Effects of Hesperidin on Oestrus Synchronisation and Fertility Parameters in Thermally Stressed Yankasa Ewes

Francis Elisha Saayinzat (saayinzat@gmail.com)
University of Jos https://orcid.org/0000-0002-7773-8658
D. Ogwu
Ahmadu Bello University

Research Article

Keywords: oestrus synchronisation, ewes, hesperidin, fertility-parameters, thermal-stress, antioxidants

Posted Date: September 19th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1999051/v1

Abstract

Hesperidin is an exogenous antioxidant obtained from citrus fruits. Recent studies have demonstrated its therapeutic and biological properties in ameliorating oxidative stress through scavenging for free radical species. The study was aimed at evaluating the effect of hesperidin on oestrus synchronisation and fertility parameters in thermally stressed Yankasa ewes. The study was carried out during the dry and hot seasons of the year in Vom, Plateau State, Nigeria. Forty-six (46) maiden Yankasa ewes with average body condition score of 2.5 and aged between 5–8 months, weighed between 15–20 kg were randomly allocated into two groups of twenty-seven ewes each. Group A served as the treatment group, which were given oral hesperidin supplement (200 mg/kg body weight) on a weekly basis throughout the experiment. Group B severed as the control animals, which received 10 mL of mix dimethyl sulphate and normal saline throughout the study. Three rams aged 18 months to 2 years, weighing between 35–40kg were used as teaser and breeding rams. The time of onset of oestrus, oestrus duration, oestrus response rate, control internal drug release retention rate, pregnancy and lambing rates, fecundity, gestational length, lambing weight and postpartum oestrus interval were evaluated. The results obtained showed that hesperidin had significant ($P < 0.05$) effects on the CIDR retention (95 7.10% and 75.0 ± 7.1%), oestrus response rate (ORR) (80.00 ± 14.1% and 65.0 ± 7.1%), onset of oestrus (2.8 ± 1.0 and 6.0 ± 1.4 days), duration of oestrus (30.5 ± 2.1 and 25.6 ± 2.4 hours), pregnancy rate (85% and 75%), lambing rate (95% and 80%), lambing weight (2.52 ± 0.69 kg and 2.24 ± 0.73), postpartum oestrus interval (37.88 ± 1.13 and 39.33 ± 0.67 days), and gestation length (149.38 ± 1.39 and 151.4 ± 1.14 days) for the treatment and control groups respectively. The present study demonstrated that hesperidin administration increased significantly ($P < 0.05$) the TOO, ORR, OD, CIDR retention, lambing weight, pregnancy and lambing rates in thermally stressed Yankasa ewes.

Introduction

Sheep production is an important component of Nigerian livestock industry and an agro-preneurial venture that promises high return on investment (Akubuo et al., 2020). Sheep supplies mutton, milk, wool, skin and other products, and also serve as flexible financial reserves as they are sold when needed by smallholder farmers and during migratory practices by Fulani nomads (Sa'Ayinzat, 2021). It also plays other socio-cultural roles in the customs and traditions of Nigerian societies (Lawal-Adebowale, 2012). Yankasa breed of sheep are commonly kept by small holder farmers and Fulani herders due to their hardy nature, resilience and productivity (Stenning, 1957; Ducrotoy et al., 2018). The other breeds raised include Ouda, Balami and West African Dwarf (Sa'Ayinzat, 2021). Unfortunately, the reproductive performance of these breeds has been generally poor due to the harsh and severe tropical environment, nutritional stress due to scarcity of feed especially during the dry season, disease burdens and other thermal stress conditions, resulting in oxidative stress, which undermines their reproductive performance (Sa'ayinzat et al., 2021a). Although, efforts have been made to improve their reproductive performance through improvement of genetic materials to boost their reproductive efficiency and profitability (Kiplagat et al., 2012; Pohler et al., 2016), the successes of these trials have been limited to research institutes in Nigeria (Matemilola and Elegbede, 2017).

In order to minimize some of the constraints and improve conception rates, oestrus synchronisation evolved to enhance induction of oestrus and its detection in ruminants and other animal species (Oke-Egbodo et al., 2018; Yu et al., 2018; Pal and Dar, 2020; Skliarov et al., 2021; Yu et al., 2022). Oestrus synchronisation is a management tool for the manipulation of oestrus to maximise reproductive efficiency (Musa-Azara et al., 2011; da Silva et al., 2020). Different methods of oestrus synchronisation have been extensively discussed and includes progesterone based protocols, gonadotropin releasing hormone (GnRH)/pregnant mare serum gonadotropin (PMSG) based protocol, use of prostaglandin F2α, and use of combination-based protocols and the male effect (introduction or presence of the ram) (Macmillan and Burke, 1996; Wildeus, 2000; Naderipour, 2011; Xu, 2011; Omontese et al., 2014; Omontese et al., 2016; Yu et al., 2018; da Silva et al., 2020; Pal and Dar, 2020; Skliarov et al., 2021). The techniques include protocols aimed at manipulating the follicular phase by allowing the follicle stimulating hormone (FSH) and luteinising hormone (LH) to maximise their effects and cause follicular maturation and ovulation; or altering the luteal lifespan by prolongation of progesterone and/or lysing of the corpus luteum through the use of prostaglandin F2α to shorten the luteal phase, and thus, remove the progesterone blockade and enable early ovulation (Xu, 2011; Hashemi and Safdarian, 2017; Oke-Egbodo et al., 2018; Pal and Dar, 2020). Despite the use of different oestrus synchronisation methods, thermal stress still limits reproductive performance due to excess generation of free radical species in the body, and thus, disrupting the redox reaction and when in excess, they generate pathological conditions that affect the overall animal performance and therefore reduced fertility, profitability and results in economic loss (Celi et al., 2014; Abubakar et al., 2018; Celik et al., 2021; Sa’ayinzat et al., 2021a).

The use of exogenous antioxidants has been employed in order to stem the excess generation of free radical species in animals and thus, improve their reproductive performance (Sa’Ayinzat et al., 2021b). Hesperidin as an exogenous antioxidant obtained mainly from citrus fruits, have demonstrable biologic and therapeutic properties such as scavenging for free radical species, anti-inflammatory properties, antimicrobial and antiviral properties (Sa’ayinzat et al., 2021b). Through its scavenging properties, hesperidin ameliorates oxidative stress due to severe environmental conditions, and thus, may improve reproductive performance. Hence, the current study investigated the use of hesperidin as a potent exogenous antioxidant aimed at improving oestrus synchronisation and fertility in thermally stressed Yankasa ewes.

Materials And Methods

Study Location

The experiment was carried out in the Livestock Investigation Department (LID) of the National Veterinary Research Institute (NVRI), Vom, Nigeria between September 2016 - January 2017. LID is located on the Jos Plateau, which is situated between latitude 9o44 North of the equator and longitude 8o47 East, with an altitude of about 1,285 metres above the sea level. It has an average relative humidity of 55% (Ntem, 2015). The average monthly ambient temperature ranges from 17oC to 29oC, from November to February, the average night time temperatures drop as low as 10oC resulting in chilly nights during the cold harmattan season and a temperature-humidity-index range of 14 – 25. It receives an average annual rainfall of 1300 mm, with July to September being the months with the highest rainfall. The average rainfall during the months of October to March is 13.3 mm (Ntem, 2015).

Meteorological Data

Daily temperature readings were taken using wet and dry bulb thermometer (Brannan, England) throughout the duration of the experiment. The data obtained was complemented with that provided by Nigeria Meteorological Agency. The data were analysed and classified based on the modification of Marai et al. (2007) and Papanastasiou et al. (2015) to demonstrate the impact of thermal environmental stressors on ewes.

Ethical Approval

The use of animals was approved by the Animal Use and Care Committee of the National Veterinary Research Institute, Vom, Plateau State, Nigeria, with the number AEC/02/36/17.

Animal Sourcing and Groupings

Forty-six (46) cycling maiden Yankasa ewes weighed between 15 – 20 kg, aged 5 – 8 months and three rams aged 18 months to 2 years weighed between 35 - 40kg were sourced from Tilde Fulani market in Bauchi state, Nigeria and were used for the study. The animals were kept for a period of four weeks to get acclimatized, in a stone-built dwarf-walled fence and was roofed with corrugated roofing sheet in a well-ventilated house. Concentrates containing 2500 mKcal and 15% crude protein compounded by the Institute's (NVRI) Feedmill and mix of maize offal, sorghum waste and silage were provided as supplementary feed during the dry season (Appendix Table 1). Clean drinking water was provided ad libitum.

Screening of Experimental Animals

The animals were kept for a stabilisation period of four weeks during which the animals were screened and treated for ecto-, endo- and haemo-parasites. They were treated with ivermectin 1% (Ivomec® - Boehringer Ingelheim Animal Health USA Inc.), given subcutaneously at a dose of 1 mL/50 kg body weight; albendazole (Kepro BV Holland); given orally at the dose of 0.8 ml/kg, diminazen diaceturate (Animal Care®) at dose of 5 mg/kg body weight by deep intramuscular route and oxytetracycline (Kepro B VR Holland) at the rate of 20 mg/kg by deep intramuscular injection. Physical evaluation of the reproductive system of the rams was also undertaken.

Source and Constitution of Hesperidin

Three kilograms of high-grade commercial hesperidin powder (98.5% purity) was obtained from ANIMED, Connecticut, USA and was used for the experiment. The powder was dissolved in 30 mL dimethyl sulphoxide (DMSO) (Honywell Riedel-de Haen, Germany, 99.5% purity). The solution obtained was diluted five times with normal saline to a final concentration of 200 mg/ml.

Experimental Groupings and Treatment Regime

The ewes were weighed and assigned into two groups of 27 ewes each. Group A served as the treatment group, while group B served as the control group. The treatment group was administered constituted hesperidin orally based on body weight once weekly throughout the duration of the experiment spanning over 6 oestrous cycles. The ewes in the control group ewes were administered 10 mL of a mix of DMSO and normal saline on weekly basis throughout the duration of the experiment spanning over 6 oestrous cycles. Both groups were administered EAZI-Breed control internal drug release (CIDR) containing 300 mg of impregnated progesterone during the 1st (baseline stage of the study) and during 2nd and 3rd oestrous cycles. The CIDR are T-shaped devices with a silicone-coated nylon core with the silicone coating impregnated with progesterone and were inserted intra-vaginally using a specialized applicator. After withdrawal of CIDR on the 11th day and the immediate deep intramuscular injection of 1mL of lutylase (20%) (dinoprost tromethamine, Zoetis Inc, Spain) the ewes were monitored for oestrus (heat). During the 4th and 5th oestrous cycles, the ewes in the treatment group were given constituted hesperidin orally on weekly basis while the control group received DMSO and normal saline (Table I). During the 6th oestrous cycle, the ewes were allowed to come into heat naturally without any treatment in both groups (Table 1).

Table 1: Treatment Regime

Oestrous Cycle	Treatment Group Remarks	Control Group Remarks
1st (baseline)	CIDR + lutylase	CIDR + lutylase
2nd	CIDR + lutylase + hesperidin	CIDR + lutylase + DMSO + NS
3rd		
4th	Hesperidin given to treatment group	DMSO + NS
5th		
6th	no CIDR, no lutylase, and no hesperidin	no CIDR, no lutylase, and no hesperidin

Oestrus Detection

Apronated rams were used to detect ewes on oestrus throughout the oestrus cycle studies. Ewes standing to be mounted was considered as the hallmark indicating oestrus. The oestrus detection was carried out daily after withdrawal of CIDR and deep intramuscular injection of lutylase between 6 – 11.00 a.m. and between 2 – 6.00 p.m. Ewes that showed visible standing oestrus were considered to be on heat (oestrus) and refusal to be mounted after showing oestrus was considered as end of heat (Parsons & Hunter, 1967; Roelofs et al., 2008). Upon detection of oestrus during the 6th oestrous cycle, the ewes were bred naturally in both groups.

Pregnancy Diagnosis

The ewes were restrained in dorsal recumbency after shaving the transabdominal region. Each ewe was scanned using real time B-mode scanner (Medison SA600V, made in Germany), which was equipped with a 3.5 MHz convex transducer on the 21st day post-mating to determine the presence of gestational sac, which indicated conception.

Determination of CIDR Retention Rate, Pregnancy and Lambing Rates and Fecundity

CIDR Retention Rate

The CIDR refers to controlled internal drug release, which is a progesterone impregnated device used for oestrous synchronisation through intravaginal insertion. Its retention had to do with the proportion of ewes with intravaginal CIDR intact at the end of the experiment in comparison with the total number of ewes in the group that had intravaginal CIDR inserted (Omontese et al., 2014).

Pregnancy Rate

The fertility/pregnancy rate was, therefore, defined as the number of ewes lambing as a proportion of the number of females of reproductive age that were available for mating (Salifu, 2014). This was calculated according the formula:

$$\text{Pregnancy Rate} = \frac{\text{Number of pregnant ewes} \times 100}{\text{Number of ewes mated in the group}}$$

Lambing rate

The lambing rate was considered as the proportion of the number of ewes lambing in the group mated or exposed (Ataman & Aköz, 2006).

$$\text{Lambing rate} = \frac{\text{Number of ewes lambing} \times 100}{\text{Number of ewes mated in the group}}$$

Gestational length

Gestational length is the period from mating to delivery of the foetus, which last for a period of about 5 months or ranged between 145 – 150 days (Senger, 2007).

Fecundity: number of lambs born/number of ewes synchronized (Zohara et al., 2014).

Data Analysis

The experimental layout was completely a randomised independent t-test. Data generated were analysed and expressed using descriptive statistics. Variable such as ORR was expressed in percentage, while TOO, OD, pregnancy and lambing rates were expressed as mean (days/hours) ± SEM. Data obtained from all experiments were subjected to independent t-test using the Statistical Analysis System (SAS, Institute Inc., Release 8.2, Cary, NC, USA, 2013). Significant differences among treatment means were separated using the Least Significant Difference (LSD). Line and bar charts were used to construct the graphical distribution of the variables. Values of $P < 0.05$ were considered significant.

Results

The meteorological data during the oestrus cycle study ranged between 9oC and 31.5oC for mean ambient temperature with the mean ambient temperature ranging between 18.50 ± 0.29oC and 22.77 ± 0.34oC. The relative humidity ranged between 8% - 98% and the mean relative humidity fluctuated between 18.95 ± 1.35% and 69.52 ± 2.69%. The wind speed ranged between 4.75 m/s and 10 m/s, while solar radiation fluctuated between 3,941.4 and 6,100.2 w/m2 (Appendix Table 1).

CIDR Retention Rate, Oestrus Response Rate, Time of Onset of Oestrus and Oestrus Duration in Hesperidin Fed Yankasa Ewes

The effect of hesperidin on oestrous cycle parameters are summarised in Appendix Table 1. The effect of hesperidin on response to CIDR Retention is presented in Fig. 1. The CIDR retention, which was significantly ($P < 0.05$) higher with 26 (95%) in the ewes treated with CIDR, lutylase and hesperidin; and 20 (75%) ewes in the control group. The CIDR retention was significantly ($P < 0.05$) higher with 24 (90.25%) in the hesperidin treated group while 16 (60%) in the control group. CIDR retention was detected to be significantly ($P < 0.05$) higher in 22 (80%) of the ewes in the non-treated group and 14 (50%) in the control group.

The effect of hesperidin on response to Oestrus Response Rate (ORR) is presented in Fig. 2. The ORR was significantly ($P < 0.05$) higher in 22 (80%) of the ewes treated with CIDR, lutylase and hesperidin; and 18 (65%) ewes in the control group. There was a significantly ($P < 0.05$) higher ORR in 22 (81.25%) of the ewes in the hesperidin treated group and 16 (60%) in the control group. The ORR was significantly ($P < 0.05$) higher in 17 (62%) of the ewes in the non-treated group and 11 (40%) in the control group.

The effect of hesperidin on time of onset of oestrus (TOO) is presented in Fig. 3. The TOO was significantly ($P < 0.05$) shorter with 2.8 ± 1.0 days in ewes treated with CIDR, lutylase and hesperidin; and 6.0 days in ewes in the control group. The TOO was significantly ($P < 0.05$) shorter in 16.80 ± 1.70 days in ewes treated with hesperidin and 19.41 ± 2.4 days in the control group. The TOO was significantly ($P < 0.05$) shorter 16.7 days in the ewes in the non-treated group and 18 days in the control group.

The effect of hesperidin on oestrus duration (OD) is presented in Fig. 1 below The OD was significantly ($P < 0.05$) higher with 30.5 ± 2.1 hours in ewes treated with CIDR, lutylase and hesperidin; and 25.6 ± 2.4 hours in ewes in the control group. The OD was significantly ($P < 0.05$) higher 33.00 ± 4.24 hours in ewes treated with hesperidin and 23.30 ± 2.40 hours in the control group. The OD was significantly ($P < 0.05$) higher with 29.5 hours in the ewes in the non-treated group and 24 hours in the control group.

Fertility Parameters in Hesperidin Fed Yankasa Ewes

The effect of hesperidin on fertility parameters in thermally-stressed Yankasa ewes are summarized in Appendix Table 5. The effect of hesperidin on pregnancy rate (PR) is presented in Fig. 5. The PR was significantly ($P < 0.05$) higher 85% in ewes in the treatment group than in the control group with 75%. The lambing rate (LR) was significantly ($P < 0.05$) higher 95% in the hesperidin treated group while it was 80% in the control group.

The effect of hesperidin on lambing weight (LW) is presented in Fig. 6. The LW was significantly ($P < 0.05$) higher with 2.52 ± 0.69 Kg in ewes in the non-treated group and 2.24 ± 0.73 (50%) in the control group.

The effect of hesperidin on postpartum oestrus interval (PPOI) is presented in Fig. 7 below The PPOI was significantly ($P < 0.05$) shorter with 37.88 ± 1.13 days in the treated group while the control had 39.33 ± 0.67 days.

The effect of hesperidin on gestation length (GL) is presented in Fig. 8. The GL was significantly ($P < 0.05$) shorter 149.38 ± 1.30 days in the treated group when compared with the control (151.4 ± 1.14 days).

The effect of hesperidin on fecundity is presented in Fig. 9. The fecundity was not significantly ($P < 0.05$) different with 1.13 in treated group and 1.04 in the control group.

Discussion

The mean ambient temperature (AT) and relative humidity (RH) documented in this study were outside the thermoneutral zone (TNZ) of 22 – 30 oC and 28 – 60 %, respectively, established for sheep under tropical environment (Suprayogi et al., 2006; Khalek, 2007; Marai et al., 2007; Papanastasiou et al., 2015). The lowest AT recorded during the harmattan season was 14^{o}C during the morning hours and 10^{o}C during the night hours, which indicated that, the animals were subjected to extreme cold environmental conditions. The TNZ is the comfort zone or the zone of indifference of the animal where the animals' performance is maximized with no compensatory efforts required by the animal for the maintenance of its homeostasis (Bianca, 1976; Silanikove, 2000).

CIDR retention rate improves oestrus synchronisation, and therefore, the oestrus response rate (ORR), which resulted in higher pregnancy rates in ewes (Moeini et al., 2007; Sidi et al., 2016). The higher value of CIDR retention rate and therefore higher oestrus response rate in the treatment groups obtained in the present study may be as a result of hesperidin ability to scavenge toxic free radical species, combat inflammation and ameliorate oxidative stress induced by the CIDR insertion and exposure of the animals to severe thermal stress. This resulted in higher oestrus synchronisation, demonstrating the ameliorative effects of hesperidin in improving oestrus synchronisation in thermally stressed Yankasa ewes. The finding of this study agrees with the findings of Omontese et al. (2010) and Omontese et al. (2014) who administered ascorbic acid to does and had CIDR retention of 85% and to Yankasa ewes with CIDR retention of 90%, respectively. CIDR losses were found to be higher in the control group and this agrees with the findings of Romano (2004), who carried out similar experiment and obtained similar results in Nubian goats, though no antioxidants were used in the study. High losses of CIDR in ewes have been reported by several authors (Ainsworthl and Doww, 1986; Maxwell and Barnes, 1986; Rhodes and Nathanielsz, 1988; Wheaton et al., 1993) and might have been due to lack of use of the CIDR applicator and methods of insertion of the CIDR. When CIDR are not carefully inserted intravaginally, it causes irritation of the vaginal mucosa, which may result in inflammation and predisposes the ewes to infection and probably loss of the CIDR and lower oestrus synchronisation rate and oestrus response rates (Swelum et al., 2015).

The significant ORR values obtained in the present study may be due to the radical scavenging ability of hesperidin, which resulted in higher ORR. The results of the present study resonate with the findings of Musa et al. (2018), who found higher ORR values in antioxidant supplemented Yankasa ewes. Oxidative stress is associated with the different phases of the oestrous cycle in addition to that from severe environmental conditions, during which excess ROS are produced, resulting in poor oestrous outcomes. The effect of selenium (Se) supplementation on the reproductive performance of Merino ewes mated out of the normal breeding season was investigated by Sánchez et al. (2008) and found that though selenium supplementation had a positive effect on oestrus synchronisation in ewes mated out of the breeding season, it did not improve significantly ewe fertility or lamb birth weight, even though selenium supplemented ewes had higher lambing rate and produced more lambs than those not synchronized. In their study they associated selenium supplementation at the early stages of pregnancy to result in selenium toxicity and embryonic mortality. In another study by (Mashamaite, 2019) on South Africa indigenous goats, selenium supplementation did not have any significant effect on the number and size follicles, oestrus response and duration, oestrus onset, pregnancy and kidding rates, gestation length and litter size. Earlier studies by (Sánchez et al., 2008) had indicated that selenium supplementation to Merino sheep had inhibitory effects resulting in embryonic mortality during earlier pregnancy. With hesperidin supplementation, ROS are scavenged and destroyed, thus resulting in enhanced ORR. However, the findings of current study disagree with the findings of Gore (2016), who investigated the effect of β-carotene (an antioxidant radical scavenger) supplementation on oestrus synchronisation and milk production in Saanen goats and found that β-carotene supplementation had no effect on ORR. The discrepancies could be due to species variation, location, health status and season during which the study was conducted.

The overall beneficial effects of hesperidin resulted in shorter TOO, which falls within the normal range of 13 – 19 days reported by Greyling and Brink (1987). Hesperidin as an antioxidant, with ability to scavenger excess reactive oxygen species (ROS) resulted in better cell wall and other cellular components often damaged by excess ROS associated with thermal stress and reproductive processes. Its anti-inflammatory, antibacterial, and antiviral properties improved TOO in Yankasa ewes. The findings of this study disagree with the findings of Trout et al. (1998), who investigated the characteristics of oestrous cycle and antioxidant status in lactating dairy cattle exposed to heat stress, and observed that there was no variation in TOO in the antioxidant treatment and control groups. The findings of the current study are also contrary to the result of Vaadala et al. (2019), who reported that the use of the flavonoid, baicalein, in female mice prolonged oestrus and also suppressed fertility output.   This differences in findings may be due to species variation and the season during the studies were carried out. The current study was carried out in Yankasa ewes during the cold-dry harmattan season with chilly night time temperatures of 10oC and under a montane vegetation. The study by Trout et al., (1998) was conducted in a heat stressed environment in cattle, while that of Vaadala et al. (2019) was conducted in female mice under laboratory conditions.

The higher oestrus duration (OD) (hours) obtained in this study corroborates the findings of Sejian et al., (2014), who obtained a significant increase in oestrus duration (36.68 ± 2.42 hours) in Malpura ewes administered mineral and antioxidant supplementation, while other parameters like oestrous response rate (100%) and length of oestrous cycle (14.29 ± 0.18) were not different. The mean oestrus duration (hours) fell within the range of 24 – 36 hours reported by various researchers (Vivanco, 1986; Jarquin et al., 2014; Zohara et al., 2014). This shows that hesperidin improved the OD in Yankasa ewes. This might have been due to free radical scavenging capacity of hesperidin thereby enabling the animals to cope with the harsh thermal stress during the harmattan season. However, the result of the current study disagrees with the findings of Gore, (2016) who investigated the effect of β-carotene (an antioxidant radical scavenger) supplementation on oestrus synchronisation and milk production in Saanen goats and found that β-carotene supplementation had no effect on OD. The discrepancies in the findings could be due to species and breed variations, location and the season during which the study was carried out. Furthermore, the current study was carried out during the cold dry harmattan season, while Gore, (2016) conducted his study in goats indicating species variations and under sub-tropical conditions. Different climatic factors have been noted to influence onset and oestrus duration with prolong higher temperatures shortening the duration of oestrus and reducing the intensity of oestrus behaviour in ewes (Romano and Fahning, 2013). Cold stress induces shorter oestrus length in West Bengal goats in treatment group than the control (Kumar et al., 2015), which agrees with the findings of this study. Cold stress has been reported to shorten OD, and may even result in total loss of the oestrous cycle event in rats (Tumenbayar et al., 2019). Extreme cold stress is associated with the depletion of the energy reserves resulting negative energy balance and increased metabolic activity in ewes and other farm animals, which adversely influences homeostasis and cause overall poor reproductive performance (Gebregeziabhear and Ameha, 2015). OD may be influenced by season, species, breed, location, health status, management style, nutrition and the stage of the oestrous cycle (Omontese et al., 2017).

Residual effect observed in this study after withdrawal of hesperidin is an indication of a drug's continued effect in the body and expresses the long-term drug effects. Drug residual effects is well studied in cases of drug abuse in humans (Roehrs et al., 1986; Spencer & Boren, 1990; Fitzgerald and Vietri, 2015) and in animal studies (Atabaki et al., 2020; Sharma et al., 2021). It is, however, poorly documented in animals. In this study hesperidin demonstrated significant residual effects after two weeks of withdrawal of treatment, by improving ORR, OD and shortening of the TOO in Yankasa ewes. The findings of this study resonate with the findings of Pinna and Sala, (2019), who found that hesperidin and genistein mix elicited residual vasorelaxations effect after L-NAME pretreatment were blocked by incubation with glybenclamide. Their findings concluded that regular moderate consumption of citrus fruit or juice may confer protection to both mother and foetus, and might reduce blood pressure, and the risk of foetal vascular complications such as preeclampsia and intrauterine growth restriction. Also, semi-professional cyclists were administered a single dose each of 500 mg of hesperidin had enhanced physical performance due to the amelioration of oxidative status in the volunteers (Martínez-Noguera et al., 2019; Ávila-gálvez et al., 2021).

The higher pregnancy and lambing rates observed in this study might have been as a result of the ability of hesperidin to ameliorate oxidative stress associated with severe thermal stress and pregnancy and parturition (Agarwal et al., 2005). The finding agrees with the result of a study conducted by (Safarnavadeh and Rastegarpanah, 2011) in rats using oil from *Satureja khuzestanica*, which showed a 93.33 % pregnancy rate. *Satureja khuzestanica* oil contains flavonoids, such as p-cymene and carvacrol, which through their antioxidant capacity had the ability to combat oxidative stress, improve oocyte quality and pre-implantation embryo survival, thus, improving pregnancy rates (Safarnavadeh and Rastegarpanah, 2011). The supplementation with vitamin C (ascorbic acid) in women resulted in higher pregnancy rates in women who had luteal phase defect indicating the beneficial effect of ascorbic acid as an antioxidant (Henmi et al., 2003). Another study using supplementation composed of vitamin E, iron, zinc, selenium and L-arginine showed an increase in ovulation and pregnancy rates in women and, thus, supporting the findings of the current study (Westphal et al., 2004). The findings of this study are contrary to the results obtained by Ozyurtlu et al. (2010), who investigated the characterization of oestrus synchronisation and other fertility parameters in Awassi ewes during the non-breeding season and found no variations in parameters studies. Such results might have been influenced by breed variation and genetic make-up, location, nutrition, environmental conditions and the healthy status of the ewes.

The shorter gestation length found in this study may be associated with the radical scavenging capacity of hesperidin. Oxidative stress is associated with severe environment conditions and pregnancy due to physiologic and metabolic processes that are necessary for the development of the offspring. The findings of this study agree with the report of Mukasa-Mugerwa et al. (1994), Fogarty et al. (2005), Hucal, (2011), Petrovic et al. (2013) and Menatian et al. (2010). The findings of this study found the gestation length to fall within the normal range established for sheep with 138 – 157 days reported by Tilton, (1964). Iyiola-Tunji et al. (2010) reported a different range of 150.3 ± 0.61 to 153.3 ± 0.60 days for all Nigerian breed genotypes (Balami, Uda and Yankasa) investigated, except for the pure Balami breed which had a shorter gestation length (137.1 ± 0.81 days). The findings of Iyiola-Tunji et al. (2010) on gestation length was carried out on genotypes not pure Yankasa breed and may show variation in gestation length. Gestation length in ewes is dependent upon several factors including: genotype, health status of the dam, body condition score, breed, nutritional status, age, number of foetuses, sex of the foetus, foetal birth weight, environmental conditions associated with the breeding seasons including the effect of thermal stress and the sire used for breeding (Tilton, 1964; Forbes, 1967; Anderson et al., 1981; Oztirk and Aktas, 1996; Iyiola-Tunji et al., 2010; Hucal, 2011; Petrovic et al., 2013). Higher lambing weight is reported to induce earlier lambing whether single or twin pregnancies and male offspring tend to result to earlier lambing than female offspring due to their body size and weight (Salifu, 2014; Parraguez et al., 2020; Sales et al., 2020). Higher foetal weight induce stress which activates the generation of cortisol and initiate earlier lambing (Senger, 2007; Salifu, 2014). Though studies regarding antioxidant effect on lambing weight are somewhat mixed and varied with some finding increase in lambing rates (Capper et al., 2005), others did not find any variation (Ali et al., 2004; Sterndale et al., 2018). They attributed the variations to be due to use of different doses of vitamin E, routes of administration, and duration of treatments, in addition to eventual differences in sheep pregnancy rank and breed and other undefined factors.

The higher lambing weights in the treatment group obtained in this study agrees with the findings of (Sales et al., 2019) who administered Vit C and E to ewes and found that the lambs from supplemented ewes had higher lambing weights than the control in both single and twin pregnancies. Melatonin supplementation given to pregnant ewes under heat stressed conditions improved the redox status of heat-stressed ewes and increased the mean number and bodyweight of lambs born per ewe, as well as the milk production (Bouroutzika et al., 2020). Higher lamb birth weights were also obtained from undernourished pregnant ewes given supplementation of vitamins C and E, which resulted in counteraction of hypoxemia and oxidative stress associated with intrauterine growth restriction (Parraguez et al., 2022a and b). Supplementation with vitamins C and E alone or in combination with concentrate on pregnancy outcomes and growth and survival of lambs during early postnatal stages (lactation) showed increased birth weight and higher body weight (BW) at weaning in ewes and higher lamb survival rates (Parraguez et al., 2020; Parraguez et al., 2022a). This demonstrates the antioxidant capacity of ascorbic acid and vitamin E in improving foetal oxygenation by counteracting maternal hypoxia and oxidative stress. Without the antioxidants the undernourished pregnant ewes might have experienced lipid peroxidation and impairment of redox homeostasis, and thus, reducing the oxygenation capacity of the red blood cells and therefore, decreased foetal body weight (Nawito et al., 2016; Parraguez et al., 2020; Sales et al., 2020). Antioxidants supplementation has been associated with increased umbilical flow that favoured foetal growth, increased angiogenesis, favoured placental function and foetal development (Kasimanickam et al., 2010; Thakor et al., 2010; Parraguez et al., 2013). Improved placental efficiency and lambing weight have been reported in pregnant undernourished rats (Richter et al., 2009). This is further supported by the findings of Parraguez et al., (2011) who obtained increased placental efficiency between 10% and 45% in single ovine pregnancies developed under oxidative stress in chronically hypoxic environment on high plateaus. Foetal hypoxia has been reported to predisposes the offspring to congenital anomalies and chronic diseases in future life (Silvestro et al., 2020). However, the use of several antioxidants such as melatonin, erythropoietin, vitamin C, resveratrol and hydrogen, have demonstrated potential protective effects in prenatal hypoxia (Silvestro et al., 2020). Hesperidin as a free radical scavenger, ameliorated oxidative stress through impairment of lipid peroxidation and improvement of cell wall integrity, improved oxygenation between the dam and foetus, higher lambing weights and therefore better performance.

No statistically significant differences were recorded between the two treatments regarding the fecundity. This finding is consistent with the work of Ozyurtlu et al. (2010) who investigated the effect of oestrus synchronisation in sheep on fertility parameters and found no variation. The studies of Ataman and Aköz, (2006) and Ozyurtlu et al., (2010) also obtained similar results implying hesperidin supplementation did not alter fecundity in sheep. Discrepancies above may be caused by some factors such as genotype, nutrition, environmental conditions, housing and management. Contrary to the findings of this study on fecundity, Kamiloğlu et al. (2017) obtained significantly higher fecundity rates in Tuj sheep. They attributed their findings to the inclusion of testosterone immunization and its synergy with oestrus synchronisation agents administered to the ewes. The results of this study showed that fecundity was not influenced by hesperidin treatment.

In conclusion it was observed that hesperidin significantly increased oestrus synchronisation outcomes and fertility parameters in Yankasa ewes.

It is therefore recommended that farmers in Plateau State, Nigeria could be advised to administer hesperidin to Yankasa ewes during thermally-stressed conditions. The study involved a limited number of ewes on the Jos Plateau, it is therefore also recommended that further studies involving more ewes be carried out in other thermally stressed environments where Yankasa ewes are raised. Further studies are also required to elucidate on the molecular mechanism of action of hesperidin in ameliorating thermal stress in Yankasa ewes.

Declarations

ACKNOWLEDGEMENT

The authors are grateful to colleagues who read through the article before final submission for publication.

FUNDING SUPPORT

The authors did not receive any specific grant from any funding agency for this work, whether from public, commercial or not-for-profit sector.

AUTHORS CONTRIBUTION

All authors contributed to the study conception and design. Francis Elisha Sa'Ayinzat participated in following of the trial, evaluation. and statistical analysis of the results and writing and publishing of the manuscript. The first draft of the manuscript was written by Francis Elisha Sa'Ayinzat and all authors commented on all versions of the manuscript. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data of this study are available from the corresponding author upon reasonable request.

CONSENT FOR PUBLICATION

All authors give consent for publication.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest associated with the publication of the outcomes of this scientific study.

References

1. Abubakar, O., Olabisi, O., Asuquo, A., Carols, U., Daureen Gift, U., & Author, C. (2018). Physiological variations and oxidative status in West African Dwarf male sheep and goat in semi-intensive management system. Animal Research International, 15(1), 2898–2905. .
2. Agarwal, A., Gupta, S., & Sharma, R. (2005). Oxidative stress and its implication in female infertility - a clinician's perspective. Reproductive Biomedicine Online, 11(5), 641–650.
3. Ainsworthl, L., & Doww, B. R. (1986). A controlled internal drug release containing progesterone for the control of estrus cycle of ewes. Theriogenology, 26(6), 847–856.
4. Akubuo, A. U., Ahaotu, E. O., Ihenacho, R. O., & Osuagwu, C. O. (2020). Management Practices and Problems of Sheep Farmers in Oru West Local Government Area of Imo State. International Journal of Animal Science, 4(7), 1–7. https://doi.org/10.36876/ijas565888.
5. Ali, A., Morrical, D. G., Hoffman, M. P., & Al-Essa, M. F. (2004). Evaluation of Vitamin E and Selenium Supplementation in Late Gestation on Lamb Survival and Pre-Weaning Growth. Professional Animal Scientist, 20(6), 506–511. https://doi.org/10.15232/S1080-7446(15)31355-3.
6. Anderson, B., Bradford, G. E., & Cupps, P. T. (1981). Length of gestation in ewes carrying lambs of two different breeds. Theriogenology, 16(1), 119–129.
7. Atabaki, R., Roohbakhsh, A., Moghimi, A., & Mehri, S. (2020). Protective effects of maternal administration of curcumin and hesperidin in the rat offspring following repeated febrile seizure:

Role of inflammation and TLR4. International Immunopharmacology, 86, 1567–1569. https://doi.org/10.1016/j.intimp.2020.106720.

8. Ataman, B. M., & Aköz, M. (2006). GNRH-PGF 2α AND PGF 2α-PGF 2α Synchronisation in Akkaraman cross-bred sheep in the breeding season. Bull Vet Inst Pulawy, 50, 101–104.
9. Ávila-gálvez, M. Á., Giménez-bastida, J. A., González-sarrías, A., & Espín, J. C. (2021). New insights into the metabolism of the flavanones eriocitrin and hesperidin: a comparative human pharmacokinetic study. Antioxidants, 10(3), 1–18. https://doi.org/10.3390/antiox10030435.
10. Bianca, W. (1976). The significance of meteorology in animal production. International Journal of Biometeorology, 20(2), 139–156.
11. Bouroutzika, E., Kouretas, D., Papadopoulos, S., Veskoukis, A. S., Theodosiadou, E., Makri, S., Paliouras, C., Michailidis, M. L., Caroprese, M., & Valasi, I. (2020). Effects of melatonin administration to pregnant ewes under heat-stress conditions, in redox status and reproductive outcome. Antioxidants, 9(3). https://doi.org/10.3390/antiox9030266.
12. Capper, J. L., Wilkinson, R. G., Kasapidou, E., Pattinson, S. E., Mackenzie, A. M., & Sinclair, L. A. (2005). The effect of dietary vitamin E and fatty acid supplementation of pregnant and lactating ewes on placental and mammary transfer of vitamin E to the lamb. British Journal of Nutrition, 93(4), 549–557. https://doi.org/10.1079/bjn20051376.
13. Celi, P., Chauhan, S.S., Cottrell, J.J., Dunshea, F.R., Lean, I. J., Leury, B. J. and Liu, F. (2014). Oxidative stress in ruminants: enhancing productivity through antioxidant supplementation. Broadening Horizons, 11. Retrieved from: http://www.feedipedia.org/content/oxidative-stress-ruminants-enhancing-productivity-through-a, 2nd September, 2015, 1.45 p.m.
14. Çelik, H. T., Aslan, F. A., Altay, D. U., Kahveci, M. E., Konanç, K., Noyan, T., & Ayhan, S. (2021). Effects of transport and altitude on hormones and oxidative stress parameters in sheep. PLoS ONE, 16(2 Febuary), 1–11. https://doi.org/10.1371/journal.pone.0244911.
15. da Silva, R. O., de Oliveira, R. P. M., Silva, A. F., de Oliveira, F. F., Rufino, J. P. F., & da Silva, M. L. M. (2020). Effect of different protocols for estrus synchronization on reproductive performance of santa inês ewes under amazon environmental conditions. Acta Scientiarum - Animal Sciences, 43(1), 1–7. https://doi.org/10.4025/actascianimsci.v43i1.48954.
16. Ducrotoy, M. J., Majekodunmi, A. O., Shaw, A. P. M., Bagulo, H., Bertu, W. J., Gusi, A. M., Ocholi, R., & Welburn, S. C. (2018). Patterns of passage into protected areas: Drivers and outcomes of Fulani immigration, settlement and integration into the Kachia Grazing Reserve, northwest Nigeria. Pastoralism, 8(1). https://doi.org/10.1186/s13570-017-0105-1.
17. Fitzgerald, T., & Vietri, J. (2015). Residual Effects of Sleep Medications Are Commonly Reported and Associated with Impaired Patient-Reported Outcomes among Insomnia Patients in the United States. Sleep Disorders, 2015, 1–9. https://doi.org/10.1155/2015/607148.
18. Fogarty, N. M., Ingham, V. M., Gilmour, A. R., Cummins, L. J., Gaunt, G. M., Stafford, J., Edwards, J. E. H., & Banks, R. G. (2005). Genetic evaluation of crossbred lamb production. 1. Breed and fixed effects

for birth and weaning weight of first-cross lambs, gestation length, and reproduction of base ewes. Australian Journal of Agricultural Research, 56(5), 443–453. https://doi.org/10.1071/AR04221.

19. Forbes, J. M. (1967). Factors affecting the gestation length in sheep. Journal of Agricultural Science, Camb, 68, 191–194.
20. Gebregeziabhear, E., & Ameha, N. (2015). The Effect of stress on productivity of animals: a review. Journal of Biology, Agriculture and Healthcare, 5(3), 165–173. .
21. Gore, D. (2016). Effect of β carotene supplementation on oestrous synchronisation and milk production of Saanen goats. A thesis submitted in fulfilment of partial requirements for the degree MSc (Agric) Animal Science, Faculty of Natural and Agricultural Sciences, University of Pretoria, South Africa.
22. Greyling, J. P. C., & Brink, W. C. J. (1987). Synchronization of oestrus in sheep: The use of controlled internal drug release (CIDR) dispensers. South Africa Journal of Animal Science, 17(3), 128–132.
23. Hashemi, M., & Safdarian, M. (2017). Efficiency of different methods of estrus synchronization followed by fixed time artificial insemination in Persian Downy does. Animal Reproduction, 14(2), 413–417. https://doi.org/10.21451/1984-3143-AR825.
24. Henmi, H., Endo, T., Kitajima, Y., Manase, K., Hata, H., & Kudo, R. (2003). Effects of ascorbic acid supplementation on serum progesterone levels in patients with a luteal phase. Fertility and Sterility, 80(2), 459–461. https://doi.org/10.1016/S0015-0282(03)00657-5.
25. Hucal, E. (2011). Managing the Lambing Enterprise. A Dissertation submitted in partial fulfilment of the requirements for award of BSc Degree in Animal Science, Faculty of Animal Science, California State Polytechnic University, San Luis Obispo.
26. Iyiola-Tunji, A. O., Akpa, G. N., Nwagu, B. I., Adeyinka, I. A., Osuhor, C. U., Lawal, T. T., & Ojo, O. A. (2010). Relationship between gestation length and birth weight in Nigerian sheep and their crosses. Animal Production, 12(3), 135–138.
27. Jarquin, S., Roldan, A., Zarco, L., Berruecos, J., & Valencia, J. (2014). Effect of stage of the estrous cycle at the time of initial exposure to rams on the ovarian activity of Pelibuey ewes. Original Paper Czech Journal of Animal Science, 59(11), 504–510.
28. Kamiloğlu, N. N., Kaçar, C., Güven, A., Yildiz, B., Kuru, M., Kaya, S., Eroğlu, H. A., & Koç, E. (2017). Testosteron antikoru ile pasif immunizasyon ve A-E vitamini kombinasyonu uygulanmiş Tuj koyunlarinda döl verimi, glutatyon ve lipid peroksidasyonda meydana gelen değişikler. Kafkas Universitesi Veteriner Fakultesi Dergisi, 23(3), 459–465. https://doi.org/10.9775/kvfd.2016.17053.
29. Kasimanickam, R. K., Kasimanickam, V. R., Rodriguez, J. S., Pelzer, K. D., Sponenberg, P. D., & Thatcher, C. D. (2010). Tocopherol induced angiogenesis in placental vascular network in late pregnant ewes. Reproductive Biology and Endocrinology, 8(86). http://www.rbej.com/content/8/1/86.
30. Khalek, T. M. M. A. (2007). Thermoregulatory responses of sheep to starvation and heat stress conditions. Egyptian Journal of Animal Production, 44(2), 137–150.

31. Kiplagat, S. K., Limo, M. K., & Kosgey, I. S. (2012). Genetic Improvement of Livestock for Milk Production. In Milk Production - Advanced Genetic Traits, Cellular Mechanism, Animal Management and Health (pp. 77–96). InTech. https://doi.org/10.5772/50761.
32. Kumar, B., Ishwar, A. K., Choudhary, P. K., & Akhatar, T. (2015). Effect of temperature variation on hormonal concentration at various gestation stages in black Bengal goat. Veterinary World, 8(9), 1137–1142. https://doi.org/10.14202/vetworld.2015.1137-1142.
33. Lawal-Adebowale, O. A. (2012). Dynamics of Ruminant Livestock Management in the Context of the Nigerian Agricultural System. In Livestock Production (pp. 61–71). InTech. https://doi.org/10.5772/52923.
34. Macmillan, K. L., & Burke, C. R. (1996). Effects of oestrous cycle control on reproductive efficiency. Animal Reproduction Science, 42(1996), 307–320.
35. Marai, I. F. M., El-Darawany, A. A., Fadiel, A., & Abdel-Hafez, M. A. M. (2007a). Physiological traits as affected by heat stress in sheep-A review. In Small Ruminant Research (Vol. 71, Issues 1–3, pp. 1–12). https://doi.org/10.1016/j.smallrumres.2006.10.003.
36. Martínez-Noguera, F. J., Marín-Pagán, C., Carlos-Vivas, J., Rubio-Arias, J. A., & Alcaraz, P. E. (2019). Acute effects of hesperidin in oxidant/antioxidant state markers and performance in amateur cyclists. Nutrients, 11(8), 1–20. https://doi.org/10.3390/nu11081898.
37. Mashamaite, M. O. (2019). Effect of dietary selenium supplementation and oestrous synchronisation on reproductive performance of South African indigenous goats. MSc Dissertation, Agriculture (Animal Science), Department of Animal and Wildlife, Faculty of Natural and agricultural Sciences, University of Pretoria, South Africa. Viewed 23 08 2022 by 1.30 p.m.
38. Matemilola, S., & Elegbede, I. (2017). The Challenges of Food Security in Nigeria. Open Access Online Library Journal, 04(12), 1–22. https://doi.org/10.4236/oalib.1104185.
39. Maxwell, W. M. C., & Barnes, D. R. (1986). SHORT NOTE Induction of oestrus in ewes using a controlled internal drug release device and PMSG. Journal of Agricultural Science, Camb, 106, 201–203.
40. Menatian, S., Mirzaei-Alamounti, H. R., Fathnia, F., & Masoumi, R. (2010). Effects of Pre-Pubertal plane of nutrition on skeletal growth, lamb mortality, IGF-1 concentrations, quantity and quality of colostrum production in Kurdish female lambs. Iranian Journal of Applied Animal Science, 6(4), 841–847. .
41. Moeini, M. M., Moghaddam, A. A., Bahirale, A., & Hajarian, H. (2007). Effect of breed and progestin source on estrus synchronisation and rates of fertility and fecundity in Iranian Sanjabi and Lori ewes. Iranian Journal of Biological Sciences, 10(21), 3801–3807.
42. Mukasa-Mugerwa, A. E., Said, A. N., Lahlou-Kassi, A., Sherington, J., & Mutiga, E. R. (1994). Birth weight as a risk factor for perinatal lamb mortality, and the effects of stage of pregnant ewe supplementation and gestation weight gain in Ethiopian Menz sheep. Preventive Veterinary Medicine, 19, 45–56.

43. Musa-Azara, S. I., Bitto, I. I., & Ayoade, J. A. (2011). Oestrus Response to synchronisation using different progesterone treatments in Yankasa ewes. Nigerian Veterinary Journal, 32(3), 218–221.
44. Musa, S. I., Bitto, I. I., Ayoade, J. A., & Oyedipe, O. E. (2018). Effects of Vitamin E and Selenium on fertility and lamb performance of Yankasa sheep. Open Journal of Veterinary Medicine, 08(09), 167–173. https://doi.org/10.4236/ojvm.2018.89015.
45. Naderipour, H. (2011). The effects of three methods of synchronization on estrus induction and hormonal profile in Kalkuhi ewes: A comparison study. African Journal of Biotechnology, 11(2), 530–533. https://doi.org/10.5897/ajb11.2718.
46. Nawito, M. F., Abd El Hameed, A. R., Sosa, A. S. A., & Mahmoud, K. G. M. (2016). Impact of pregnancy and nutrition on oxidant/antioxidant balance in sheep and goats reared in South Sinai, Egypt. Veterinary World, 9(8), 801–805. https://doi.org/10.14202/vetworld.2016.801-805.
47. Ntem, G. I. (2015). The role of weather on the occurrence of common diseases in Jos North Local Government Area, Plateau State, Nigeria [Thesis]. MSc Degree Dissertation, Department of Geography, Faculty of Science, Ahmadu Bello University.
48. Oke-Egbodo, B. E., Bawa, E. K., Nwannenna, A. I., Oke, P. O., & Hassan, R. (2018). Fertility Parameters in Crossbred Sows Treated with Cloprostenol Sodium (Synchromate®) in Zaria, Nigeria. Nigerian Veterinary Journal, 38(4), 288. https://doi.org/10.4314/nvj.v38i4.2.
49. Omontese, B. O., Adewuyi, A. B., Rekwot, P. I., Nwannenna, A. I., & Rwuaan, J. S. (2017). Effect of ascorbic acid on the conception rates of Yankasa ewes after oestrous synchronisation. Revue d'élevage et de Médecine Vétérinaire Des Pays Tropicaux, 70(1), 9–12. https://doi.org/10.19182/remvt.31390.
50. Omontese, B. O., Rekwot, P. I., Ate, I. U., Ayo, J. O., Kawu, M. U., Rwuaan, J. S., Nwannenna, A. I., Mustapha, R. A., & Bello, A. A. (2016). An update on oestrus synchronisation of goats in Nigeria. In Asian Pacific Journal of Reproduction (Vol. 5, Issue 2, pp. 96–101). Elsevier (Singapore) Pte Ltd. https://doi.org/10.1016/j.apjr.2016.01.002.
51. Omontese, B. O., Rekwot, P. I., Makun, H. J., Obidi, J. A., Ruwaan, J. S., & Chiezey, N. P. (2010). Synchronisation of oestrus using EAZI-Breed CIDR and FGA-30 intravaginal sponge in pre-partum Yankasa ewes. Research Journal of Animal Sciences, 4(1), 53–57.
52. Omontese, B. O., Rekwot, P. I., Ruaan, J. S., Ate, I. U., & Makun, H. J. (2014). Induction of oestrus in Ouda ewes with different oestrus synchrony protocols. Revue de Medecine Veterinaire, 165(7–8), 241–244. .
53. Oztirk A, A., & Aktas, A. H. (1996). Effect of environmental factors on gestation length in Konya Merino sheep. Small Ruminant Research, 22(1996), 85–88.
54. Ozyurtlu, N., Kucukaslan, I., & Cetin, Y. (2010). Characterization of oestrous induction response, oestrous duration, fecundity and fertility in awassi ewes during the non-breeding season utilizing both cidr and intravaginal sponge treatments. Reproduction in Domestic Animals, 45(3), 464–467. https://doi.org/10.1111/j.1439-0531.2008.01246.x.

55. Pal, P., & Rayees Dar, M. (2020). Induction and Synchronization of Estrus. In Animal Reproduction in Veterinary Medicine (pp. 1–14). https://doi.org/http://dx.doi.org/10.5772/intechopen.90769.
56. Papanastasiou, D. K., Bartzanas, T., & Kittas, C. (2015a). Classification of potential sheep heat-stress levels according to the prevailing meteorological conditions. http://www.cigrjournal.org.
57. Parraguez, V. H., Atlagich, M., Araneda, O., García, C., Muñoz, A., de Los Reyes, M., & Urquieta, B. (2011). Effects of antioxidant vitamins on newborn and placental traits in gestations at high altitude: Comparative study in high and low altitude native sheep. Reproduction, Fertility and Development, 23(2), 285–296. https://doi.org/10.1071/RD10016.
58. Parraguez, V. H., Sales, F., Peralta, O. A., Narbona, E., Lira, R., de Los Reyes, M., & González-Bulnes, A. (2020). Supplementation of underfed twin-bearing ewes with herbal vitamins C and E: Impacts on birth weight, postnatal growth, and pre-weaning survival of the lambs. Animals, 10(4). https://doi.org/10.3390/ani10040652.
59. Parraguez, V. H., Sales, F., Peralta, O., de los Reyes, M., & Gonzalez-Bulnes, A. (2022a). Oxidative Stress and Fetal Growth Restriction Set Up Earlier in Undernourished Sheep Twin Pregnancies: Prevention with Antioxidant and Nutritional Supplementation. Antioxidants, 11(7), 1287. https://doi.org/10.3390/antiox11071287.
60. Parraguez, V. H., Sales, F., Peralta, O., de los Reyes, M., & Gonzalez-Bulnes, A. (2022b). Oxidative Stress and Fetal Growth Restriction Set Up Earlier in Undernourished Sheep Twin Pregnancies: Prevention with Antioxidant and Nutritional Supplementation. Antioxidants, 11(7), 1287. https://doi.org/10.3390/antiox11071287.
61. Parraguez, V. H., Urquieta, B., de Los Reyes, M., González-Bulnes, A., Astiz, S., & Muñoz, A. (2013). Steroidogenesis in sheep pregnancy with intrauterine growth retardation by high-altitude hypoxia: Effects of maternal altitudinal status and antioxidant treatment. Reproduction, Fertility and Development, 25(4), 639–645. https://doi.org/10.1071/RD12020.
62. Parsons, S. D., & Hunter, G. L. (1967). Effect of the ram on duration of oestrus in the ewe. Journal of Reproduction and Fertility, 14, 61–70.
63. Petrovic, C. v, Petrovic, M. P., Ilic, Z., Petrovic, M. M., Milosevic, B., Ruzic-Muslic, D., & Maksimovic, N. (2013). Effect of genotype, sire, sex, gestation length on birth weight of lambs. Biotechnology in Animal Husbandry, 29(4), 685–693. https://doi.org/10.2298/bah1304685c.
64. Pinna, C., & Sala, A. (2019). Sex-specific activity of hesperidin, diosmin and genistein on human umbilical vein. Biomedical Research and Clinical Practice, 4(4), 1–5. https://doi.org/10.15761/brcp.1000196
65. Pohler, K. G., Franco, G. A., Reese, S. T., Dantas, F. G., Ellis, M. D., & Payton, R. R. (2016). Past, present and future of pregnancy detection methods (pp. 251–258). Applied Reproductive Strategies in Beef Cattle.
66. Rhodes1, L., & Nathanielsz, P. W. (1988). Comparison of a controlled internal drug release device containing progesterone with intravaginal medroxyprogesterone sponges for estrus synchronisation in ewes. Theriogenology, 831–836.

67. Richter, H. G., Hansell, J. A., Raut, S., & Giussani, D. A. (2009). Melatonin improves placental efficiency and birth weight and increases the placental expression of antioxidant enzymes in undernourished pregnancy. Journal of Pineal Research, 46(4), 357–364. https://doi.org/10.1111/j.1600-079X.2009.00671.x.
68. Roehrs, T., Kribbs, N., Zorick, F., & Roth, T. (1986). Hypnotic residual effects of benzodiazepines with pepeated administration. Sleep, 9(2), 309–316. https://academic.oup.com/sleep/article/9/2/309/2742890.
69. Roelofs, J. B., Soede, N. M., Voskamp-Harkema, W., & Kemp, B. (2008). The effect of fenceline bull exposure on expression of oestrus in dairy cows. Animal Reproduction Science, 108(1–2), 226–235. https://doi.org/10.1016/j.anireprosci.2007.08.002.
70. Romano, J. E. (2004). Synchronization of estrus using CIDR, FGA or MAP intravaginal pessaries during the breeding season in Nubian goats. Small Ruminant Research, 55(1–3), 15–19. https://doi.org/10.1016/j.smallrumres.2003.10.015.
71. Romano, J. E., & Fahning, M. L. (2013). Comparison between 7 vs 9 days of controlled internal drug release inserts permanency on oestrus performance and fertility in lactating dairy cattle. Italian Journal of Animal Science, 12(3), 390–394. https://doi.org/10.4081/ijas.2013.e63.
72. Sa'Ayinzat, F. E. (2021). Effects of hesperidin on oestrous cycle, pregnancy, lambing weight, postpartum oestrus interval and haemato-biochemical parameters in Yankasa ewes in Vom, Nigeria. [Thesis]. A Thesis submitted to the School of Postgraduate Studies, in fulfilment of the Award of Doctor of Philosophy Degree, Department of Theriogenology and Production, Faculty of Veterinary Medicine, Ahmadu Bello University.
73. Sa'Ayinzat, F. E., Bawa, E. K., Ogwu D., & Ayo, J. O. (2021b). Hesperidin-Sources, chemistry, extraction, measurement and biologic effects on reproduction in animals: A review. International Journal of Veterinary Sciences and Animal Husbandry, 6(4), 1–8. https://doi.org/10.22271/veterinary.2021.v6.i3a.360.
74. Sa'ayinzat, F. E., Bawa, E. K., Ogwu, D., & Ayo, J. O. (2021a). Oxidative stress and its effects on reproductive performance in thermally-stressed ewes. International Journal of Veterinary Science and Animal Husbandry, 6(4), 9–17. https://doi.org/10.22271/veterinary.2021.v6.i4a.361.
75. Safarnavadeh, T., & Rastegarpanah, M. (2011). Review article Antioxidants and infertility treatment, the role of Satureja Khuzestanica: A mini-systematic review. Iranian Journal of Reproductive Medicine, 9(2), 61–70.
76. Sales, F., Parraguez, V. H., Freitas-de-Melo, A., & Ungerfeld, R. (2020). Maternal nutrition and antioxidant supplementation: Effects on mother–young behaviors in a Patagonian sheep extensive grazing system. Applied Animal Behaviour Science, 228. https://doi.org/10.1016/j.applanim.2020.105010.
77. Sales, F., Peralta, O. A., Narbona, E., McCoard, S., Lira, R., de Los Reyes, M., González-Bulnes, A., & Parraguez, V. H. (2019). Maternal supplementation with antioxidant vitamins in sheep results in

increased transfer to the fetus and improvement of fetal antioxidant status and development. Antioxidants, 8(3). https://doi.org/10.3390/antiox8030059.

78. Salifu, S. (2014a). Reproductive Performance of Djallonke sheep in the Northern Region of Ghana. A Thesis submitted to the School of Postgraduate Studies, in fulfilment of the requirement for the Award of Masters of Philosophy Degree, College of Agriculture and Natural Resources, University of Science and Technology, Kumasi, Ghana.
79. Sánchez, J., Jiménez, A., Regodón, S., & Andrés, S. (2008a). Inhibitory effect of selenium supplementation on the reproductive performance in synchronized Merino sheep at range conditions in a selenium-deficient area. Reproduction in Domestic Animals, 43(3), 328–332. https://doi.org/10.1111/j.1439-0531.2007.00904.x.
80. Sejian, V., Singh, A. K., Sahoo, A., & Naqvi, S. M. K. (2014). Effect of mineral mixture and antioxidant supplementation on growth, reproductive performance and adaptive capability of Malpura ewes subjected to heat stress. Journal of Animal Physiology and Animal Nutrition, 98(1), 72–83. https://doi.org/10.1111/jpn.12037.
81. Senger, P. L. (2007). Placentation, the Endocrinology of Gestation and Parturition. In: Pathways to Pregnancy and Parturition (2nd ed., Vol. 2).
82. Sharma, P., Kumari, S., Sharma, J., Purohit, R., & Singh, D. (2021). Hesperidin Interacts With CREB-BDNF Signaling Pathway to Suppress Pentylenetetrazole-Induced Convulsions in Zebrafish. Frontiers in Pharmacology, 11. https://doi.org/10.3389/fphar.2020.607797.
83. Sidi, S., Umaru, M., Jibril, A., Umaru, A., & Saulawa, M. (2016). Effect of Cloprostenol, CIDR and Their Combination on Estrus Synchronization in Red Sokoto Doe. IOSR Journal of Agriculture and Veterinary Science, 9(2), 38–43. https://doi.org/10.9790/2380-09213843.
84. Silanikove, N. (2000). Effects of heat stress on the welfare of extensively managed domestic ruminants. Livestock Production Science, 67, 1–18. .
85. Silvestro, S., Calcaterra, V., Pelizzo, G., Bramanti, P., & Mazzon, E. (2020). Prenatal hypoxia and placental oxidative stress: Insights from animal models to clinical evidences. In Antioxidants (Vol. 9, Issue 5). MDPI. https://doi.org/10.3390/antiox9050414.
86. Skliarov, P., Pérez, C., Petrusha, V., Fedorenko, S., & Bilyi, D. (2021a). Induction and synchronization of oestrus in sheep and goats. Journal of Central European Agriculture, 22(1), 39–53. https://doi.org/10.5513/JCEA01/22.1.2939.
87. Stenning, D. J. (1957). Transhumance, Migratory Drift, Migration; Patterns of Pastoral Fulani Nomadism. In Source: The Journal of the Royal Anthropological Institute of Great Britain and Ireland (Vol. 87, Issue 1).
88. Sterndale, S., Broomfield, S., Currie, A., Hancock, S., Kearney, G. A., Lei, J., Liu, S., Lockwood, A., Scanlan, V., Smith, G., & Thompson, A. N. (2018). Supplementation of Merino ewes with vitamin e plus selenium increases α-tocopherol and selenium concentrations in plasma of the lamb but does not improve their immune function. Animal, 12(5), 998–1006. https://doi.org/10.1017/S1751731117002300.

89. Suprayogi, A., & Astuti, D. A. (2006). Physiological Status of Indoor Sheep in the Tropical Rain Forest (HPGW) Environment. 66–70. https://repository.ipb.ac.id/handle/123456789/36222.
90. Swelum, A. A. A., Alowaimer, A. N., & Abouheif, M. A. (2015). Use of fluorogestone acetate sponges or controlled internal drug release for estrus synchronization in ewes: Effects of hormonal profiles and reproductive performance. Theriogenology, 84(4), 498–503. https://doi.org/10.1016/j.theriogenology.2015.03.018.
91. Thakor, A. S., Richter, H. G., Kane, A. D., Dungster, C., Kelly, F. J., Poston, L., & Giussani, D. A. (2010). Redox modulation of the fetal cardiovascular defence to hypoxaemia. Journal of Physiology, 588(21), 4235–4247.
92. Tilton, J. E. (1964). Factors influencing length of gestation in sheep. A dissertation submitted to the Graduate School in partial fulfilment of the requirements for the award of MSc. Degree, Oklahoma State University of Agriculture and Applied Science, Oklahoma, USA.
93. Trout, J. P., Mcdowell, L. R., & Hansen, P. J. (1998). Physiology and management characteristics of the estrous cycle and antioxidant status of lactating holstein cows exposed to heat stress. Journal of Dairy Science, 81, 1244–1250.
94. Tumenbayar, B., Tsolmon, D., Suvdaa, B., Enkhzu, l B., & Chimegsaihan, S. (2019). The Study of cold stress - induced changes in rat mesovarium's mast cell size and structure in relation with oestrous cycle. Journal of Cytology and Histology, 10(1), 1–7.
95. Vaadala, S., Ponneri, N., Karnam, V. S., & Pamuru, R. R. (2019). Baicalein, a flavonoid causes prolonged estrus and suppressed fertility output upon prenatal exposure in female mice. Iranian Journal of Basic Medical Sciences, 22(4), 452–459. https://doi.org/10.22038/ijbms.2019.33376.7972.
96. Vivanco, H. W. (1986). Recent developments in reproductive techniques of sheep and goats. Small Ruminant Production in Developing Countries., 1–17. http://www.fao.org/3/ah221e/AH221E03.htm#ch3.
97. Westphal, L. M., Polan, M. L., Trant, A. S., & Mooney, S. B. (2004). Pregnancy Rates in Women. Journal of Reproductive Medicine, 49, 289–293.
98. Wheaton, J. E., Carlson, K. M., Windels, H. F., & Johnston, L. J. (1993). CIDR: A new progesterone-releasing intravaginal device for induction of estrus and cycle control in sheep and goats. In Animal Reproduction Science (Vol. 33).
99. Wildeus, S. (2000). Current concepts in synchronization of estrus: Sheep and goats. Journal of Animal Science, 77(E-Suppl), 1. https://doi.org/10.2527/jas2000.00218812007700es0040x.
100. Xu, Z. Z. (2011). Control of estrous cycles: synchronization of estrus. In Reproduction, Events and Management (pp. 448–453). Elsievier. https://doi.org/10.1016/B978-0-12-374407-4.00452-0.
101. Yu, X., Bai, Y., Yang, J., Zhao, X., Zhang, L., & Wang, J. (2022). Comparison of Five Protocols of Estrous Synchronization on Reproductive Performance of Hu Sheep. Frontiers in Veterinary Science, 9. https://doi.org/10.3389/fvets.2022.843514.

102. Yu, X. J., Wang, J., & Bai, Y. Y. (2018). Estrous synchronization in ewes: The use of progestogens and prostaglandins. In Acta Agriculturae Scandinavica A: Animal Sciences (Vol. 68, Issue 4, pp. 219–230). Taylor and Francis Ltd. https://doi.org/10.1080/09064702.2019.1674373.
103. Zohara, B. F., Azizunnesa, A., Islam, Md. F., Shahi, Md. G., & Bari, F. Y. (2014). Reproductive Performances of Indigenous Ewes in Bangladesh. IOSR Journal of Agriculture and Veterinary Science, 7(5), 64–72. https://doi.org/10.9790/2380-07516472.

Figures

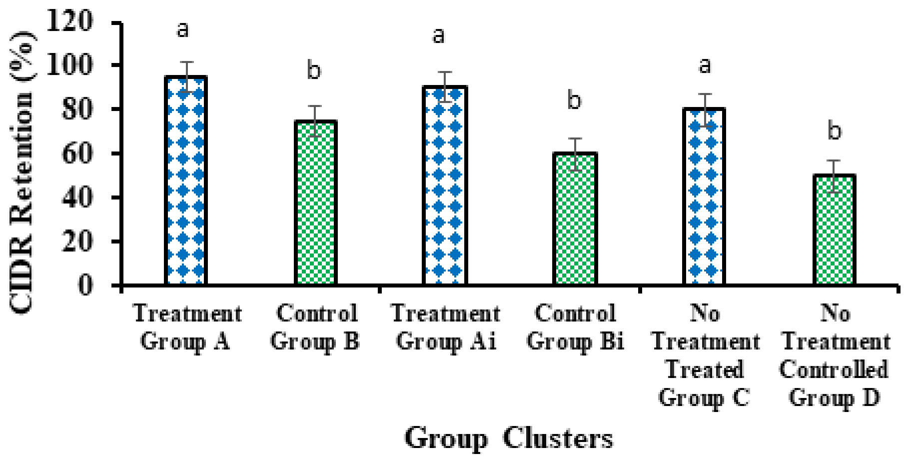

Figure 1

CIDR Retention Rates (%) in hesperidin fed Yankasa ewes. abBar Chart with different superscript differ significantly (P < 0.05).

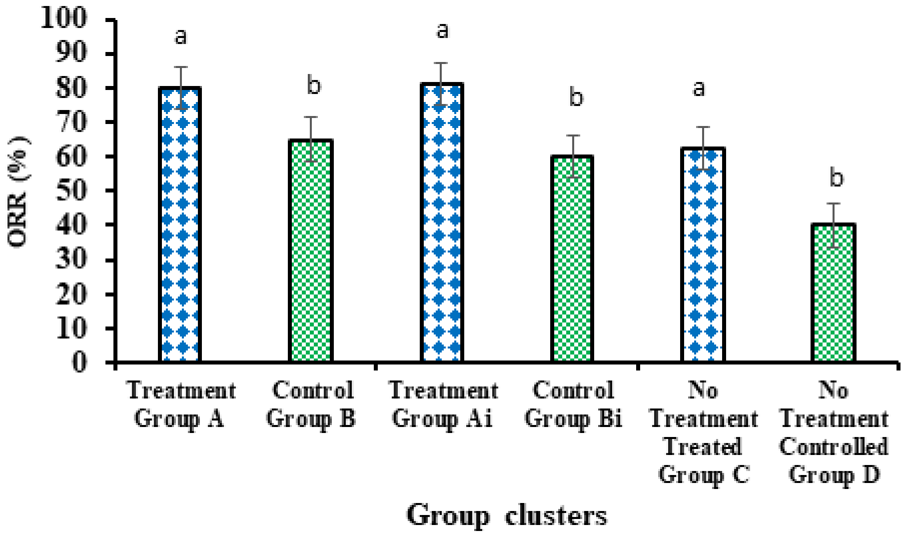

Figure 2

Oestrus Response Rate (ORR) (%) in hesperidin fed Yankasa ewes. abBar Chart with different superscript differ significantly (P < 0.05).

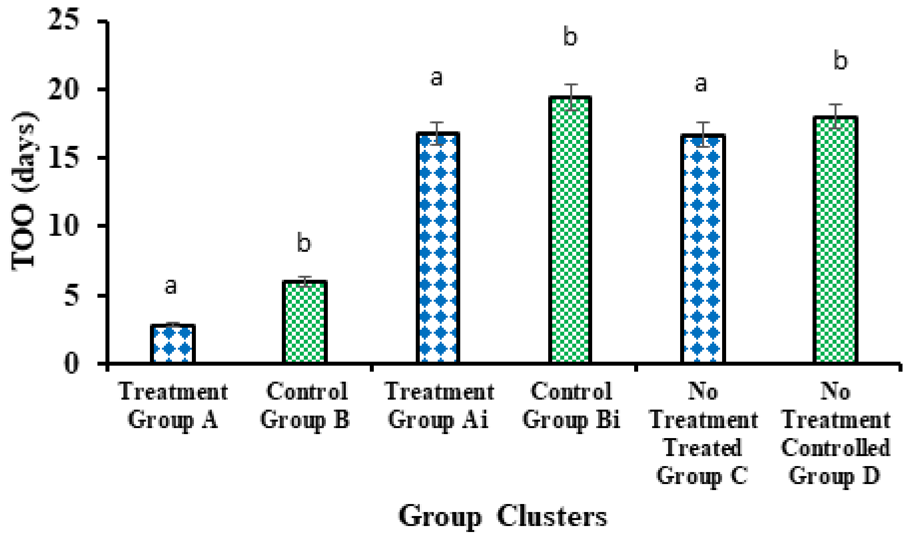

Figure 3

Time of onset of oestrus (TOO) (days) in hesperidin fed Yankasa ewes. abBar Chart with different superscript differ significantly (P < 0.05).

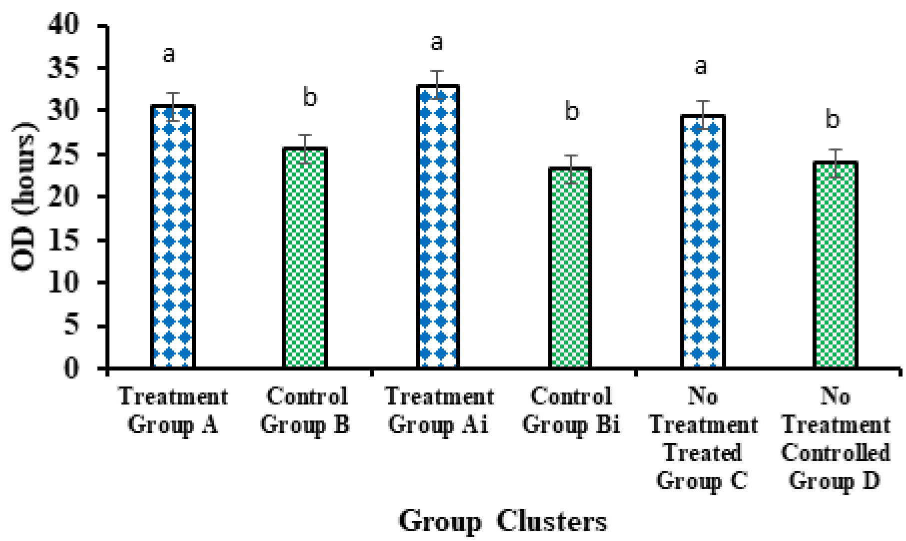

Figure 4

Oestrus duration (hours) in hesperidin fed Yankasa ewes. abBar Chart with different superscript differ significantly (P < 0.05).

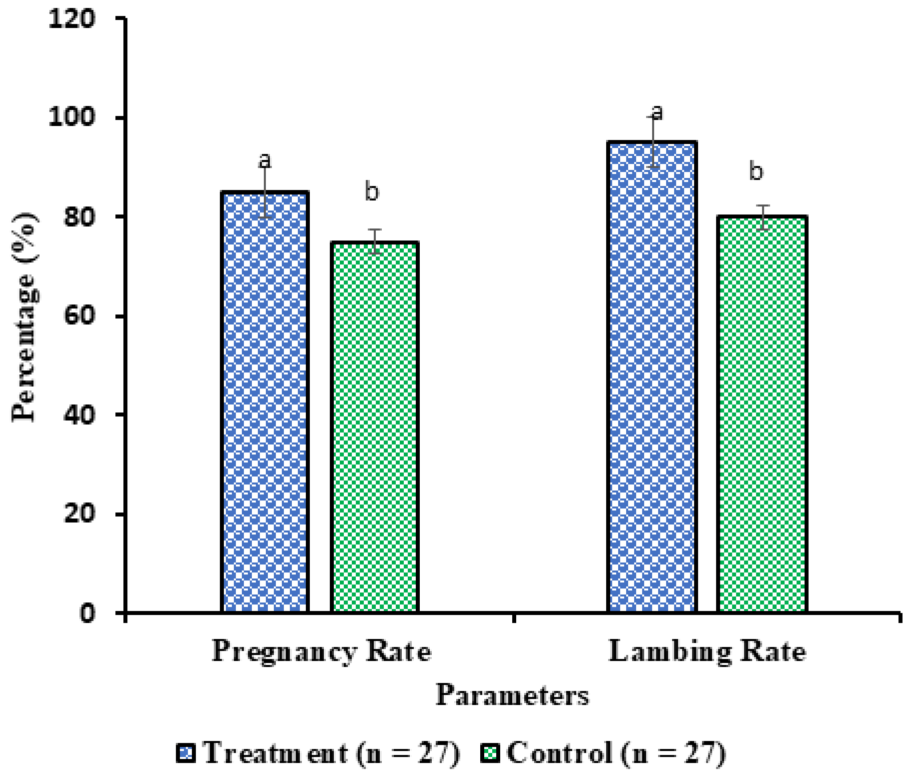

Figure 5

Pregnancy and lambing rates in hesperidin fed Yankasa ewes. abBar Chart with different superscript differ significantly (P < 0.05).

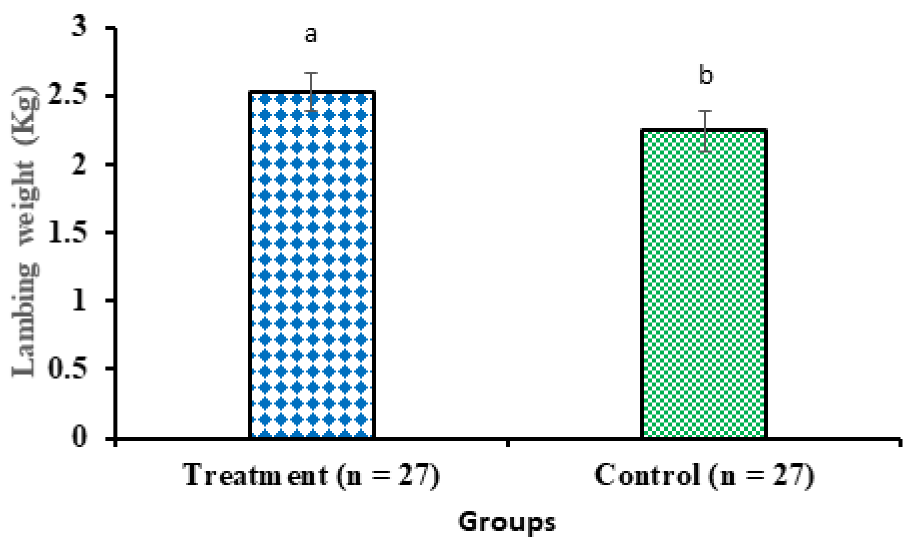

Figure 6

Lambing weights in hesperidin fed Yankasa ewes. abBar Chart with different superscript differ significantly (P < 0.05).

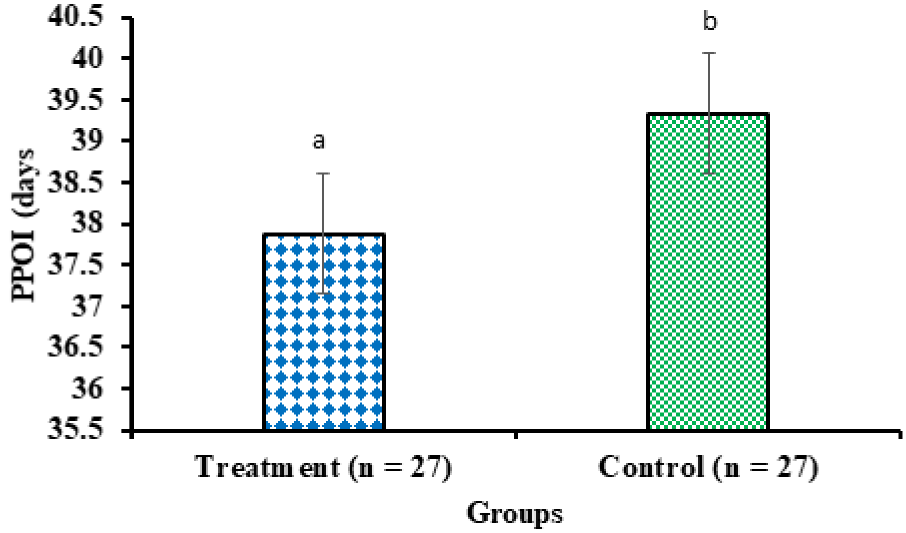

Figure 7

Postpartum oestrus interval in hesperidin fed Yankasa ewes. abBar Chart with different superscript differ significantly (P < 0.05).

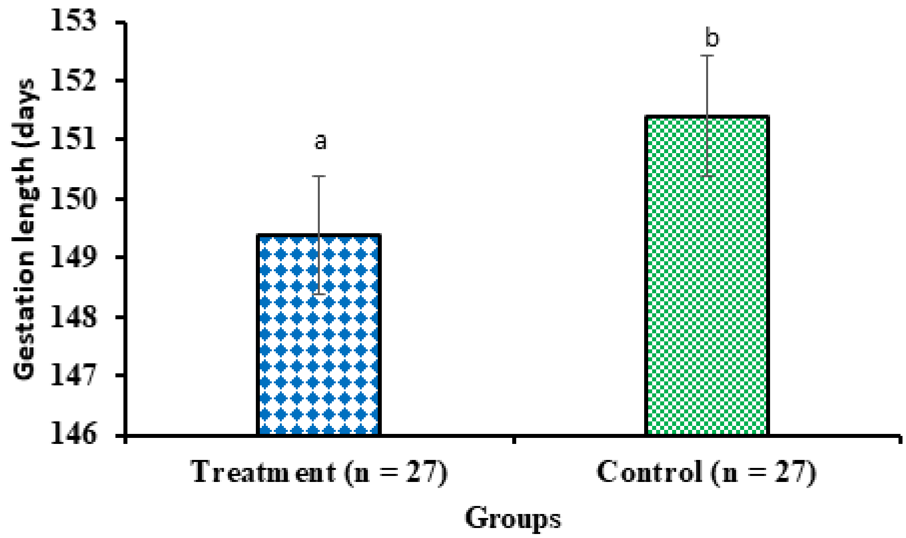

Figure 8

Gestation Length in hesperidin fed Yankasa ewes. abBar Chart with different superscript differ significantly (P < 0.05).

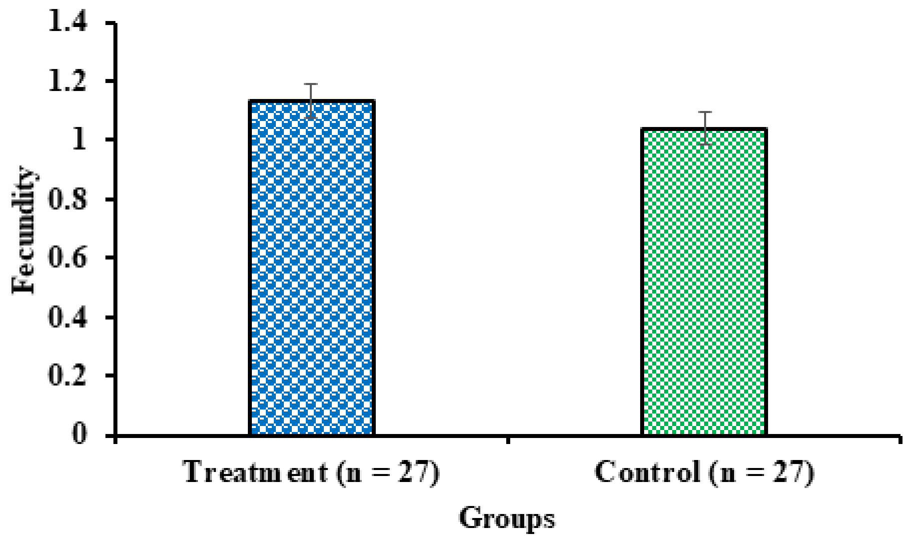

Figure 9

Fecundity in hesperidin fed Yankasa ewes. abBar Chart with different superscript differ significantly ($P < 0.05$).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryMaterialFSaayinzat30082022.docx