



International Journal of Veterinary Sciences and Animal Husbandry



ISSN: 2456-2912

NAAS Rating (2026): 4.61

VET 2026; 11(3): 328-332

© 2026 VET

www.veterinarypaper.com

Received: 02-12-2025

Accepted: 09-01-2026

Chanabasayya Hiremath

Department of Veterinary,
Gynaecology and Obstetrics,
Veterinary College, Hebbal,
Bengaluru, Karnataka,
Veterinary, Animal and Fisheries
Sciences University, Nandinagar,
Bidar, India

Narasimha Murthy

Department of Veterinary
Gynaecology and Obstetrics,
Veterinary College, Hebbal,
Bengaluru, India

Sudha G

Department of Veterinary
Gynaecology and Obstetrics,
Veterinary College, Hebbal,
Bengaluru, India

BM Ravindranth

Department of Veterinary
Gynaecology and Obstetrics,
Veterinary College, Hebbal,
Bengaluru, India

AM Kotresh

Department of Veterinary
Biochemistry, Veterinary
College, Hebbal, Bengaluru,
India

KM Srinivasa Murthy

Department of Veterinary
Surgery and Radiology,
Veterinary College, Hebbal,
Bengaluru, India

Corresponding Author:

Chanabasayya Hiremath

Department of Veterinary,
Gynaecology and Obstetrics,
Veterinary College, Hebbal,
Bengaluru, Karnataka,
Veterinary, Animal and Fisheries
Sciences University, Nandinagar,
Bidar, India

Study on comparative efficacy of different protocols in estrus synchronization of sheep

**Chanabasayya Hiremath, Narasimha Murthy, Sudha G, BM
Ravindranth, AM Kotresh and KM Srinivasa Murthy**

DOI: <https://www.doi.org/10.22271/veterinary.2026.v11.i3f.3148>

Abstract

Estrus synchronization plays an important role in improving reproductive efficiency and facilitating planned breeding in sheep. The present study was conducted to evaluate the comparative efficacy of different estrus synchronization protocols in ewes. Eighteen healthy ewes were randomly divided into three groups consisting of six animals each. Group I received Avikasil-S® progesterone intravaginal sponge for seven days followed by prostaglandin F α injection, Group II received oral clomiphene citrate (150 mg) for five days followed by PGF $_{2\alpha}$ injection and Group III received letrozole intravaginal sponge for seven days followed by PGF $_{2\alpha}$ injection. Sponge retention rate, estrus response rate, interval to estrus, duration of estrus and conception rate were recorded. In both Group I and Group III, 100 per cent sponge retention rate observed. The estrus response rate was highest in the Avikasil-S® progesterone sponge group (83.33%) followed by clomiphene citrate (66.67%) and letrozole (66.67%) groups. The interval to onset of estrus was significantly shorter in Group I (36 hrs), compared to Group II (81.5 hrs) and Group III (57 hrs). The duration of estrus did not differ significantly among the three groups and ranged from 26.4 to 30 hrs. And the conception rates were 60 per cent in Group I and 50 per cent in both Group II and Group III. This study concluded that progesterone sponge protocol provided earliest and most predictable estrus onset (tight synchrony). Whereas, letrozole sponges showed moderate synchrony. Clomiphene citrate exhibited weak synchrony with delayed estrus.

Keywords: Estrus synchronization, progesterone sponge, clomiphene citrate, letrozole, sheep

1. Introduction

Sheep husbandry is an important component of the livestock sector in India, providing livelihood and nutritional security for millions of rural farmers. Estrus synchronization is an important reproductive biotechnology used to control the timing of estrus and ovulation in sheep. It facilitates planned breeding, artificial insemination and embryo transfer programs (Kusina *et al.*, 2000; Jainudeen *et al.*, 2000) [15, 12].

Progesterone based intravaginal devices such as Avikasil-S® sponges are widely used for estrus synchronization because they mimic the luteal phase and suppress ovulation until removal of the sponge (Kumar *et al.*, 2016; Mahendra, 2016; Yadav *et al.*, 2020) [14, 18, 25].

Recently, non-steroidal drugs such as clomiphene citrate and aromatase inhibitors like letrozole have been explored as alternatives to conventional hormonal protocols due to concerns regarding hormone residues in animal products (Land and Scaramuzzi, 1979; Rateb *et al.*, 2019; Gupta *et al.*, 2021) [16, 22, 10].

Clomiphene citrate (CC), a selective estrogen receptor modulator (SERM) that acts by blocking hypothalamic estrogen receptors, thereby reducing negative feedback and stimulating GnRH, FSH and LH release, which in turn promotes follicular development and ovulation. Its advantages include low cost and ease of oral administration, making it attractive for low-input production systems. And letrozole inhibits the aromatase enzyme and suppresses estrogen synthesis, thereby increasing gonadotropin secretion and promoting follicular development (Goss and Strasser, 2001; Casper and Mitwally, 2012) [9, 3]. Therefore, the present study was conducted to compare the efficacy of progesterone sponge, clomiphene citrate and letrozole

based estrus synchronization protocols in ewes.

2. Materials and Methods

The study was conducted on eighteen healthy (aged one to four years) non pregnant, cycling ewes maintained under semi-intensive management conditions. Animals were randomly divided into three groups with six animals in each group.

Group I: Avikesil-S® progesterone intravaginal sponge inserted for 7 days followed by intramuscular injection of cloprostenol sodium (PGF₂α) at sponge removal.

Group II: Oral clomiphene citrate (150 mg) administered for five consecutive days followed by intramuscular injection of cloprostenol sodium (PGF₂α) on fifth day.

Group III: Letrozole intravaginal sponge (7.5 mg) inserted for seven days followed by intramuscular injection of cloprostenol sodium (PGF₂α) at sponge removal.

Letrozole sponges were prepared by using polyurethane material 30 mm length × 20 mm width × 20 mm thickness and thread of 15 cm length. Sponges were autoclaved and stored in the air tight polythene bags. The sponges were loaded with 7.5 mg of letrozole (3 tablets of Letroz® 2.5 mg suspended in one mL distilled water (w/v) and sponge were dipped in suspended and dried before intravaginal insertion for ewes.

2.1 Estrus detection and mating

All the study animals were observed for the behavioural estrus twice daily for 30 minutes each time (06:00 - 07:00 and 18:00 - 19:00 hour) for five days after PGF₂α injection. Stand to be mounted by the Ram till it refuse to mate. Ewes were isolated and exposed to the sexually active ram to aid estrus detection. Stand to be mounted by the ram was considered to be in estrus.

2.2 Determination of pregnancy

Pregnancy diagnosis was performed 50 days of post mating using ultrasonography and (Honda, HS/2000, Japan) with a 3.5-10 MHz linear array rectal transducer.

The parameters recorded included sponge retention rate, estrus response rate, interval to onset of estrus, duration of estrus and conception rate.

3. Results and Discussion

3.1 Intravaginal sponge retention rate

In the present study, all ewes in Group I (Avikesil-S® progesterone sponge) and Group III (letrozole sponge) retained the intravaginal sponges throughout the 7-day treatment period, resulting in a 100 per cent sponge retention rate (Table 1 and Figure 1). None of the animals exhibited signs of estrus while the sponges were in situ and no abnormal behavioural changes were observed except mild turbid vaginal discharge, indicating good tolerance of the devices under field conditions. The high retention rate observed in the present study may be attributed to factors such as sponge material characteristics (polyurethane), duration of insertion, vaginal anatomy, breed differences and parity of the animals.

Comparable results were also reported with Avikesil-S® sponges applied for 7 to 12 days in different ewe breeds

(Mahendra, 2016; Kumar *et al.*, 2016; Gangadharaiah, 2017; Yadav *et al.*, 2020; Suhas *et al.*, 2021) [18, 14, 7, 25, 23].

Similarly, Abdel Dayem *et al.* (2020) [1] reported complete retention of letrozole intravaginal sponges in Farafra ewes. However, slightly lower retention rates (94%) have been reported with longer treatment durations (14 days) (Swelum *et al.*, 2018)²⁴. Overall, these findings confirm that intravaginal sponges are reliable and well tolerated for estrus synchronization in ewes.

3.2 Estrus response rate

The estrus response rate recorded in the present study was 83.33 per cent (5/6) in Group I, 66.67 per cent (4/6) in Group II, and 66.67 per cent (4/6) in Group III, and no significant difference was observed among the groups ($p > 0.05$) (Table 2 and Figure 2).

The estrus response observed in Avikesil-S® treated ewes was comparable to earlier reports where 90 to 100 per cent estrus response was achieved using progesterone sponge protocols in combination with gonadotropins (Mahendra, 2016; Kumar *et al.*, 2016; Yadav *et al.*, 2020; Suhas *et al.*, 2021) [18, 14, 25, 23]. Similarly, De *et al.* (2015; 2016) [5, 6] reported estrus responses of 79 to 83 per cent in Malpura and Kheri ewes.

In clomiphene citrate treated ewes, the estrus response rate was also 66.67 per cent, which is lower than reports in goats where response rates above 90% have been documented (Murugan, 2020; Gupta *et al.*, 2021; Rateb *et al.*, 2019) [20, 10, 22]. Variations in estrus response may be attributed to breed differences, dosage, season, and drug absorption in ruminants. The letrozole treated group showed a moderate estrus response (66.67%), which is slightly lower than reports by Pujara (2022) [21] and Gavimath *et al.* (2023) [8] who observed responses 83.33 and 87.5 per cent. Similarly, Abdel Dayem *et al.* (2020) [1] reported 100 per cent estrus induction in Farafra ewes using letrozole sponges.

3.3 Mean time to onset of estrus

The mean interval from PGF₂α injection to onset of estrus was 36.00 ± 3.79 hours in Group I, 81.50 ± 5.85 hours in Group II, and 57.00 ± 5.75 hours in Group III. The interval was significantly longer in the clomiphene citrate group ($p < 0.05$) compared to the other treatments (Table 3 and Figure 3).

The estrus onset observed with Avikesil-S® sponges was consistent with previous reports indicating estrus within 24 to 48 hours after sponge removal (Karaca *et al.*, 2009; Mahendra, 2016; Kumar *et al.*, 2016; Yadav *et al.*, 2020) [13, 18, 14, 25].

The delayed estrus onset in the clomiphene citrate group agrees with reports in goats and sheep where estrus appeared 48 to 120 hours after treatment (Murugan *et al.*, 2020; Gupta *et al.*, 2021; Rateb *et al.*, 2019) [20, 10, 22].

The letrozole group showed an intermediate interval to estrus (57 hours), which is comparable to findings by Abdel Dayem *et al.* (2020) [1] who reported estrus onset around 54 hours in ewes treated with letrozole sponges.

These results indicate that progesterone-based synchronization provides earlier and more predictable estrus onset compared to non-steroidal protocols.

3.4 Duration of estrus

The mean duration of estrus recorded in the present study was 26.40 ± 2.40 hours in Group I, 30.00 ± 3.47 hours in Group II, and 30.00 ± 3.47 hours in Group III, with no significant difference among groups ($p > 0.05$) (Table 3 and Figure 4).

These values fall within the normal physiological estrus duration in ewes, which ranges between 24 and 36 hours (Hafez and Hafez, 2000) ^[11]. Similar durations have been reported in progesterone synchronized ewes by Yadav *et al.* (2020) ^[25] and Gangadharaiah (2017) ^[17].

Letrozole treated animals also showed estrus durations comparable to those reported by Abdel Dayem *et al.* (2020) ¹ and Gavimath *et al.* (2023) ^[8]. Overall, although synchronization protocols influenced the timing of estrus onset, the duration of estrus remained relatively consistent across treatments.

3.5 Conception rate

The conception rate observed in the present study was 60 per cent in Group I, 50 per cent in Group II, and 50 per cent in

Group III, with no significant difference among treatments ($p>0.05$) (Table 4 and Figure 5).

The conception rate obtained with Avikesil-S[®] sponges was comparable to previous reports using progesterone-based synchronization protocols (Cavalcanti *et al.*, 2012; Lombardo *et al.*, 2020; Martemucci and D'Alessandro, 2011) ^[4, 17, 19].

Similarly, the clomiphene citrate group showed a conception rate of 50 per cent, though previous studies have reported variable results depending on species and treatment protocols (Alamdar *et al.*, 2022; Rateb *et al.*, 2019; Gupta *et al.*, 2021) ^[2, 22, 10].

The letrozole group showed a moderate conception rate (50%), which is slightly lower than reports by Abdel Dayem *et al.* (2020) ^[1] and Pujara (2022) ^[21] where conception rates above 70 per cent were achieved.

Table 1: Sponge retention rate (per cent) in ewes (Group I and Group III)

Groups	Number of animals sponge applied	Number of animals sponge retained	Sponge retention rate (%)
Group I (Avikesil-S [®])	6	6	100
Group III (Letrozole)	6	6	100

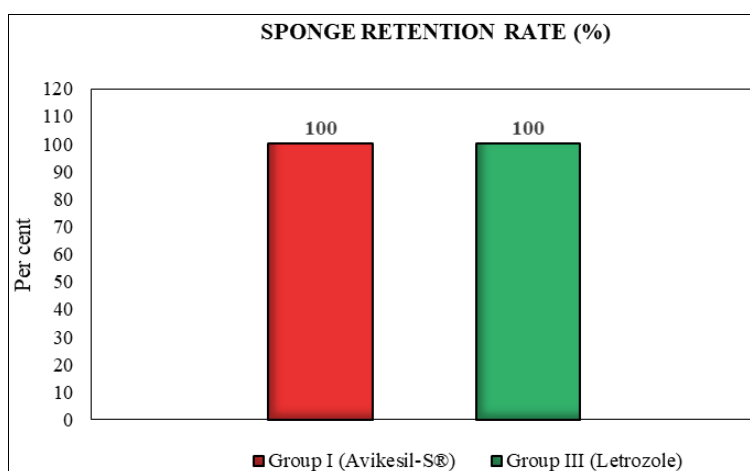


Fig 1: Sponge retention rate (per cent) in ewes (Group I and Group III)

Table 2: Effect of different estrus synchronization protocols on the estrus response rate (per cent) in ewes (n=18)

Treatment	Number of Animals Treated	Number of Animals Responded	Estrus Response Rate (%)	p value
Group I (Avikesil-S [®])	6	5	83.33	0.76 ^{ns}
Group II (Clomiphene Citrate)	6	4	66.67	
Group III (Letrozole)	6	4	66.67	

Note: ns - non significant

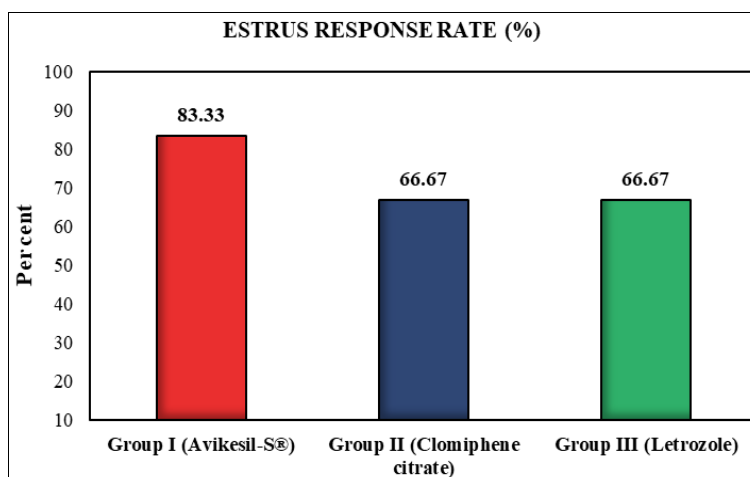
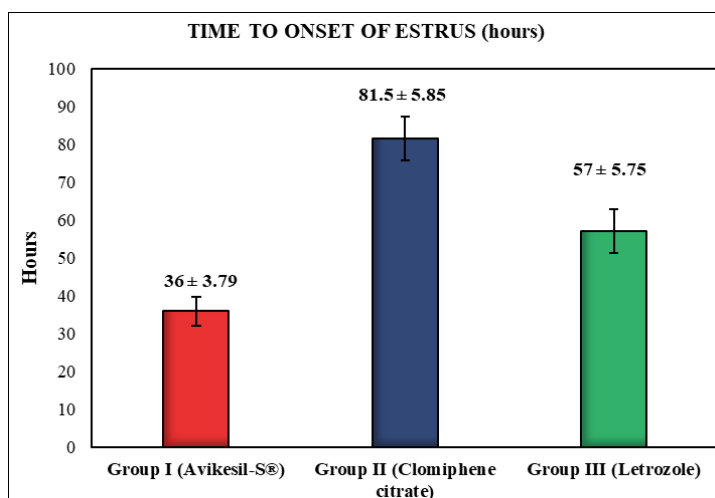
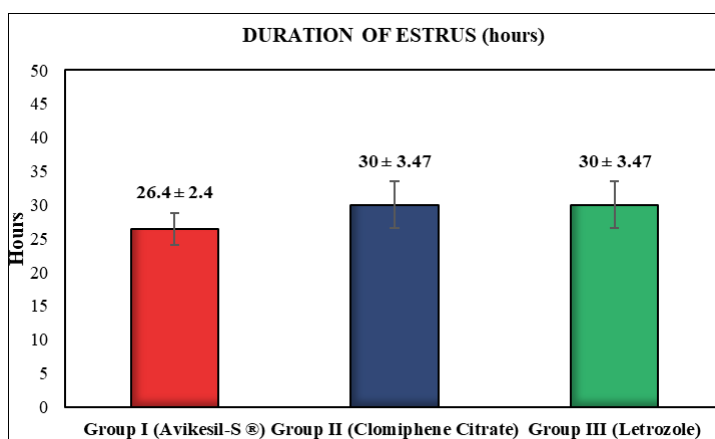


Fig 2: Effect of different estrus synchronization protocols on the estrus response rate (per cent) in ewes (n=18)

Table 3: Effect of different estrus synchronization protocols on the time to onset of estrus (hours) and duration of estrus (hours) in ewes (Mean $\pm$ SE)

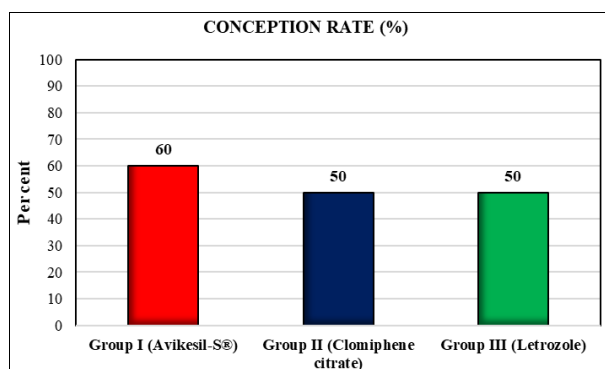
Parameter	Time to onset estrus (hours)	Duration of estrus (hours)
Group I Avikesil-S® Sponge + PGF2 α (n = 5)	36 $\pm$ 3.79 ^a	26.40 $\pm$ 2.40 ^x
Group II CC + PGF2 α (n = 4)	81.50 $\pm$ 5.85 ^b	30.00 $\pm$ 3.47 ^y
Group III Letrozole Sponge + PGF2 α (n = 4)	57.00 $\pm$ 5.75 ^c	30.00 $\pm$ 3.47 ^z

Note: Mean $\pm$ SE bearing superscripts (a, b, c) within column vary significantly at $p < 0.05$, Mean $\pm$ SE bearing superscripts (x, y, z) within column no significant difference

**Fig 3:** Effect of different estrus synchronization protocols on the time to onset of estrus (hours) in ewes (Mean $\pm$ SE)**Fig 4:** Effect of different estrus synchronization protocols on the duration of estrus (hours) in ewes (Mean $\pm$ SE)**Table 4:** Effect of different estrus synchronization protocols on the conception rate (per cent) in ewes

Treatment	Number of animals mated	Number of animals positive	Conception rate (%)	p value
Group I (Avikesil-S®)	5	3	60.00	0.94 ^{ns}
Group II (Clomiphene citrate)	4	2	50.00	
Group III (Letrozole)	4	2	50.00	

Note: ns - non significant

**Fig 5:** Effect of different estrus synchronization protocols on the conception rate (per cent) in ewes**Fig 6:** Transrectal ultrasonography showing foetal parts and caruncles

4. Conclusion

In conclusion, intravaginal progesterone sponges produced the most predictable and earliest estrus expression with robust luteal-phase progesterone support and resulted in tight synchrony. Letrozole sponges offered a non-steroidal alternative that delayed but still effectively induced estrus that is intermediate estrus onset and achieved comparable conception under these conditions. Whereas, oral clomiphene citrate yielded the least synchronized response with a markedly prolonged interval to estrus despite similar estrus duration. Given the smaller sample size, these findings support the viability of letrozole as a promising non-steroidal option but indicate that larger studies are needed to optimise dosing, timing and to confirm fertility outcomes and pharmacokinetic behaviour before field adoption.

References

1. Abdel Dayem AM, Abd El-Hameed NE, Hussein HA. Effect of aromatase inhibitor (letrozole) on estrus synchronization and reproductive performance in Farafr ewes. *Small Ruminant Research*. 2020;188:106122.
2. Alamdar A, Nouri M, Baniadam A. Evaluation of clomiphene citrate for estrus induction and fertility in Afshari ewes. *Veterinary Research Forum*. 2022;13(3):395-401.
3. Casper RF, Mitwally MFM. Aromatase inhibitors for ovulation induction. *Journal of Clinical Endocrinology and Metabolism*. 2012;97(3):743-751.
4. Cavalcanti AS, Brandão FZ, Nogueira LAG, Fonseca JF. Effects of estrus synchronization protocols on reproductive performance of ewes. *Theriogenology*. 2012;78(6):1322-1328.
5. De K, Kumar D, Singh B. Estrus synchronization in Malpura ewes using progesterone-based protocols. *Indian Journal of Small Ruminants*. 2015;21(2):225-228.
6. De K, Kumar D, Singh B. Reproductive performance of Kheri ewes following estrus synchronization protocols. *Indian Journal of Animal Reproduction*. 2016;37(1):62-65.
7. Gangadharaiah BP. Studies on conception rate following synchronization of estrus in ewes. Bidar: Karnataka Veterinary, Animal and Fisheries Sciences University; 2017.
8. Gavimath S, Murthy N, Sahadev A, Raju SB, Gavisiddappa K, Bajanthri S, *et al*. Intravaginal non-steroidal drug, an alternative to steroidal drug in estrus synchronization of does. *Journal of Pharmaceutical Innovation*. 2023;12(2):3167-3170.
9. Goss PE, Strasser K. Aromatase inhibitors in breast cancer therapy. *Journal of Clinical Oncology*. 2001;19(3):881-894.
10. Gupta S, Sharma A, Singh M. Evaluation of clomiphene citrate for estrus induction in goats. *Indian Journal of Animal Reproduction*. 2021;42(2):45-48.
11. Hafez ESE, Hafez B. *Reproduction in farm animals*. 7th ed. Lippincott Williams and Wilkins; 2000.
12. Jainudeen MR, Wahid H, Hafez ESE. Sheep and goat reproduction. In: Hafez ESE, Hafez B, editors. *Reproduction in farm animals*. 7th ed. Lippincott Williams and Wilkins; 2000. p. 172-181.
13. Karaca F, Ataman MB, Çoyan K. Synchronization of estrus with short-term progestagen and PGF_{2α} treatments in ewes. *Reproduction in Domestic Animals*. 2009;44(1):59-64.
14. Kumar S, Naqvi SMK, Maurya VP, Mittal JP. Estrus synchronization and fertility in Nellore Jodipi ewes using progesterone sponges. *Indian Journal of Small Ruminants*. 2016;22(1):37-41.
15. Kusina NT, Tarwirei F, Hamudikuwanda H, Agumba G, Mukwena J. A comparison of progesterone sponges and PGF_{2α} for estrus synchronization in Mashona goat does. *Theriogenology*. 2000;53(8):1567-1580.
16. Land RB, Scaramuzzi RJ. Use of clomiphene citrate to induce ovulation in sheep. *Journal of Reproduction and Fertility*. 1979;56(2):395-401.
17. Lombardo F, Di Trana A, Di Gregorio P. Effects of estrus synchronization protocols on reproductive performance in sheep. *Animals*. 2020;10(9):1611.
18. Mahendra K. Studies on estrus synchronization and fertility in ewes using progesterone sponges. Bidar: Karnataka Veterinary, Animal and Fisheries Sciences University; 2016.
19. Martemucci G, D'Alessandro AG. Synchronization of estrus and ovulation in sheep. *Small Ruminant Research*. 2011;99(1):1-10.
20. Murugan M, Ramesh K, Kumar R. Estrus induction using clomiphene citrate in Kanni Adu goats. *Indian Journal of Small Ruminants*. 2020;26(2):210-213.
21. Pujara R. Evaluation of letrozole-based estrus synchronization in sheep. *Indian Journal of Animal Reproduction*. 2022;43(2):79-83.
22. Rateb SA, Hussein HA, Abdel Dayem AM. Effect of clomiphene citrate on estrus induction and reproductive performance in Damascus goats. *Veterinary World*. 2019;12(10):1600-1605.
23. Suhas G, Manjunatha BM, Rao S. Fertility response following estrus synchronization in ewes using progesterone sponge. *Indian Journal of Small Ruminants*. 2021;27(1):93-97.
24. Swelum AA, Saadeldin IM, Ba-Awadh H. Estrus synchronization protocols in sheep: A review. *Veterinary Medicine International*. 2018;2018:1-9.
25. Yadav P, Yadav MC, Kumar A. Estrus synchronization and fertility in crossbred ewes using progesterone intravaginal sponge. *Indian Journal of Small Ruminants*. 2020;26(1):44-48.

How to Cite This Article

Hiremath C, Murthy N, Sudha G, Ravindranth BM, Kotresh AM, Murthy KMS. Study on comparative efficacy of different protocols in estrus synchronization of sheep. *International Journal of Veterinary Sciences and Animal Husbandry*. 2026;11(3):328-332.

Creative Commons (CC) License

This is an open-access journal, and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 International (CC BY-NC-SA 4.0) License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.