Original Research Article ISSN (Print) 2786-0272 ISSN (Online) 2786-0280

Comparative Clinicopathological Study on the Impact of Intrauterine Infusion of Eugenol Versus Ceftiofur on Experimentally Induced Endometritis in Baladi Female Goats

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Received at: 2025-01-10 Accepted at: 2025-02-04

ABSTRACT: Goats are highly vulnerable to various reproductive disorders, including endometritis that adversely affect their productivity and hinder breeding programs. The limitations and side effects of conventional treatments have prompted the research for alternative therapies to treat endometritis. Eugenol, a major component of clove essential oil, is known for its potent anti-inflammatory and antioxidant properties. This study aimed to evaluate the efficacy of eugenol as an alternative to ceftiofur for treating experimentally induced endometritis in female goats by assessing selected clinicopathological parameters. Twenty pluriparous Baladi (n=20) does (female goats) were assigned into four equal groups, each comprising five goats. Estrus synchronization was achieved using synthetic prostaglandin to ensure all goats had the same luteal phase. The control group (Control) received 3 ml of normal saline, while the remaining three groups underwent experimental induction of endometritis via intrauterine infusion of 3 ml of 95% ethanol. Among these, the endometritis group (ENM) received no treatment. The (ENM+EGL) group was treated with 3 ml of eugenol (16 mg/ml, single dose), and the (ENM+CEF) group was treated with 3 ml of ceftiofur (125 mg, single dose). Blood samples were collected two weeks post-induction to evaluate the leukogram profile, serum biochemical variables, oxidative stress, and antioxidant biomarkers. Results indicated significant increases in the serum concentration of alanine aminotransferase (ALT), aspartate transaminase (AST), sorbitol dehydrogenase (SDH), urea, creatinine, and hydrogen peroxide (H_2O_2), alongside superoxide dismutase (SOD), total protein, albumin, and globulin were reduced considerably. The histopathological findings revealed severe lesions in the endometrium of affected does. Both eugenol and ceftiofur mitigated these changes, although ceftiofur demonstrated superior efficacy.

KEYWORDS: Clinicopathological studies, Endometritis, Eugenol, Ceftiofur, Female goats

1. Introduction

Small ruminants, including sheep and goats, play a considerable role as a source of livelihood for villagers to develop sustainable and robust production systems. Providentially, God has endowed sheep and goats with genetic, morphological, physiological, and behavioral characteristics constituting key adaptation mechanisms to withstand heat-stressed and drastic environments [1]. Goats are of great socioeconomic influence in rural regions in Egypt which hold nearly 3.4 million live goats that are mainly reared for their meat but with lesser significance for milk production that is constricted to the coastal areas and oases [2]. The goat industry constitutes one of the key components of animal production in Egypt and a significant source of red meat, where during the period between 2015 and 2019 goat meat production was approximately thirty thousand tons representing about 4.14% of the average total red meat production in Egypt [3]. Goats are prone to several lesions affecting the reproductive tract, particularly the uterus and ovary which can contribute to sterility. Affections of the reproductive tract decrease the efficacy of feed conversion leading to reduced milk production, decreased pregnancy rate, and increased culling rates [4]. Stillbirth, abortion, and retention of the placenta are the major reproductive disorders in goats with the

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uterus being the most commonly affected organ, exhibiting the highest prevalence of genital lesions (14.6%) [4]. However, it is found that endometritis and ovarian cysts are among the most frequently encountered conditions after slaughtering the ewes [5].

Endometritis is an inflammation affecting the endometrium which is a prevalent reproductive disorder in female domesticated animals, with subsequent ovarian dysfunction, abortion, and infertility. Many predisposing factors contribute to endometritis including dystocia, uterine prolapse, placental retention, and unhygienic conditions, resulting in significant financial loss for the animal owners [6, 7]. The use of active compounds derived from plant sources is of great importance in treating diseases affecting farm animals because of the high rates of resistance to commonly used conventional antibiotics [8]. Medicinal plants are considered an affluent origin of various bioactive compounds that exhibit pharmacological characteristics that prevent and treat inflammatory conditions [9]. Eugenol, also named 4-allyl-2-methoxyphenol, is one of the volatile phenols belonging to the phenylpropanoid class, which is considered the prime constituent of clove (Syzygium aromaticum) essential oil, comprising 45–90% extracted from the buds of Eugenia caryophyllata and its leaves. Also, eugenol is present in cinnamon, bay leaves, basil, and nutmeg. It can be administered to the body through various routes [10, 11, 12]. In addition, eugenol serves as a functional constituent of various products associated with the industry of food, pharmaceuticals, and cosmetics within limited concentrations, besides this, it reveals a vast array of biological activities, including antioxidant, anti-inflammatory, antimicrobial, antitumor, antipyretic, antifungal, analgesic, and anesthetic activities [10, 11] . Moreover, it has been evidenced that eugenol can counteract the harmful effects of toxic substances on folliculogenesis. This is achieved through its hormonal balancing properties, which include antiandrogenic, estrogenic, and antioxidant effects[13]. The antioxidant effects of eugenol and other phenolic compounds are attributed to their structure-function relationship and their ability to donate hydrogen atoms. Eugenol can stabilize the radicals due to its reducing capability by donating electrons from the hydroxyl group [14]. It further exhibits antioxidant properties by swiftly scavenging free radicals, inhibiting ROS production, and preventing lipid peroxidation [12]. More than that, eugenol possesses potent anti-inflammatory properties by inhibiting the activity of pro-inflammatory cytokines, including interleukin-6 (IL-6), interleukin-1 beta (IL-1β), prostaglandin E2 (PGE2) and tumor necrosis factor-alpha (TNF-α) [15].

Ceftiofur is a third-generation broad-spectrum cephalosporin with potent antibacterial efficacy against gram-negative and gram-positive bacteria [16]. As a β-lactam antibiotic, it works by inhibiting the crosslinking between the bacterial enzyme dd-transpeptidase and peptidoglycan, which is crucial for bacterial cell wall synthesis. This disruption in cell wall synthesis leads to cell lysis and ultimately bacterial death [17]. Intrauterine administration of ceftiofur has been shown to improve uterine health in dairy cows with uterine infections; however, it has no significant impact on subclinical endometritis or reproductive performance [18].

Successful reproduction is essential for optimizing goat flock numbers and enhancing productivity. However, goats are highly vulnerable to various reproductive disorders that negatively impact their production and hinder their breeding development plans [3]. The side effects associated with conventional treatments have led to the development of alternative therapies for managing endometritis [19]. In this context, the present study aimed to evaluate the efficacy of eugenol as an alternative to ceftiofur for treating experimentally induced endometritis in goats. Additionally, the study assessed the differences between eugenol and ceftiofur in terms of their impact on leukogram profiles, selected serum biochemical parameters, oxidative stress, and antioxidant markers, and

the histopathological changes of the endometrium in does with experimentally induced endometritis.

2. Materials and Methods

The current research was conducted in compliance with the regulations and procedures approved by the Medical Ethics Committee "Institutional Review Board" IRB local approval number (04-2023-200251).

2.0.1. Animals:

Twenty multiparous Baladi female goats (n = 20) were picked up from local farms in New Valley governorate, aged between 1 and 3 years and weighing 15.465±0.378 (mean ± SE) with a history of normal parturition with no postpartum diseases. All animals were clinically healthy, exhibiting normal appetite, mucous membrane coloration, heart rates of 69–90 beats/minute, respiratory rates of 10–20 breaths/minute, rectal temperatures ranging from 38.5 to 39.5°C [20], and a bright, alert, and responsive mental state. Also, the external genital examinations revealed no abnormal vaginal discharge [21]. The goats were dewormed to ensure freedom from internal and external parasites and were regularly vaccinated [22, 23, 24]. They were housed freely in well-ventilated pens and provided with diets meeting standard nutritional requirements, along with unlimited access to fresh water [25]. Prostaglandin was administered to synchronize estrus, ensuring all animals were in the same luteal phase for the study [26].

2.0.2. Drugs & Chemicals

Synthetic prostaglandin (Estrumate) was purchased from (Vet Pharma Friesoythe GmbH, Germany) for synchronization of estrus. Ethyl alcohol (95%) was obtained from (Egyptian company for chemicals, Egypt) for the induction of endometritis. Eugenol extracted from clove (syzygium aromaticum) (>99% pure) was obtained from (Prevest DenPro Limited, India). Vials of Ceftiofur sodium were from (Badr Pharma for Pharmaceutical Industries). Turky's solution for the leukocytic count, Methanol 95% Merk, Germany, Giemsa stain used for staining recently prepared blood film to be examined for differential leukocytic count. Kits for measurement of serum concentrations of alanine aminotransferase (ALT), aspartate aminotransferase (AST), total protein, albumin, urea, and creatinine were obtained from (Chema Diagnostica, Italy). Sorbitol dehydrogenase (SDH) kits were from (BioAssay Systems, USA), serum oxidative stress and antioxidant markers including hydrogen peroxide (H2O2), and superoxide dismutase (SOD).

2.0.3. Experimental design

Twenty goats were assigned into four equal groups, each of which consisted of five goats. The first group served as the control group (Control), which received 3 ml of normal saline, and the other three groups where endometritis was experimentally induced by intrauterine infusion of 3 ml of 95% ethanol [27]. One of these three groups was designated as the endometritis group (ENM). The other two groups received treatments via intrauterine infusion as follows: the (ENM+EGL) group was treated with 3 ml of eugenol (single dose) at a concentration of 16 mg/ml [28], while the (ENM+CEF) group received 3 ml containing 125 mg (single dose) of ceftiofur [18].

2.0.4. Induction of endometritis

Goats in the experimental groups received 3 ml of 95% ethanol in each uterine cavity [27] , using a 10 ml industrial syringe that has a needle with a blunt tip to avoid any injury to the cervix [29].

2.0.5. Blood sampling

At the end of the 2nd week post-induction of endometritis (10 days after treatment), blood samples were collected from the jugular vein, where two separate blood samples were collected from each doe. One sample was taken in a single-use vacutainer tube containing EDTA anticoagulant produced by (Hebei Xinle Sci & Tech Co. LTD, China) for leukogram examination. The 2nd blood sample was withdrawn to plain vacutainers and placed at room temperature for (20) minutes in a tilted position. All these

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vacutainers were stored in the fridge to arrest glycolysis and allow the blood clot to retract fully. Subsequently, the samples were centrifuged at 3000 rpm for ten minutes to separate the clear serum, which was carefully collected and transferred into Eppendorf tubes. The serum samples were then stored at –20°C until biochemical analysis was performed.

2.0.6. *Total and differential leukocytic count*

Manual leukocytic count and differential leukocytic count were performed according to [30] utilizing a diluting fluid called Turkey's solution and an improved Neubauer hemocytometer.

2.0.7. *Serum biochemical analysis*

The frozen serum samples were used for the analysis of selected serum biochemical variables, including a kinetic method for the determination of AST and ALT [31, 32], SDH [33], a quantitative colorimetric method for the determination of total protein (TP) [34], a photometric colorimetric test fo determination of albumin [35, 36], globulin concentration, and A/G ratio were analyzed according to [37, 38], an enzymatic colorimetric method for determination of urea [39] and a liquicolor photometric colorimetric test for kinetic measurement method without deproteinization for determination of creatinine [31, 36]. The concentrations of the investigated serum biochemical variables were measured by using a semi-automatic photometer(RIELE Photometer 5010 V5+, Germany).

2.0.8. *Serum oxidative stress and antioxidant markers*

The stored frozen serum samples were used and analyzed for selected serum concentrations of antioxidant and oxidative stress markers including SOD [40], and H2O2 [41]. Antioxidant and oxidative stress parameters were assayed with the aid of ELISA Reader (Hyperion) Model: Hyperion 4 Plus, Hyperion Inc.,136th street, Miami, Florida, USA).

2.0.9. *Histopathological examination*

Samples were obtained from the uterine horns (both right and left) and the uterine body of the does. Each specimen measured approximately 1 cm^3. The collected tissue specimens were fixed in neutral buffered formalin, followed by dehydration and clearing. Subsequently, the specimens were embedded in paraffin to create blocks. Thin sections, 5 µm thickness, were cut from the paraffin blocks and stained with hematoxylin and eosin (H&E). Finally, the prepared slides were examined under a microscope [42].

2.0.10. *Statistical Analysis*

Statistical analysis of all variables was conducted using analysis of variance (ANOVA) to compare means in the different groups, performed with the SPSS software (version 25) for Microsoft Windows. Post hoc multiple comparison tests (One-Way ANOVA: LSD and Duncan) were applied [43, 44] to identify significant mean differences. Results are presented as mean ± SEM, with a statistical significance level of $p<0.05$.

3. Results

3.1. *Leukogram*

The leukogram picture mean (±S.E.) in goats exposed to experimentally induced endometritis before and after treatment with eugenol versus ceftiofur are depicted in Figure. 1(1-5). At the end of the 2nd-week post induction of endometritis (10 days after treatment): The (ENM) does revealed a significant elevation in the TLC, neutrophils, and monocytes as compared to the (control) does. However, the TLC, neutrophils, and monocytes decreased significantly in (ENM+EGL) and (ENM+CEF) groups in comparison with the (ENM) group. On the other hand, the leukogram showed insignificant changes between (ENM+EGL) and (ENM+CEF) groups.

3.2. *Serum biochemical variables*

The serum biochemical variables (mean±S.E.) in goats exposed to experimentally induced endometritis before and after treatment with eugenol versus ceftiofur are demonstrated in Figure. 1 (6-8) Figure. 2 (9-14) At the end of the 2nd-week post induction of endometritis (10 days after treatment): The endometritis (ENM) group showed a

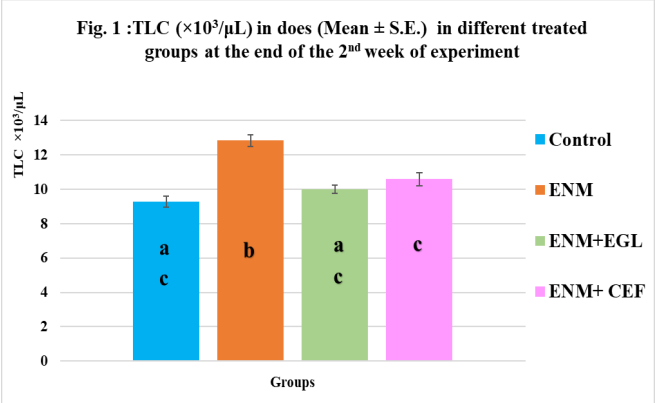
Fig. 1 :TLC (×10³/µL) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment
TLC ×10³/µL
14
12
10
8
6
4
2
0
a
c
b
a
c
c
Control
ENM
ENM+EGL
ENM+ CEF
Groups

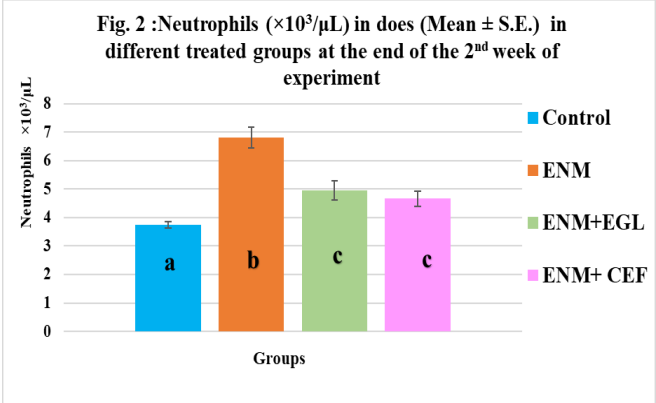
Fig. 2 :Neutrophils (×10³/µL) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment
Neutrophils ×10³/µL
8
7
6
5
4
3
2
1
0
a
b
c
c
Control
ENM
ENM+EGL
ENM+ CEF
Groups

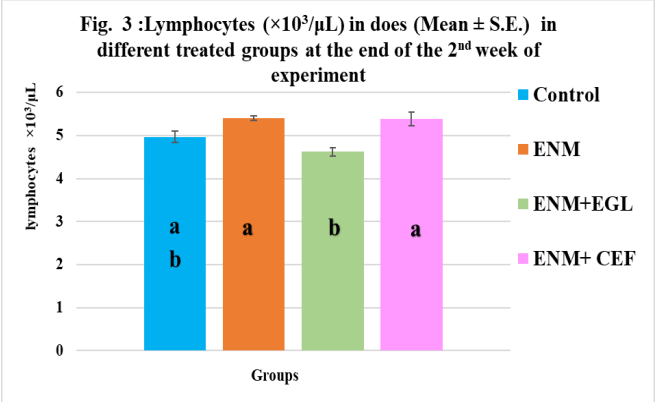
Fig. 3 :Lymphocytes (×10³/µL) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment
lymphocytes ×10³/µL
6
5
4
3
2
1
0
a
b
a
b
a
a
Control
ENM
ENM+EGL
ENM+ CEF
Groups

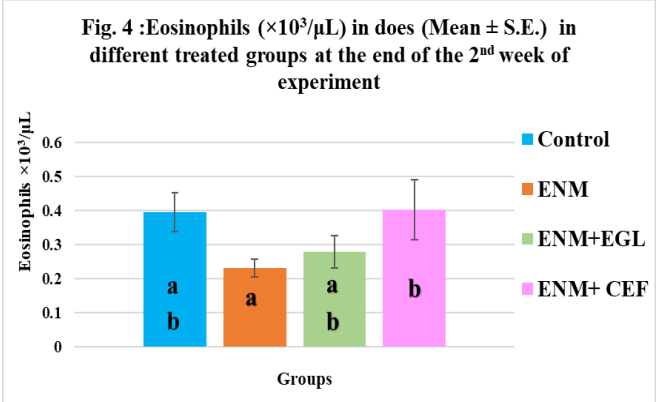
Fig. 4 :Eosinophils (×10³/µL) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment
Eosinophils ×10³/µL
0.6
0.5
0.4
0.3
0.2
0.1
0
a
b
a
a
b
b
Control
ENM
ENM+EGL
ENM+ CEF
Groups

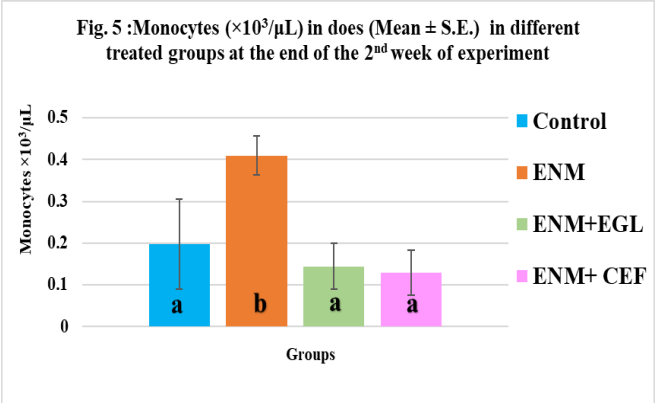
Fig. 5 :Monocytes (×10³/µL) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment
Monocytes ×10³/µL
0.5
0.4
0.3
0.2
0.1
0
a
b
a
a
Control
ENM
ENM+EGL
ENM+ CEF
Groups

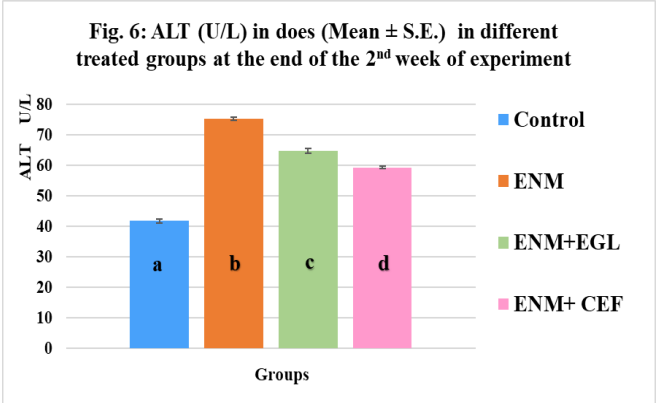
Fig. 6: ALT (U/L) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment
ALT U/L
80
70
60
50
40
30
20
10
0
a
b
c
d
Control
ENM
ENM+EGL
ENM+ CEF
Groups

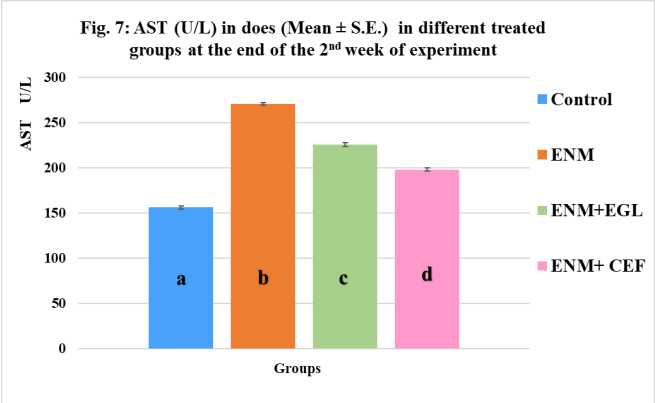
Fig. 7: AST (U/L) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment
AST U/L
300
250
200
150
100
50
0
a
b
c
d
Control
ENM
ENM+EGL
ENM+ CEF
Groups

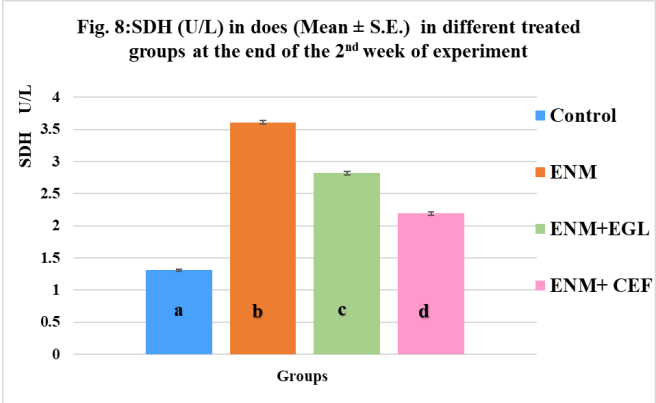
Fig. 8:SDH (U/L) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment
SDH U/L
4
3.5
3
2.5
2
1.5
1
0.5
0
a
b
c
d
Control
ENM
ENM+EGL
ENM+ CEF
Groups

Figure 1

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Fig. 9:TP (g/dl) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment

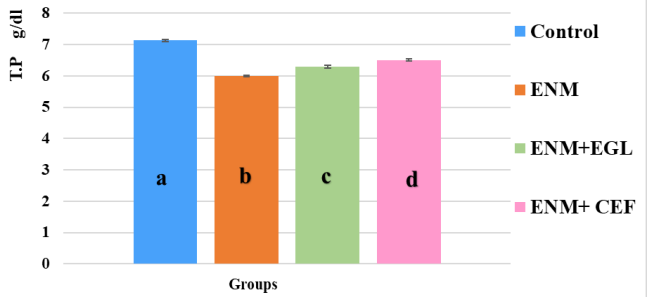

Fig. 10:Albumin (g/dL) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment

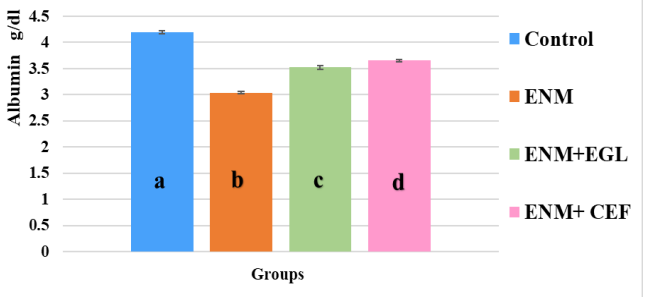

Fig. 11 :Globulin (g/dl) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment

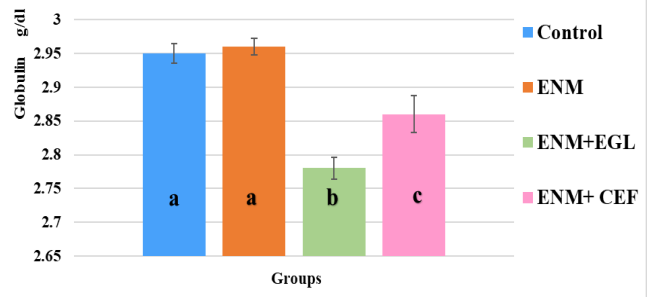

Fig. 12 :A/G ratio in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment

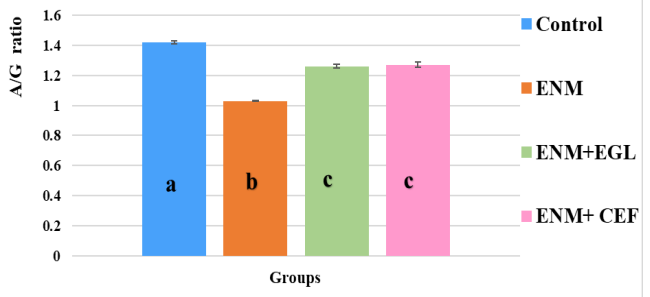

Fig. 13:Urea (mg/dl) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment

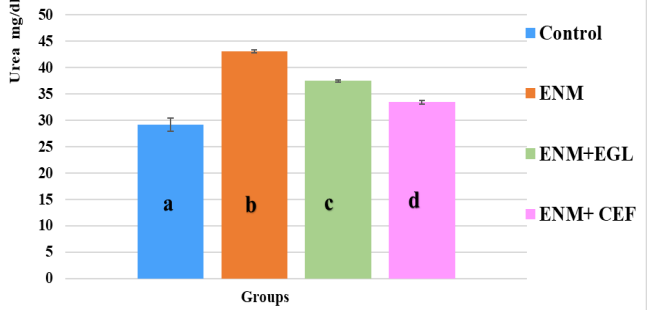

Fig. 14:Creatinine (mg/dl) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment

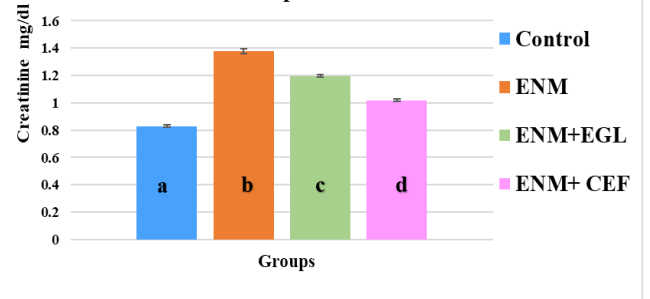

Fig. 15:SOD (pg/ml) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment

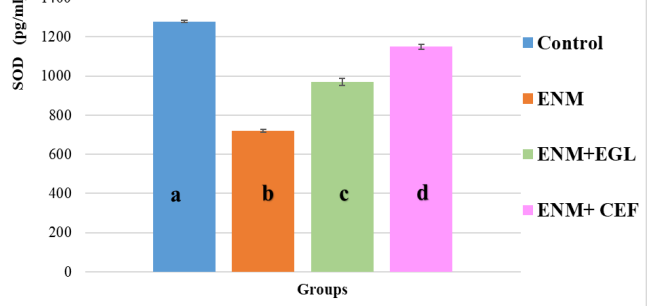

Fig. 16: H_2O_2(mU/ml) in does (Mean ± S.E.) in different treated groups at the end of the 2nd week of experiment

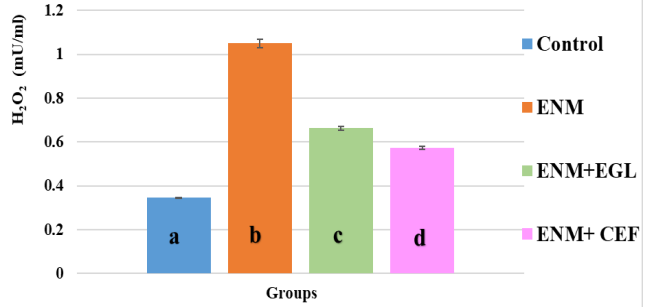

Figure 2

significant increase in ALT, AST, SDH, urea, and creatinine concentrations in comparison with (control) group. On the other hand, these variables were significantly decreased in (ENM+EGL) and (ENM+CEF) groups as compared to the (ENM) group. In addition, the (ENM+CEF) group revealed a significant reduction in the concentrations of these variables compared to (ENM+EGL) group. Serum concentrations of TP, albumin, and A/G ratio revealed a significant reduction in the (ENM) group compared to the (control) group. However, they were significantly elevated in (ENM+EGL) and (ENM+CEF) groups as compared to the (ENM) group. On the other hand, globulin level was insignificantly changed between the (ENM) group compared to the (control) group but significantly decreased in (ENM+EGL), and (ENM+CEF) groups compared to the (ENM) group. While, the serum concentrations of TP, albumin, and globulin showed a significant elevation in the (ENM+CEF) group in comparison with (ENM+EGL) group. Serum antioxidant and oxidative stress and biomarkers: The serum antioxidant oxidative stress and biomarkers mean (±S.E.) in goats exposed to experimentally induced endometritis before and after treatment with eugenol versus ceftiofur are evidenced in Figure. 2 (15–16). At the end of the 2nd-week post induction of endometritis (10 days after treatment): The (ENM) group showed a significant reduction in SOD levels in comparison with the (control) group. On the other hand, its levels were significantly increased in (ENM+EGL) and (ENM+CEF) groups as compared to the (ENM) group. However, the (ENM+EGL) group revealed a significant reduction in the serum concentration of SOD as compared to (ENM+CEF) group. The serum concentration of H2O2 significantly increased in the (ENM) group in comparison with the (control) group. In contrast, treatment groups (ENM+EGL) and (ENM+CEF) groups showed a significant decrease in H2O2 levels compared to (ENM) group. In addition, the (ENM+CEF) group revealed a significant reduction in the serum concentrations of H2O2 in comparison with (ENM+EGL) group.

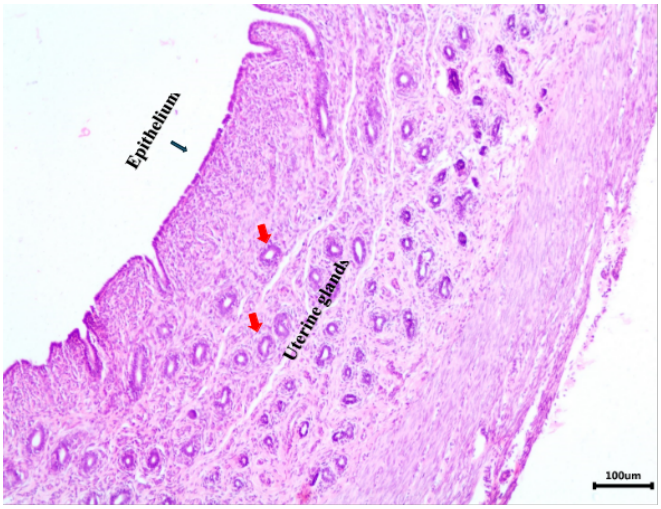

Figure 3: Uterus of doe with normal endometrium of control negative group showing intact epithelial lining of endometrium (Black arrow) and the columnar epithelium lining the uterine glands (Red arrow) with mild inflammatory cells infiltration. H&E stain. Scale bar =100 µm.

3.3. Histopathological findings

Histopathological examination of uterine sections from the endometritis (ENM) group showed severe lesions including necrosis and sloughing of epithelial lining of endometrium, endometrial edema in the lamina propria, atrophy of endometrial glands, Fibrosis around blood vessels with inflammatory cells infiltration (Figure. 4) in comparison with the (control) group (Figure. 3). While, the endometrium of treatment group (ENM+EGL) showed moderate lesions including degeneration of epithelial lining, inflammatory edema with inflammatory cells infiltration in the lamina propria, mild fibrosis around the uterine glands (Figure. 5). However, the endometrium in (ENM+CEF) group exhibited the best response to the treatment with mild lesions, where it showed intact epithelial lining of endometrium, reduction of inflammatory edema with mild inflammatory cell infiltration in the lamina propria (Figure. 6) as compared to (ENM) group (Figure. 4).

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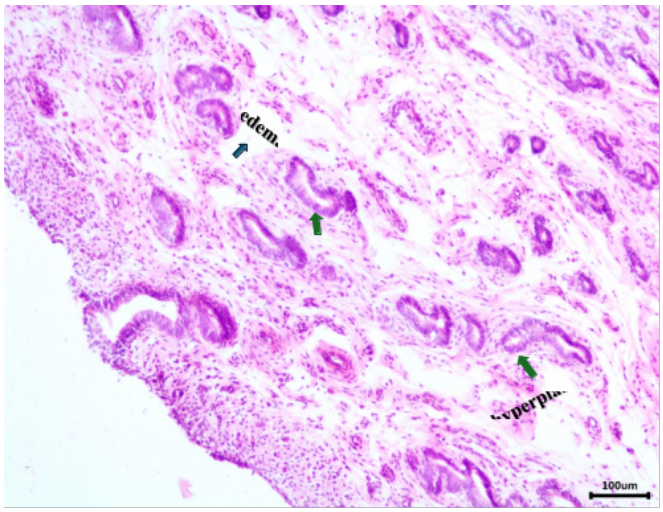

Figure 4: Uterus of doe with endometritis of ENM group showing sloughing and necrosis of epithelial lining of endometrium, inflammatory edema (**black arrow**) with large amount of inflammatory cell infiltration in lamina propria. Note atrophy and periglandular fibroses of endometrial glands. H&E stain. Scale bar =100 µm.

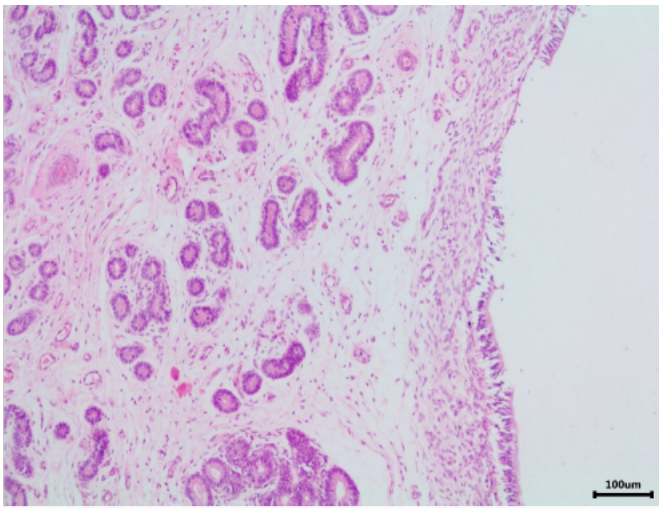

Figure 5: Uterus of does with endometritis treated by eugenol (ENM + EGL) showing mild degenerative changes of epithelial lining, inflammatory edema with inflammatory cells infiltration in lamina propria

4. Discussion

Endometritis is a localized inflammation of the uterine endometrial lining, typically occurring during the postpartum period, and is a major cause of significant economic losses [45, 46]. During inflammation, immune cells release various chemokines and cytokines to recruit more immune cells to the site of infection or oxidative stress. In turn, the increased ROS production by immune cells at the

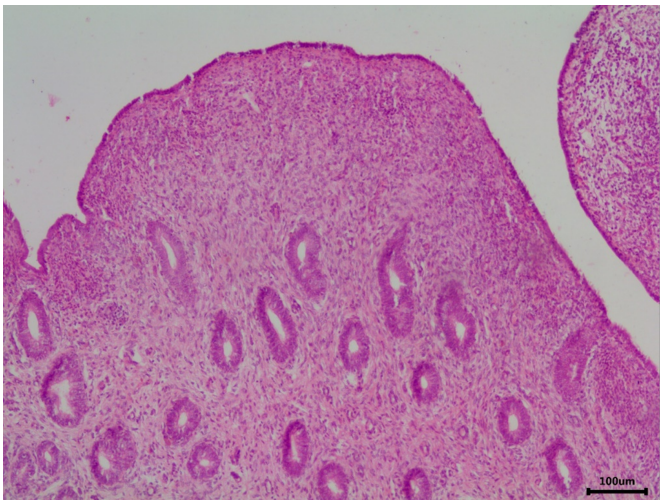

Figure 6: Uterus of does with endometritis treated by ceftifofur (ENM + CEF) showing intact epithelial lining of endometrium, normal uterine glands, reduction of endometrial edema and inflammatory cells infiltration in lamina propria H & E

site of inflammation exacerbates oxidative stress, leading to tissue damage [47]. In the current study, the leukogram picture in does with induced endometritis (ENM) revealed leukocytosis, neutrophilia, monocytosis compared to the control group. Leukocytosis could be due to the secretion of acute phase proteins and inflammatory mediators such as tumor necrosis factor that stimulate the release of neutrophils at the site of the inflammation [48]. In addition, leukocytosis may result from oxidative stress which stimulates the secretion of adrenocorticotropic hormone (ACTH) from the pituitary gland, leading to increased production of corticosterone from the adrenal cortex, thereby causing a rise in WBC count [49, 50]. The obtained data are consistent with Hanafi et al., and Heidarpour et al., [51, 52]. in cows and Darwish et al.,[53] in ewes. Also, the collected data aligns with Islam et al., [54] who observed a leukocytosis with high circulating neutrophils caused by stress at parturition or increased levels of cortisol and MDA in postpartum endometritis. On the other hand, the leukogram of (ENM+EUG) group showed a significant decrease in the total leukocytic count, neutrophils and monocyte as compared to (ENM) group which could be due to the antioxidant effect of eugenol. The antioxidative properties of eugenol are attributed to its chemical

structure, which enables it to neutralize phenoxy radicals by donating hydrogen atoms. Its antioxidant activity can be assessed through its ability to form complexes with reduced metals. Both eugenol and isoeugenol are believed to strongly inhibit lipid peroxidation by scavenging free radicals and forming iron-oxygen chelate complexes, thereby stabilizing iron and copper in their reduced states [55, 15]. Similarly, the leukogram of does in (ENM+CEF) group showed a significant reduction of the total leukocytic count, neutrophils, and monocytes compared to the (ENM) group. The results obtained match with [52, 56, 57]. Ceftiofur is a third-generation cephalosporin broad-spectrum antibiotic [56, 58]. It is effective against Gram-positive, Gram-negative, and β-lactamase producing bacteria. Ceftiofur is an antibiotic developed mainly for veterinary use. In addition, it is effective against anaerobic bacteria [59]. It is an effective antibiotic used for the treatment of metritis and clinical endometritis in dairy cows [60, 61]. Transaminases, also recognized as aminotransferases, are a category of enzymes that facilitate the transfer of an amine group between an amino acid and a keto acid [62]. The ALT and AST are transferases that are common biomarkers for hepatic injury. ALT is primarily a specific hepatocellular enzyme, while AST is found in various tissues including the liver, heart, and skeletal muscles [63]. Sorbitol dehydrogenase is a cytosolic enzyme primarily found in the liver, where it plays a key role in converting sorbitol into glucose, it presents in only minimal amounts in other tissues [64]. The serum activity of SDH in goats is higher than that in sheep and cattle [65]. The highest amount of AST is found in muscle cells and its concentration increases as muscle damage occurs [48]. In the current work, ALT, AST, and SDH serum levels were highly elevated in goats suffering from induced endometritis than normal control goats. This could be attributed to the hazardous effects of oxidative stress triggered by ethanol which induced endometritis [66, 67]. Oxidative stress intensifies both psychological and physiological burdens associated with stressful conditions, contributing to the development of severe pathologies through degenerative damage to cellular structures [68]. Lipid peroxidation is a prominent consequence of oxidative stress, with markedly elevated levels observed in the liver. This process arises from the peroxidation of polyunsaturated fatty acids, leading to alterations in the permeability of the cell membrane with potential membrane leakage. These changes are closely linked to increased steady-state concentrations of reactive oxygen species (ROS) and oxidative damage. Furthermore, lipid peroxidation byproducts, such as 4-HNE, contribute to the stimulation of stress-response signaling pathways, which play a pivotal function in the progression of liver fibrosis and the promotion of proinflammatory responses [69]. In the same line, Bertoni et al., and El-Deep, [70, 71] explained that this impairment of liver function could be due to proinflammatory cytokines and oxidative stress leading to oxidative damage of cells of different organs with subsequent elevation in hepatic enzymes. In addition, these results indicated that the high concentrations of acute-phase protein and impairment of liver function could be risk factors for the persistence of endometritis in cows [72]. The obtained results agree with Nasreldin et al., [24] who recorded that serum ALT and AST levels were significantly elevated in ewes with clinical and subclinical endometritis than in the control group. Also, the observed data conforms to Kaya et al., [73] who recorded a significant increase in blood levels of AST in cows with endometritis. In addition, these findings are harmonious with Burke et al., [74] who recorded a significant elevation in serum concentrations of AST and glutamate dehydrogenase during the postpartum period suggesting hepatocellular damage which disturbs the liver function, and in some cases may result in hepatic failure. In the same line, Sattler and Fürll, [75] mentioned that inflammation increased the

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permeability of cell membrane and enhanced the leakage of AST enzyme into the circulation. However, the serum concentration of ALT, AST, and SDH significantly decreased in (ENM+EUG) goats compared to those of the (ENM) group. Yildiz and Öztürk, [66] reported that the ALT and AST concentrations in blood were reduced in rats with ethanol-induced liver damage after oral administration of eugenol. These results may indicate the inhibition of the hepatotoxic effects of ethanol on the liver due to the antioxidant properties of eugenol by reducing the effect of oxidative stress on biochemical parameters and increasing the activity of the antioxidant system. Likewise, the obtained data exhibited a significant reduction in ALT, AST, and SDH serum concentrations in the (ENM+CEF) goats. These findings are in the same line with [72]. In the present research, serum concentrations of total protein, albumin, globulin, and A/G ratio significantly reduced in the (ENM) group compared to the (control) group. These results could be because endometritis stimulated the inflammatory response and impaired liver function [74]. Also, low serum concentrations of albumin indicate impaired hepatic function due to an increase in the synthesis of acute-phase proteins [76]. In addition, the proinflammatory cytokines in the liver stimulated the acute phase response through induction of the synthesis of positive acute phase proteins and the impairment of the hepatic synthesis of some negative acute phase proteins including retinol-binding protein and albumin [70]. The obtained data are harmonious with El-Sayed et al., [46] who reported a significant reduction in total protein, albumin, and globulin serum concentrations in buffalo cows with clinical endometritis, they explained that albumin is a negative acute-phase protein whose concentration decreases during acute inflammation. In addition, Jan et al., [77] recorded low serum concentrations of albumin in buffaloes with subclinical endometritis. Also, Nischala & Sireesha, [78] mentioned that the serum concentrations of total protein and albumin were significantly lower, while the serum concentrations of globulin and the A/G ratio were significantly increased in the buffaloes with endometritis as compared to the healthy animals. In the present research, the serum concentrations of total protein, albumin, globulin, and the A/G ratio were significantly higher in (ENM+EUG) goats compared to the (ENM) group. These findings may be attributed to the indirect anti-inflammatory and antioxidant properties of eugenol, which exhibits a strong free radical scavenging capacity and reduces inflammation by regulating oxidative stress and lowering inflammatory mediators [11, 79]. These findings align with the results obtained by El-Hafez et al., [80], who recorded normal serum levels of total protein, albumin, and globulin in cisplatin-induced immunodeficient rats following oral administration of clove aqueous extract. This effect was attributed to the immunomodulatory properties of clove extract, primarily due to its polyphenolic compounds and flavonoid content. The total protein, albumin, globulin, serum concentrations, and the A/G ratio were significantly elevated in the (ENM+CEF) group compared to the (ENM) ones. These results are in the same line with Patil et al., [81] who reported that buffaloes with postpartum metritis treated by a single dose of subcutaneous (SC) injection of ceftiofur with a dose of 6.6 mg/kg body weight showed higher plasma concentrations of total protein, albumin, and globulin on day 6 after treatment. In this study, serum concentrations of both urea and creatinine showed significant elevation in (ENM) group compared to the (control) group. This could be due to oxidative stress and the disequilibrium between the pro-oxidant and antioxidant activities which may contribute to renal dysfunction [82]. Also, oxidative stress plays a significant role in the pathophysiology of acute and chronic kidney diseases, where within one week only a sudden loss of kidney function may result in acute renal diseases which accumulate the toxic end products of nitrogen metabolism and creatinine in the bloodstream [83]. In addition, oxidative stress accelerates the progression

of renal injury. At the same time, inflammation exacerbates renal function deterioration, evidenced by increased concentrations of inflammatory markers, like cytokines and C-reactive protein, as renal function declines [84]. Cytokines are pivotal in the pathogenesis of acute renal injury, with cytokine-mediated inflammatory response that serves as a central element in the pathophysiology of acute renal failure, irrespective of its original cause [85]. Furthermore, these results could be due to the liberation of high levels of β-hydroxybutyrate (BHB), non-esterified free fatty acids (NEFAs), and triglyceride in the peripheral circulation which become a burden on both kidneys because of the negative energy balance and high lipolysis of the body fats to obtain energy. Also, oxidative stress leads to oxidative damage of cells [53, 86, 87]. In the same line, Kaya et al., [73] explained that higher concentrations of urea in cow's blood suffering from endometritis could be due to uterine PH alteration and local immune system suppression. The obtained data agreed with Darwish et al., and Nasreldin et al., [24, 53] who reported significantly elevated serum urea and creatinine concentrations in ewes suffering from endometritis. In the current work, the serum urea and creatinine concentrations were significantly declined in (ENM+EUG) does compared to those in (ENM) group. Similarly, Markakis et al., [85] reported that oral administration of eugenol in rats with experimentally induced acute pancreatitis revealed reduced urea and creatinine serum levels. Also, Said,[88] mentioned that the oral administration of eugenol alleviated nephrotoxicity induced by gentamicin in rats through normalization of the serum levels of urea and creatinine, suggesting that it could be due to the protective influence of eugenol against renal toxicity achieved by attenuating oxidative stress. The serum concentrations of urea and creatinine were decreased in female goats with induced endometritis and treated by ceftiofur (ENM+CEF) as compared to the endometritis (ENM) group. In the present work, the obtained results revealed that the serum H_2O_2 was significantly elevated, but the serum SOD level was reduced considerably in (ENM) group compared to the control group. This could be due to the endometritis induced by ethanol. Inflammation is a defense mechanism against injuries, tissue damage, and infections. It can generate reactive oxygen species, leading to oxidative stress. The overabundance of ROS can surpass antioxidant defenses, causing cellular damage and disturbances in homeostasis [9]. Ethanol is a potent inducer of oxidative stress, disrupting the balance between the oxidant and antioxidant systems and enhancing the production of free radicals [66]. Oxidative stress arises when there is an imbalance between the generation of ROS and the availability of antioxidants or radical scavengers. Excessive ROS can lead to the oxidation of biomolecules or structural alterations in proteins and genes, thereby initiating signaling pathways that drive the development and progression of inflammatory diseases. Additionally, ROS activates transcription factors and pro-inflammatory genes trigger inflammation [47]. Free radicals play a crucial role in the pathogenesis of endometritis by altering nitric oxide synthase levels within the endometrium [87]. Ethanol-derived free radicals are produced after ethanol administration through two pathways: Fenton-type reaction from endogenous H_2O_2 and CYP2E1-mediated, independent of hydroxyl radicals. These ethanol-derived free radicals, along with increased ROS production, may cause cell injury due to the increased production of ROS [67]. The obtained findings are ensured by the severe histopathological changes in the endometrium in (ENM) goats that include necrosis and sloughing of the epithelial lining of endometrium, inflammatory edema in the lamina propria with inflammatory cells infiltration, perigladular fibrosis and atrophy of endometrial glands. On the contrary, the findings in (ENM+EUG) goats showed a significant decrease in serum H_2O_2 along with a significantly increased SOD comparable to (ENM) group. This could be due to the antioxidative effect of eugenol through

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the allyl group present in its structure. It inhibits lipid peroxidation with subsequent neutralizing and destruction of the free radicals. Also, it has a remarkable reducing ability and provides phenolic hydroxyl groups which react with free radicals thus reducing oxidative stress, making it a desirable antioxidant [89]. Eugenol has been found to enhance the activity of enzymatic antioxidant factors, such as SOD and catalase in the liver of rats with carrageenan-induced arthritis. SOD converts superoxide radicals into molecular oxygen and hydrogen peroxide, which are then converted into H_2O and O_2 by catalase. Also, eugenol elevated the levels of GSH, while reducing the production of thiobarbituric acid reactive substances (TBARS) indicating its potential to scavenge free radicals in cases of induced arthritis [90]. These findings correspond to El Mottaleb et al., [91] who reported the protective effect of the low dose of eugenol against liver damage induced by ischemia/reperfusion injury in rats by decreasing the concentrations of the liver content of MDA and increasing GSH levels. In addition, the oral administration of eugenol in rats with myocardial infarction induced by isoproterenol improved the cardiac biomarkers injury, improved the heart biomarkers injury, decreased inflammatory mediators, and increased cardiac SOD activities [92]. Moreover, Kumar et al., [93] demonstrated that the oral administration of eugenol had a very potent anti-oxidative and anti-inflammatory effect in rats with Cadmium-induced hepatic toxicity via significant reduction of MDA and NO content and marked improvement of SOD, catalase, and GSH levels in liver tissue of treated rats. Moreover, eugenol increased antioxidant enzymes including SOD and catalase in mice with lipopolysaccharide-induced acute lung injury [94]. The results indicated the protective effect of eugenol against the damage of the free radicals by reduction of lipid peroxidation in the treated animals. In addition, intraperitoneal injection of eugenol at 30-60 mg/kg was able to protect the ovarian tissue against oxidative stress and tissue damage caused by torsion and detorsion in adult female rats through the significant reduction of plasma levels of MDA and increase the concentrations of SOD and GPx after treatment [95]. Our results are confirmed by the moderate histopathological lesions observed in the endometrium of (ENM+EUG) goats in comparison with the (ENM) group which showed only degeneration of epithelial lining, edema with inflammatory cells infiltration in the lamina propria, and mild fibrosis around the uterine glands. In this regard, the study of histopathological changes in the endometrium helps to determine the pathogenesis of endometritis. These changes in the uterus are highly crucial for the assessment of the disease prognosis in conditions with endometritis [45]. The observed results showed a significant reduction in the serum H2O2 along with a significant increase in SOD in (ENM+CEF) compared to (ENM) group. The obtained results are in consonant with Heidarpour et al., and Yildiz and Balikci, [72, 96] who found that cows with clinical endometritis and treated with ceftiofur showed a significant reduction in serum concentration of MDA. Similarly, Yildiz and Balikci, [95] reported a significant increase in the serum levels of SOD and GPx in cows treated with ceftiofur. These findings are supported by the current histopathological examination, which revealed an intact epithelial lining of the endometrium, a reduction in endometrial edema, and mild inflammatory cell infiltration in the lamina propria. These observations indicate mild lesions and a highly favorable response to the intra-uterine infusion of ceftiofur for treatment of experimentally induced endometritis as demonstrated in comparison with (ENM) and (ENM+EUG) goats. It could be concluded that eugenol has corrected the deleterious effect of endometritis experimentally induced in goats but to a lesser extent as compared to ceftiofur which was superior in the experimental findings including leukogram picture, selected serum biochemical variables, oxidative stress and antioxidant biomarkers, We recommend further studies on

eugenol using different concentrations and with different doses.

ACKNOWLEDGMENT

This paper is based upon work supported by Science, Technology & Innovation Funding Authority (STDF) under grant PGSG-call 2 (Project ID: 48573). The authors sincerely express their gratitude and appreciation to the STDF for its financial support.

CONFLICT OF INTERESTS

The authors affirm that they have no competing interests.

References

[1] H. Berihulay, A. Abied, X. He, L. Jiang and Y. Ma, *Animals*, 2019, **9**, 75.

[2] A. Sallam, H. Reyer, K. Wimmers, F. Bertolini, A. Aboul-Naga, C. Braz and A. Rabee, *BMC genomics*, 2023, **24**, 573.

[3] A. Mosaad, S. El, N. Ferial, H. El, R. Ahmed, M. Atef and G. Morsy, *Tropical Animal Health and Production*, 2024, **56**, 1–12.

[4] V. Beena, R. Pawaiya, K. Gururaj, D. Singh, A. Mishra, N. Gangwar and A. Kumar, *Veterinary World*, 2017, **10**, 964–972.

[5] K. Tafti and A. Davari, *Iran. J. Vet. Res*, 2013, **14**, 140–144.

[6] C. Thasmi, T. Siregar, S. Wahyuni, D. Aliza, B. Panjaitan, N. Nazaruddin, F. F.N. and M. Fallatanza, *Journal of Advanced Veterinary and Animal Research*, 2018, **5**, 445.

[7] J. Xiao, S. Li, R. Zhang, Z. Wang, X. Zhang, A. Wang and P. Lin, *Animals*, 2021, **11**, 2593.

[8] R. Paiano, J. Bonilla, R. Sousa, A. Moreno and P. Baruselli, *The journal of infection in developing countries*, 2020, **14**, 177–183.

[9] R. Damasceno, J. Pinheiro, L. Rodrigues, R. Gomes, A. Duarte, J. Emídio, D. L. L. and D. Sousa, *Pharmaceuticals*, 2024, **17**, 1505.

[10] S. Nejad, H. Özgüneş and N. Başaran, *Turkish journal of pharmaceutical sciences*, 2017, **14**, 201–206.

[11] J. Barboza, C. Silva Maia Bezerra Filho, R. Silva, J. Medeiros and D. Sousa, *Oxidative medicine and cellular longevity*, 2018, **2018**, 3957262.

[12] J. Iqbal, B. Abbasi, R. Ahmad, R. Batool, T. Mahmood, B. Ali and A. Munir, *Biomedicine & Pharmacotherapy*, 2019, **109**, 1381–1393.

[13] Z. Taghipour, M. Bahmanzadeh and R. Rahimi, *Reproductive Sciences*, 2023, **30**, 2591–2614.

[14] A. S.A., O. B.M. and O. G, *Journal of Food Biochemistry*, 2021, **45**, 13276.

[15] M. Ulanowska and B. Olas, *International Journal of Molecular Sciences*, 2021, **22**, 3671.

[16] A. Gümüşbaş and T. Bakirel, *Acta Veterinaria Eurasia*, 2022, **48**, 22–29.

[17] W. El-deeb, M. Abdelghani, A. Alhaider and M. Fayez, *Animal Reproduction*, 2022, **19**, 20220035.

[18] K. Galvão, L. Greco, J. Vilela, M. Sá Filho and J. Santos, *Journal of dairy science*, 2009, **92**, 1532–1542.

[19] A. Dawod, J. Miro, H. Elbaz, H. Fahmy and A. Abdoon, *Animals*, 2021, **11**, 1123.

[20] T. Abdisa, *International Journal of Veterinary Science and Research*, 2017, **3**, 030–049.

[21] L. Cui, Y. Zheng, H. Wang, J. Dong, J. Li, Q. Song and J. Li, *Animal Reproduction Science*, 2020, **215**, 106333.

[22] J. Lubroth, M. Rweyemamu, G. Viljoen, A. Diallo, B. Dungu and W. Amanfu, *Rev. sci. tech. Off. int. Epiz*, 2007, **26**, 179–201.

[23] N. Sharma, S. V and K. Shyma, *Veterinary World*, 2015, **8**, 590–598.

[24] N. Nasreldin, F. Abo, Z. Ali, H. Abd-elhafeez, M. Hassan, M. El-zeftawy and W. Senosy, *Animal Reproduction Science*, 2020, **219**, 106541.

[25] D. Brown, J. Ng'ambi and D. Norris, *Indian Journal of Animal Research*, 2016, **50**, 41–47.

[26] J. Fonseca, V. Maffili, A. Santos, R. Fürst, C. Prosperi, H. Rovay and C. Torres, *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*, 2012, **64**, 349–358.

[27] H. Jang, S. Myoung, J. Choe, T. Kim, Y. Cheon, Y. Kim and H. Park, *Yonsei medical journal*, 2017, **58**, 1195–1203.

[28] J. Xu, Y. Li, X. Cao and Y. Cui, *Experimental and Therapeutic Medicine*, 2013, **5**, 1667–1670.

[29] E.-R. Sma, *Journal of Veterinary Science & Animal Husbandry*, 2020, **8**, 106.

[30] B. Feldman, J. Zinkl and N. Jain, *Schalm's Veterinary Hematology*, Lippincott Williams & Wilkins, 5th edn., 2000, p. 1120–1124.

[31] *Methods of enzymatic analysis*, 1974.

[32] G. Schumann, R. Bonora, F. Ceriotti, G. Férard, C. Ferrero, P. Franck, F. Gella, W. Hoelzel, F. Schiele and H. Schimmel, ... *International Federation of Clinical Chemistry and Laboratory Medicine (2002): IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37 degrees C. International Federation of Clinical Chemistry and Laboratory Medicine*, Reference procedure for the measurement of catalytic concentration of aspartate aminotransferase. Clinical chemistry and laboratory medicine,.

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[33] A. Uzozie, P. Nanni, T. Staiano, J. Grossmann, S. Barkow-Oesterreicher, J. Shay and G. Marra, *Sorbitol dehydrogenase overexpression and other aspects of dysregulated protein expression in human precancerous colorectal neoplasms: a quantitative proteomics study*, 2014, http://doi.org/1198-1218., Molecular & Cellular Proteomics, 13(5),.

[34] C. Flack and J. Woollen, *Clinical chemistry*, 1984, **30**, 559–561.

[35] B. Doumas, H. Biggs, R. Arends and P. Pinto, *Standard Methods of Clinical Chemistry*, 1972, **7**, 175–188.

[36] C. Burtis and E. Ashwood, *Tietz textbook of clinical chemistry*, 1994, Second edition, W.B.

[37] J. Kaneko, J. WH and L. Micheal, *: Clinical Biochemistry of domestic animals*, Academic Press, New Yourk, .5th edn., 1997.

[38] S. Samanta, A. Sharma, B. Das, A. Mallick and A. Kumar, *J. Clin. Diagn. Res*, 2016, **10**, 14– 18.

[39] K. Jung, *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*, 2006, https://doi.org/10.1373/clinchem.2005.062638, Clinical Chemistry,.

[40] I. Zelko, T. Mariani and R. Folz, *Free radical biology & medicine*, 2002, **33**, 337–349.

[41] T. Votyakova and I. Reynolds, *Archives of biochemistry and biophysics*, 2004, **431**, 138–144.

[42] S. Suvarna, C. Layton and J. Bancroft, *Bancroft's Theory and Practice of Histological Techniques*, Elsevier Limited, 8th edn., 2019.

[43] D. Duncan, *Biometrics*, 1955, **11**, 1– 41.

[44] D. George and P. Mallery, *IBM SPSS Statistics 25 Step by Step: A Simple Guide and Reference*, Routledge, 15th edn., 2018.

[45] M. Demirel, S. Han, A. Tokmak, N. Ercan Gokay, M. Uludag, T. Yildirir Ustun and A. Cicek, *Naunyn-Schmiedeberg's Archives of Pharmacology*, 2019, **392**, 1577–1589.

[46] A. El-Sayed, S. Faraj, B. Marghani, F. Safhi, M. Abdo, L. Fericean, I. Banatean-Dunea, C. Alexandru, A. Alhimaidi, A. Ammari, A. Eissa and A. Ateya, *Veterinary Sciences*, 2024, **11**, 340.

[47] T. Dziubla and D. Butterfield, *Chapter*, 2016, **2**, 35–58.

[48] K. Qadri, H. Mehta, N. Singh and K. Choudhary, *Indian Veterinary Journal*, 2018, **95**, 14–17.

[49] V. Kumar, A. Abbas and J. Aster, *Robbins and Cotran Pathologic Basis of Disease*, Elsevier, Philadelphia, 9th edn., 2015.

[50] S. J. G., C. H.C., S. C. and L. N. A, *Frontiers in Neuroscience*, 2015, **8**, 1–6.

[51] E. Hanafi, W. Ahmed, S. Abd, E. Moez, H. Khadrawy, A. Abd and E. Hameed, *American-Eurasian J. Agric. & Environ. Sci*, 2008, **4**, 530–536.

[52] M. Heidarpour, M. Mohri, A. Fallah-Rad, F. Shahreza and M. Mohammadi, *Comparative Clinical Pathology*, 2014, **23**, 97–101.

[53] A. Darwish, *Alexandria Journal of Veterinary Sciences*, 2019, **62**, 16–25.

[54] R. Islam, H. Kumar and B. Krishnan, *Asian Pacific Journal of Reproduction*, 2014, **3**, 57–63.

[55] A. Khalil, U. Rahman, M. Khan, A. Sahar, T. Mehmood and M. Khan, *RSC advances*, 2017, **7**, 32669–32681.

[56] N. Lutfi, R. El-Shafe, M. El-Diasty and M. El-sayed, *Mansoura Veterinary Medical Journal*, 2019, **20**, 50–56.

[57] H. Khalil, R. Waheeb, S. El-rheem and G. El-amrawi, *Alexandria Journal of Veterinary Sciences*, 2023, **79**, 150 –157.

[58] S. Jeon, F. Cunha, R. Daetz, R. Bicalho, S. Lima and K. Galvão, *Animal Microbiome*, 2021, **3**, 15.

[59] M. EL-Taweel, T. Attia, M. El-Hewaity and E.-G. H, *Journal of Current Veterinary Research*, 2019, **1**, 95–104.

[60] T. Brick, G. Schuenemann, S. Bas, J. Daniels, C. Pinto and D. Rings, *Journal of Dairy Science*, 2012, **95**, 1894–1905.

[61] C. Mclaughlin, E. Stanisiewski, M. Lucas, C. Cornell, J. Watkins, L. Bryson, J. Tena, J. Hallberg and J. Chenault, *Journal of Dairy Science*, 2012, **95**, 4363–4371.

[62] J. Jez, in *eBook ISBN: 9780128220405, Elsevier*, 2021, vol. 1, p. 452–461.

[63] B. T. D., M. Manns, S. A.J. and D. Zakim, *Zakim and Boyer's Hepatology: a textbook of liver disease*, saunders/ Elsevier Inc, Philadephia, 6th edn., 2012, p. 201–215.

[64] H. W. M., R. C.G. and W. M. A, *Academic press*, 2013, **1**, 565–594.

[65] J. Kramer and G. Carthewt, *NEW ZEALAND VETERINARY JOURNAL*, 1985, **33**, 91–93.

[66] H. Yildiz and E. Öztürk, *Adıyaman University Journal of Science*, 2020, **10**, 83–99.

[67] O. Koch, G. Pani, S. Borrello, R. Colavitti, A. Cravero, S. Farrè and T. Galeotti, *Molecular aspects of medicine*, 2004, **25**, 191–198.

[68] N. S., S. M., B. H. and S. S, *African Journal of Biochemistry Research*, 2009, **3**, 282–287.

[69] Z. H.J., X. L., D. V.J., X. L., O. L.W. and K. K.C, *The FASEB Journal*, 2003, **17**, 2293–5.

[70] G. Bertoni, E. Trevisi, X. Han and M. Bionaz, *Journal of Dairy Science*, 2008, **91**, 3300–3310.

[71] W. El-deeb, *Journal of Zhejiang University SCIENCE B*, 2013, **14**, 33–39.

[72] M. Heidarpour, M. Mohri, F. Shahreza and M. Mohammadi, *Veterinary Record*, 2012, **171**, 219.

[73] K. S., M. O., K. C., C. A. and B. K, *Veterinary World*, 2016, **9**, 1056–1062.

[74] C. Burke, S. Meier, S. Mcdougall, C. Compton, M. Mitchell and J. Roche, *Journal of Dairy Science*, 2010, **93**, 5363–5373.

[75] T. Sattler and M. Fürll, *Journal of Veterinary Medicine Series A: Physiology Pathology Clinical Medicine*, 2004, **51**, 132–137.

[76] M. Elmetwally, G. Elshopakey, A. El-Desouky, W. Eldomany and F. Bazer, *Troprical Animal Health and Production*, 2020, **52**, 3697–3706.

[77] M. Jan, H. Kumar, S. Kumar, W. Malla and R. Sharma, *Tropical Animal Health and Production*, 2021, **53**, 1–11.

[78] S. Nischala and G. Sireesha, *Journal of Livestock Science*, 2018, **9**, 81–83.

[79] I. Adeshina, A. Jenyo-Oni, B. Emikpe, E. Ajani and M. Abdel-Tawwab, *Journal of the World Aquaculture Society*, 2019, **50**, 390–405.

[80] A. El-Hafez, M. A., G. Omnia, H. Refaat, G. and A. El-Masry Aboraya, *Journal of Applied Sciences*, 2023, **38**, 16–28.

[81] R. Patil, J. Patel and N. Khade, *Indian Journal of Field Veterinarians*, 2012, **7**, 6–11.

[82] R. H., J. A., A. M.S. and A. S.A.H, *International Journal of Molecular Sciences*, 2024, **25**, 3.

[83] G. M., G. R., B. J. and T. L', *Oxidative Medicine and Cellular Longevity*, 2020, **2020**, 5478708.

[84] V. Cachofeiro, M. Goicochea, S. Vinuesa, P. Oubiña, V. Lahera and J. Luño, *Kidney International Supplements*, 2008, **111**, 4–9.

[85] C. Markakis, A. Tsaroucha, A. Papalois, M. Lambropoulou, E. Spartalis, C. Tsigalou, K. Romanidis and C. Simopoulos, *HPB Surgery*, 2016, **2016**, 3203147.

[86] C. Tóthová, O. Nagy and G. Kovác, *Journal of Applied Animal Research*, 2014, **42**, 278–283.

[87] S. Kaya, M. Öğün, H. Özen, M. Kuru, L. Şahin, A. Kükürt and C. Kaçar, *Journal of the Hellenic Veterinary Medical Society*, 2017, **68**, 231–236.

[88] M. Said, *Fundamental and Clinical Pharmacology*, 2011, **25**, 653–775.

[89] M. Nisar, M. Khadim, M. Rafiq, J. Chen, Y. Yang and C. Wan, *Oxidative medicine and cellular longevity*, 2021, **2021**, 2497354.

[90] S. Adefegha, S. Oyeleye, B. Okeke and G. Oboh, *Journal of Basic and Clinical Physiology and Pharmacology*, 2019, **30**, 185–193.

[91] E. M. A. M., S. Selim and A. Mohamed, *Journal of*, 2014, **11**, 238–245.

[92] K. Mnafgui, R. Hajji, F. Derbali, A. Gammoudi, G. Khabbabi, H. Ellefi, A. N., K. A. and N. Gharsallah, *Cardiovascular toxicology*, 2015, **16**, 336–344.

[93] A. Kumar, N. Siddiqi, S. Alrashood, H. Khan, A. Dubey and B. Sharma, *Biomedicine & Pharmacotherapy*, 2021, **111588**, 11588.

[94] X. Huang, Y. Liu, Y. Lu and C. Ma, *International Immunopharmacology*, 2015, **26**, 265–271.

[95] B. Barghi, M. Shokoohi, A. Khaki, A. Khaki, M. Moghimian and M. Soltani, *Journal of Obstetrics and Gynaecology*, 2021, 933–938.

[96] A. Yildiz and E. Balikci, *Journal of Applied Animal Research*, 2016, **44**, 431–435.

Author contributions

N.N conceived the idea, the experimental design, and the methodology. S.kh.A and W.S Involved in were involved in the conception of the experimental design and methodology. N.N and S.A.A were involved in performing the experiment, sampling, analysis of hematology, serum biochemical parameters, oxidative and antioxidant parameters, making the statistical analysis of all results, performing data analysis preparing the tables, interpretation, and writing the original manuscript draft. S.Kh.A performed the histopathological sampling, processing, preparation, and evaluation. W.S performed the ultrasonographic examination of the female goats, synchronization of the estrus cycle of the does, performed the intrauterine infusion for induction and treatment of endometritis. S.Kh.A, W.S and N.N revised the results and the data analysis. S.Kh.A, W.S and N.N revised and edited the manuscript. All authors have read and agreed to the published version of the manuscript.