxes enough to allow the baby to leave the mother's womb through the birth canal. This is an intriguing biological process (Safdar *et al.*, 2014) ^[17].

Uterine contractions happen roughly once every 15 minutes at the start of stage 1 of calving, and by the end of this stage, they happen roughly once every three minutes. These contractions should be distinguished from the abdominal contractions that take place during stage 2 of calving since they are not easily visible from the outside. The connection between the placenta and uterus slightly breaks down with each uterine contraction (Lange *et al.*, 2017) ^[11].

Elimination of Placental Membranes

The elimination of placental membranes occurs after the calf is discharged. In stage 3 of calving, the placenta and foetal membrane attachments to the uterus disintegrate and are expelled. After the calf is delivered, uterine contractions continue and progressively lessen over the next few days. Cows having bicornuate-shaped uteruses, and their placentas are histologically of the synepitheliochorial type, which means that during pregnancy, there are five tissue layers separating the mother's and the fetus's circulation. The bovine placenta is categorized as a cotyledonary placenta based on the spread and configuration of allantochorionic villi. (Patel & Parmar 2016) ^[14].

In locations where fingers-like structures or villi generate outgrowths known as cotyledons, the allanto chorionic membrane forms an intimate connection with the uterine wall. These clusters of villi interdigitate with caruncles, which are crypts of specific regions of the uterine endometrium. Placentomes are the collective term for these cotyledon and caruncle contact regions. A pregnant cow's uterus has about 120 placentomes

The intercaruncular endometrium is only positioned in opposition to the intercotyledonary portions of the fetal membranes because an intimate connection between the uterus and the allantochorion membrane is only conceivable at the location of the placentomes. As a result, the placenta's fetal components only separate inside the placentomes. A specific length of time is required for placental evacuation, solely due to this kind of linkage and concurrent enzymatic reactions. Cows usually vomit these membranes eight to twelve hours after calving. It is best to avoid removing placental material from a recently calved cow because doing so could harm the uterine lining. Due to changes in the endocrine profile throughout the peripartum period, placental maturation plays a significant role in the separation process. Other occurrences include distortion of placentomes brought on by uterine contractions and separation of cotyledonary villi from maternal caruncular crypts due to exsanguination of the fetal section of the placenta. Shedding that lasts longer than 12 or 24 hours after calving is typically regarded as placental retention (also known as retained foetal membranes, or RFM) with a pathological background, where a variety of causes may be at play.

Involution of the Uterus

A particularly severe period of uterine involution occurs during the postpartum period, which begins immediately after calf birth and is the first stage of the puerperal phase. The process by which the tubular genitalia contract to undo the enlargement brought on by pregnancy is known as involution. The uterus shrinks as the myometrium and endometrium regenerate during involution, preparing the uterus for the

subsequent pregnancy. Following delivery, cows have regular, well-coordinated uterine contractions that resemble calving. The contractility of the typical cow uterus gradually decreases after delivery. The frequency, intensity, and length of myometrial contractions decrease by more than 50% by 24 hours after calving compared to six hours after delivery. In order to facilitate detachment, contractility stays at roughly 80% of what it was six hours after delivery if fetal membranes are kept (Sheldon, 2004) ^[18].

Shortly after parturition, contractions of the uterus gradually reduce, causing debris, fluids, and compression of the vasculature, which eventually regains its size, shape, and biometry. A number of physiological processes occur throughout the five to seven weeks that the involution takes to complete. In addition to the endometrium's physical changes, the uterus's size significantly shrinks during involution. In typical cows, the first few days following delivery are when the biggest size reduction takes place. Five days after delivery, the diameter of the previously gravid horn is cut in half, and fifteen days later, its length is cut in half. The pace of involution decreases between days 4 and 9 postpartum, then accelerates between days 10 and 14 before gradually slowing down until the process is finished. Involution follows a declining logarithmic pattern (Ioannidi *et al.*, 2020) ^[10].

The full involution process takes between 25 to 50 days following parturition, however the bovine uterus recovers to its pre-gravid form by roughly 25 days. The process of uterine involution is significantly influenced by the mechanical activity of the uterine smooth muscle. Spontaneous uterine contractility raises intrauterine pressure during the postpartum phase, aiding in the removal of fluid and debris from the uterine lumen. This is a component of the innate defense mechanism and is made possible by the contraction of the myometrium's longitudinal and circular muscle layers. Along with professional phagocytes, it supports the initial line of defense. (Abd-Elkareem *et al.*, 2025) ^[1].

The evacuation of uterine fluid and debris is aided by the physical propulsion produced by the contraction of longitudinal and circular muscles. The evacuation of lochia, which lasts for 14 to 23 days after delivery, is largely caused by the contraction of myometrial muscle fibers. Myometrial contraction is significantly influenced by nutrition. Improving uterine involution, preserving mineral homeostasis, and boosting immunity all depend on macro and microminerals. Inadequate myometrial contractions cause fluid, debris, and bacteria to be cleared more slowly, which puts the cow at risk for postpartum uterine illness. Myometrial tone and uterine involution are therefore crucial components of uterine defense. Lack of activity, infrequent nursing, and hypocalcemia are some of the causes of decreased myometrial contractility, which can lead to poor uterine clearance, lochia buildup, and an increased risk of bacterial infection (Gupta *et al.*, 2026) ^[9].

Postpartum Cows' Uterine Contractile Events

First-day postpartum activities

Abdominal straining efforts stop after the fetus is expelled, but frequent, powerful uterine contractions continue, exhibiting a high degree of regularity. The dislodgement of cotyledons from their associated caruncles and the subsequent ejection of fetal membranes are the physiological goals of this action. Actually, this is the third and last stage of the parturition process, which comes after calving. According to reports, the frequency of individual contractions at this period ranges from 12 to 30 per hour, and it decreases in the hours

that follow the calf's ejection. The frequency decreased linearly until two hours after calving, with mean values ranging from 14 to 19 contractions per hour. Amplitudes have been shown to range from 20 to 40 mmHg in the first two hours following a typical calving. Contractions spread in a tubocervical direction during the first several hours after calving. The placenta's evacuation seems to be the primary purpose of the powerful contraction waves that propagate tubocervically during this time. Following the fetal membranes shed during the first eight hours following delivery, the contractility significantly decreases.

Events during the second day postpartum

On the second day, uterine contractions appear to be propagating in a tubocervical direction even though they become weaker. After calving, uterine contractions often decreased quickly, with a significant drop occurring between 12 and 24 hours later, and by 48 hours, very little spontaneous contractility remained. Cows with retained foetal membranes (RFM) have been shown to exhibit maximal amplitudes of 50 to 80 mmHg with contraction frequencies ranging from 8.6 to 40 per hour. At 48 hours, uterine activity was considerably higher in RFM cows than in animals without RFM (Bajcsy *et al.*, 2005) ^[5].

Uterine Contractility-Related Factors

The contractions of uterine muscle cells are influenced by several situations and variables.

Intracellular calcium availability: Since intracellular calcium is one of the key elements, postpartum animals' plasma calcium levels are clinically significant. After the calf is expelled, the pattern of myometrial contractions alters, but they still occur and have a regular pattern with strong, frequent individual pressure cycles. (Arechiga-Flores *et al.*, 2022) ^[2]. However, uterine contractions significantly decrease if a cow has milk fever, which is caused by a significant drop in blood calcium content during the immediate post-calving stage. Intrauterine pressure fluctuates when a flaccid uterus is palpable. Additionally, a higher incidence rate of RFM has been linked to hypocalcemia. There is strong evidence that involution may be postponed in cows with subclinical hypocalcemia (DeGaris *et al.*, 2008) ^[8].

The direct impact of breastfeeding and milking on uterine contractility during the puerperal stage is debatable. Even if the calf was permitted to lick or nurse her mother, few studies show no variations in the uterine contractility patterns of cows with or without calves. However, some research has shown that breastfeeding has a beneficial effect and that uterine activity increases following milking, nursing, or simply having their calves close by. The decrease in uterine contractility in postpartum cows is probably caused by the detrimental impact of calf removal on oxytocin release (Bajcsy *et al.*, 2005) ^[5].

Uterine contractions can be momentarily lessened by uterine relaxants or tocolytic drugs. In parturient animals with aberrant fetal presentations, oversized fetuses, uterine displacements, or torsion, these drugs are helpful during obstetrical assistance. When performing caesarean sections on ruminants, it is frequently utilized to externalize the pregnant uterine horn. When uterine relaxants are administered to cows, the uterine contractility decreases. (Visser *et al.*, 2015) ^[21].

Repercussions of Unusual Uterine Contractility

Given its significance in later conception and pregnancy, the

uterus of early postpartum dairy cows is of particular interest. Since the business of a cattle farm depends heavily on reproduction, there is a greater probability of improving reproductive performance and, indirectly, economic effectiveness if the causes of reproductive problems are identified and removed as soon as possible. The calving interval is typically used to measure a dairy herd's reproductive efficiency. Due to reproductive abnormalities, the length of the calving interval impacts both the culling rate and milk yield. Inappropriate uterine involution affects the calving interval overall and lengthens the time between calving and conception. Uterine involution begins immediately after calving, readying the genital tract for a subsequent conception. Puerperal abnormalities during this early stage may result in a delayed restart of ovarian activity and an extension of complete uterine involution, which would lengthen the intervals between calving and conception and raise farm production expenses. The ejection of uterine contents, the cleansing of the uterine cavity, and the lowering of uterine size are all significantly influenced by uterine smooth muscle activity. However, these processes can be disrupted, leading to puerperal conditions such as endometritis or retained foetal membranes.

Ecbolics in Veterinary Medicine

Ecbolics are medications that speed up the process of uterine involution and contractions. Several ecobolic medications are utilized during the puerperal phase in bovine practice. Rather than the appropriate rationale for treatment and the recorded knowledge of their immediate and long-term effects on uterine functions, such therapies are still frequently relied on tradition or the practical experiences of veterinarians. Prostaglandin F_{2a}, oxytocin, or ergot alkaloids are examples of ecobolic or uterotonic medications utilized in bovine therapy during the postpartum period.

Myometrial oxytocin receptors are stimulated by oxytocin, which causes myometrial contractions directly. There may also be another indirect process whereby the occupation of endometrial oxytocin receptors results in the release of prostaglandins (PG), which then act on the myometrium through a paracrine pathway. Up until the second postpartum day, a 30 IU oxytocin therapy improves uterine contractility. During the first four to six days after giving birth, the benefits of oxytocin become less noticeable. Because oxytocin has a very short half-life, its uterotonic impact lasts for a brief time (Arias, 2000) [3].

Prostaglandin (PGF_{2α}) exhibits uterotonic and luteolytic properties. The presence of G-protein-coupled cell surface receptors in various uterine areas is necessary for the uterotonic action. The uterus contracts and relaxes in response to activation of two different types of receptors: FP, which is selective for PGF_{2α}, and EP₂, which is selective for PGE. It has been demonstrated that the uterine fundus has a large number of FP receptors, which, when activated, result in myometrial contractions. More EP₂ receptors, which promote myometrial relaxation and cervical dilatation, are found in the cervical area (Pate & Hughes, 2023) [13]. To maintain uterine quiescence during pregnancy, the uterus has less contractile receptors (FP) and more relaxant receptors (EP₂). In order to facilitate the start of contractions and sustain them throughout the postpartum phase, the number of FP receptors increases during the beginning of labor. In order to promote uterine clearance and involution, PGF_{2α} acts on particular FP receptors in the postpartum bovine uterus to start myometrial contractility. The naturally occurring alkaloid ergometrine is

present in ergot (*Claviceps purpurea*). It can induce uterine contractions and is categorized as a water-soluble derivative of lysergic acid. The alkaloid is typically employed in pharmaceutical products as the maleate salt (ergometrine maleate), which shows more stability than the free base. In veterinary medicine, it is utilized to prevent prolapsed uteri, regulate postpartum uterine hemorrhage, remove fluid from atonic uteri, and carefully choose when to suture the uterus following a cesarean section or replace an avorted uterus (Ashfaq *et al.*, 2024) [4]. Methylergometrine injection is a component of Nexbolic, an ecobolic with proven effectiveness. Ergometrine maleate is rapidly absorbed following intramuscular injection and oral administration. About ten minutes after an oral dose and seven and one minutes after intramuscular and intravenous injections, respectively, it starts to work. After peaking for about an hour, the activity gradually declines over many hours. Elimination appears to happen mostly through the bile after liver metabolism (Bhoi, *et al.*, 2022) [6].

Conclusion

Reproduction is crucial for efficient dairy production, with the postpartum phase being critical due to physical and hormonal changes in bovines. Key physiological events include the uterus returning to its pre-conception state, endometrial rejuvenation, and normalization of ovarian function to prepare for subsequent pregnancies. Uterine contractions, essential for expelling uterine contents after calving, are mediated by the myometrium, which consists of three layers: endometrium, myometrium, and perimetrium. Physiological uterine contractility involves phases activated by uterotropins like estrogen, while nerve control is facilitated by the sympathetic nervous system. Uterine contractions intensify during parturition, transitioning from mild contractures to strong contractions, allowing for cervical dilation and calf delivery. After calving, placental membranes are expelled, with the process influenced by the anatomy of the bovine placenta and uterine contractions. Retained membranes longer than 12 to 24 hours post-calving are considered pathological. The process of uterine involution, particularly significant during the postpartum period following calf birth, involves the contraction and regeneration of the uterus to reverse the changes induced by pregnancy. This process begins immediately after calving, characterized by regular uterine contractions that decrease in intensity and frequency over time. Initial contractions are robust and assist in the detachment of fetal membranes, with amplitudes reaching 20 to 40 mmHg in the first hours post-delivery. Substantial reduction in uterine size occurs within the first five days, and the full involution may take 25 to 50 days. Factors affecting uterine contractility include intracellular calcium levels, breastfeeding effects, and the use of tocolytic drugs, which can diminish contractions. Poor uterine contractility due to issues such as hypocalcemia may increase the risk of postpartum uterine infection. Overall, uterine involution involves intricate physiological changes critical for recovery and defense post-calving. The uterine health of early postpartum dairy cows is crucial for reproductive efficiency and economic performance. A prolonged calving interval, influenced by uterine involution issues, can lead to increased costs and lower milk production. Puerperal abnormalities, such as endometritis, can delay ovarian activity and lengthen the time between calving and conception. Ecbolics, including oxytocin, prostaglandin PGF_{2α}, and ergot alkaloids, are commonly used to enhance uterine contractions during the

puerperal phase, although their application often relies more on tradition than on comprehensive evidence of their effects. Oxytocin, for instance, improves contractions initially but has a limited duration of action post-administration. Prostaglandin PGF_{2α} helps induce contractions by activating specific uterine receptors, while ergometrine is used in various capacities, including controlling hemorrhage and facilitating uterine recovery after procedures. Fast absorption and activation of therapeutic agents like ergometrine highlight their role in managing postpartum uterine conditions in veterinary practice.

Conflict of Interest

Not available

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Not available

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