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

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Abstract

The present study evaluated the efficacy of intravaginal progesterone sponge (Avikesil-S®), Letrozole intravaginal sponge, and oral Clomiphene citrate in improving reproductive efficiency in goats. The trial was conducted from March to August 2025 at the Livestock Farm Complex, Veterinary College, Hebbal, Bengaluru, using eighteen healthy does randomly allocated into three groups. Group I received Avikesil-S® sponge for 7 days, Group II a 7.5 mg Letrozole intravaginal sponge for 7 days, and Group III 150 mg oral Clomiphene citrate (Ovulanta®) for 5 days, with all treatments combined with PGF_{2α} for estrus synchronization. Key reproductive parameters including sponge retention, estrus response, onset and duration of estrus, conception rate, and hormonal profiles (progesterone and estrogen) were assessed. Pregnancy was confirmed on day 50 post-mating by ultrasonography. A significant difference was observed in the onset of estrus among groups: 33.6±4.48 h (Avikesil-S®), 56.0±4.3 h (Letrozole), and 86.4±5.87 h (Clomiphene). Conception rates were higher in the Letrozole and Clomiphene groups (100%) compared to the Avikesil-S® group (80%). Avikesil-S® produced the highest hormonal peaks, effectively simulating the luteal phase, whereas Letrozole showed steady progesterone rise with estrogen rebound, and Clomiphene induced gradual hormonal changes. Findings highlight Letrozole and Clomiphene as promising non-steroidal alternatives to conventional progesterone sponges, offering improved conception rates and expanding options for estrus synchronization in goats.

Keywords: Goats, progesterone, estrogen, intravaginal sponge, Avikesil-S®, Letrozole and clomiphene citrate

Introduction

In goats achieving consistent productivity is often challenged by seasonal breeding, which is regulated by photoperiod-mediated changes in melatonin and dopamine that suppress gonadotropin-releasing hormone (GnRH) during longer daylight periods (Wakabayashi *et al.*, 2010; Fatet *et al.*, 2011) [9, 3]. Indigenous solutions like Avikesil-S®, a 350mg natural progesterone sponge developed by ICAR-CSWRI, have shown promising results in goats, alongside emerging non-hormonal alternatives like the "buck effect" and nutritional flushing which address consumer concerns regarding chemical residues (Babu *et al.*, 2020; Mishra *et al.*, 2023) [2, 7]. Recent pharmacological advances have further highlighted Selective Estrogen Receptor Modulators (SERMs) like clomiphene citrate and third-generation aromatase inhibitors like letrozole. These agents modulate hypothalamic-pituitary signaling and suppress estrogen synthesis to promote a controlled follicular rebound, thereby improving corpus luteum function and reducing embryonic loss (Gupta *et al.*, 2021; Yapura *et al.*, 2015) [5, 10]. This transition toward precision reproductive management not only enhances conception rates but also enables advanced techniques like embryo transfer and synchronized kidding. The present study aimed to record and compare the efficacy of these diverse synchronization protocols on the reproductive parameters and hormonal profiles of indigenous goats to optimize performance in low-input production systems.

Materials and Methods

The study was conducted at the Department of Livestock Farm Complex, Veterinary College, Hebbal, Bengaluru, from May to August 2025. Eighteen healthy, non-pregnant indigenous does (1-4 years old) with at least two prior natural estrus cycles were selected

following clinical and gynecological examinations. Animals were maintained under a semi-intensive system, grazing during the day and housed indoors at night, with ragi straw supplemented with vitamins and minerals and water provided ad libitum. All goats were dewormed with Fenbendazole (7 mg/kg BW) and confirmed non-pregnant via ultrasonography (Honda HS/2000, Japan).

Does were randomly allocated into three groups (n = 6 each). Group I received 350 mg natural progesterone-impregnated intravaginal sponges (Avikesil-S®) for seven days, followed by 125 µg Cloprostenol sodium (PGF_{2α}). Group II was treated with polyurethane sponges impregnated with 7.5 mg Letrozole for seven days, also followed by PGF_{2α}. Group III received oral drenching of 750 mg Copper Sulphate (CuSO₄) and 150 mg Clomiphene citrate daily for five days, with PGF_{2α} on Day 5.

Estrus detection was performed twice daily using teaser bucks, with “stand-to-be-mounted” behavior as the primary indicator. Synchronized does were naturally serviced by fertile bucks. Blood samples (2 mL) were collected via jugular venipuncture on the day of 0, 3, 5, 7th day of treatment and on the day of estrus and serum estrogen (E₂) and progesterone (P₄) were analyzed using ELISA (Calbiotech, Inc.). Reproductive parameters assessed included onset and duration of estrus, sponge retention, and conception rate, confirmed 50 days post-mating by ultrasonography. Statistical analysis employed Fisher’s exact test and one-way ANOVA, with significance at $p < 0.05$.

Results and Discussion

The vaginal sponge retention rate was 100% in both Group I (Avikesil-S®) and Group II (Letrozole), with all sponges remaining intact until removal. Estrus induction was observed in 83.33% of does across all three treatment groups, confirming the effectiveness of each protocol in stimulating behavioral estrus.

The onset of estrus varied among treatments. Group I (Avikesil-S®) showed the earliest response at 33.6±4.48 hours, Group II (Letrozole) exhibited onset at 56.0±4.3 hours, and Group III (Clomiphene citrate) demonstrated the longest interval at 86.4±5.87 hours. The mean duration of estrus was similar across groups, recorded as 28.8±2.94 hours in Groups I and II, and 31.2±2.94 hours in Group III.

Conception outcomes were favorable in all groups. Group I achieved pregnancies in 4 out of 5 mated does (80%), while Groups II and III recorded pregnancies in all 5 does (100%). Progesterone profiles revealed distinct treatment effects. Group I exhibited the highest peaks, with values rising from 9.98±1.11 ng/ml on Day 0 to 11.76±2.32 ng/ml on Day 7, followed by a decline to 1.16±0.14 ng/ml at estrus. Group II showed a steady increase from 4.70±2.08 ng/ml on Day 0 to 9.60±2.56 ng/ml on Day 7, with 0.89±0.23 ng/ml at estrus. Group III demonstrated moderate fluctuations, peaking at 8.66±4.51 ng/ml on Day 5.

Estrogen concentrations increased toward estrus in all groups. Group I showed the highest peak at 51.31±7.32 pg/ml, followed by Group II at 38.03±1.71 pg/ml and Group III at 31.98±0.66 pg/ml.

Table 1: Sponge retention rate (%), Estrus Response Rate (%), Time to onset estrus (h), Duration of estrus (h) and Pregnancy Rate (%)

Groups	Sponge retention rate (%)	Estrus Response Rate (%)	Time to onset estrus (h)	Duration of estrus (h)	Pregnancy Rate (%)
Group I-Avikesil	100	83.33	33.6±4.48 ^a	28.8±2.40	80
Group II-Letrozole	100	83.33	56.0±4.30 ^b	28.8±2.40	100
Group III-Clomiphene	100	83.33	86.4±5.87 ^c	31.2±2.40	100

Table 2: Progesterone profile in different estrus synchronization protocols (ng/ml)

Groups	0 th day	3 rd day	5 th day	7 th day	9 th day
Group I-Avikesil	9.98±1.11	9.95±1.24	9.9±1.9	11.76±2.32	1.16±0.14
Group II-Letrozole	4.7±2.08	6.08±1.71	7.94±2.22	9.6±2.56	0.89±0.23
Group III-Clomiphene	4.85±1.57	6.02±1.53	8.66±4.51	5.35±2.01	1.24±0.33

Table 3: Estrogen profile in different estrus synchronization protocols (pg/ml)

Groups	0 th day	3 rd day	5 th day	7 th day	9 th day
Group I-Avikesil	26.36±5.5	38.34±6.44 ^{ab}	34.42±5.37 ^a	34.71±6.92	51.31±7.32 ^{ab}
Group II-Letrozole	19.79±3.54	20.55±5.38 ^a	11.14±2.12 ^a	27.05±2.55	38.03±1.71 ^a
Group III-Clomiphene	14.4±3.84	15.05±3.95 ^b	17.56±2.49 ^b	21.94±2.00	31.98±0.66 ^b

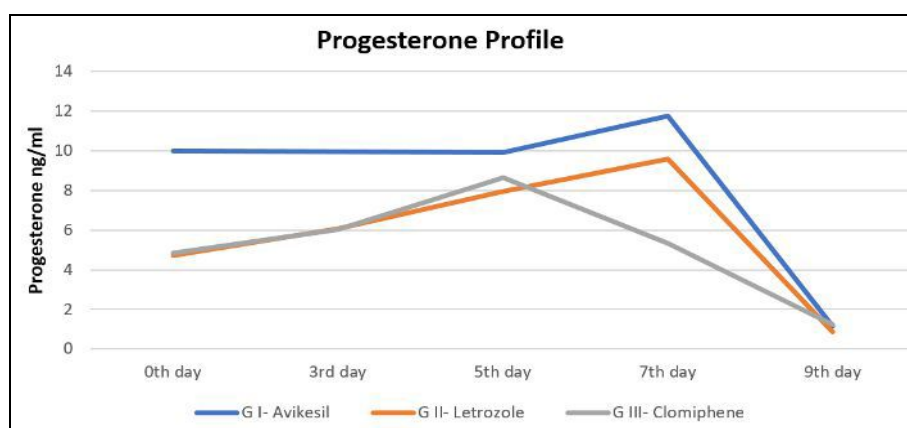


Fig 1: Progesterone profile in different estrus synchronization protocols (ng/ml)

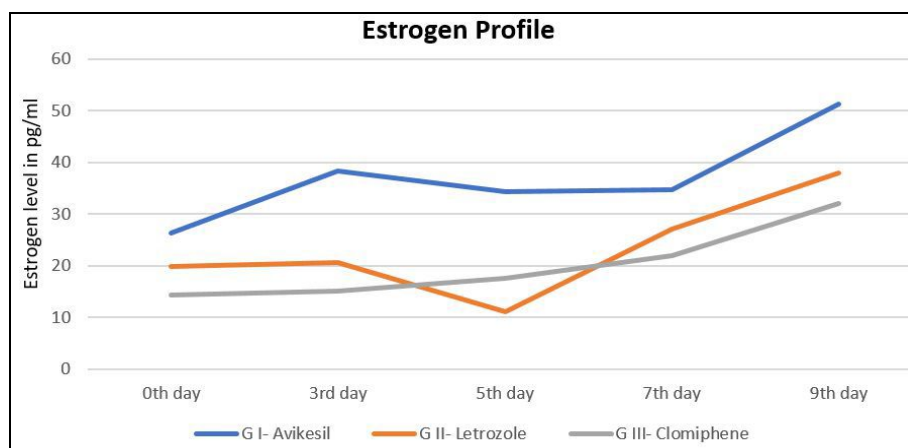


Fig 2: Estrogen profile in different estrus synchronization protocols (pg/ml)

Discussion

The 7-day polyurethane sponge protocol achieved **100%** retention in Groups I and II, corroborating reports of high retention with short-term polyurethane dispensers (Babu *et al.*, 2019, 2020; Gavimath *et al.*, 2023) ^[1, 2, 4], while shorter exposure likely minimized displacement compared with longer protocols (Jangir *et al.*, 2023) ^[6]. Estrus induction was 83.33% (5/6) across groups, indicating that progesterone, letrozole and clomiphene effectively induced behavioral heat under semi-intensive management (Shakya, 2017) ^[8]. Time to onset of estrus differed by treatment—33.6±4.48 h (Group I), 56.0±4.38 h (Group II) and 86.4±5.87 h (Group III)—reflecting the distinct pharmacokinetics of progesterone withdrawal, aromatase inhibition and clomiphene action (Yapura *et al.*, 2015) ^[10]. Estrus duration was comparable (28.8±2.40 h for Groups I and II; 31.2±2.40 h for Group III), providing an adequate mating window across protocols (Gavimath *et al.*, 2023) ^[4]. Conception rates were 80% (4/5 mated) in Group I and 100% (5/5 mated) in Groups II and III, demonstrating that non-steroidal letrozole and clomiphene supported high fertility comparable to progesterone sponges (Gupta *et al.*, 2021) ^[5]. Hormonal profiles showed pronounced P4 and E2 peaks with progesterone sponges (P4 up to 11.76 ng/ml, E2 51.31 pg/ml), a steady P4 rise and estrogen rebound with letrozole (P4 to 9.60 ng/ml, E2 38.03 pg/ml), and moderate P4 fluctuations with clomiphene (peak 8.66 ng/ml, E2 31.98 pg/ml), consistent with their mechanisms and supportive of luteal function and conception (Yapura *et al.*, 2015) ^[10].

Conclusion

The study demonstrated that all three protocols effectively induced a preovulatory E₂ peak sufficient to initiate estrus and support high conception rates. Avikesil-S® yielded the earliest onset of estrus, while letrozole and clomiphene achieved higher conception rates; despite significant variation in estrus onset, other reproductive parameters—sponge retention, estrus duration, and overall pregnancy outcomes—remained largely consistent across treatments. These findings confirm that non-steroidal protocols such as letrozole and clomiphene can match conventional progesterone preparations in efficacy, offering practical, cost-effective alternatives for precision reproductive management in indigenous goats. Ultimately, protocol selection should consider drug availability, ease of administration, and farm management practices, and further multi-breed, multi-season studies are recommended to optimize timing and dosing for broader field application.

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